PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Prior Application Art Unit: 1627 Prior Application Examiner: Sarah PIHONAK

Commissioner: This is a request for filing a

☒ Continuation ☐ Continuation-in-Part ☐ Divisional Application under 37 C.F.R. § 1.53(b) of pending prior Application No. 14/183,283, filed February 18, 2014, of Kazuyuki FUJIHARA for PHARMACEUTICAL COMPOSITION.

1. ☐ Enclosed is a complete copy of the prior application and drawings, as originally filed. The attached papers are a true copy of prior Application No. 14/183,283, filed February 18, 2014, which is a continuation of Application No. 11/919,678, filed October 31, 2007, which issued on May 20, 2014 as U.S. Patent No. 8,729,085, which is a National Stage Entry of International Application No. PCT/JP2006/310571, filed May 26, 2006, which claims priority to Japanese Patent Application No. 2005-153508, filed May 26, 2005, the content of each of which is incorporated herein by reference.

2. ☐ Certification and Request for Prioritized Examination under 37 C.F.R. § 1.102(e)

3. ☐ A Preliminary Amendment is submitted herewith.

4. ☒ A copy of a declaration submitted in prior Application No. 14/183,283 is submitted herewith.

5. ☒ An Application Data Sheet is enclosed.

Basic Utility Application Filing Fee					$280	$ 280.00
Search Fee					$600	600.00
Examination Fee					$720	720.00
Prioritized Examination Fee						
	Number of Claims		Basic	Extra		
Total Claims	35	-	20	15	x $ 80	1200.00
Independent Claims	4	-	3	1	x $420	420.00
☐ Presentation of Multiple Dep. Claim(s)					+ $780	
Size Fee: Paper Filing Total Application Pages (specification, drawings, printed sequence or computer listing, preliminary amendment)	[Total] - 100 ÷ 50 = [number]* x $400 *Rounded up to next whole number					
Additional Fee for Paper Filing New Application $400 (DELETE if filing new application via EFS Web - fee not required for EFS new application submissions)						
Size Fee: EFS-Web Filing Total Application Pages (specification, drawings, printed sequence or computer listing, preliminary amendment)	[Total] X .75 - 100 ÷ 50 = [number]* x $400 *Rounded up to next whole number					
Processing Fee, except in provisional applications - $140 *For the Track I (Prioritized Examination) Program, the processing fee is required.*						140.00
Subtotal						$ 3,360.00
Reduction by 1/2 if small entity **[for e-filing ONLY: small entity fee for Basic filing fee - $70)**						-
TOTAL FEES DUE						$ 3,360.00

6. ☒ The fee of $3,360.00 is submitted herewith.

7. ☒ The Commissioner is hereby authorized to charge any fees which may be required including fees due under 37 C.F.R. § 1.16 and any other fees due under 37 C.F.R. § 1.17, or credit any overpayment during the pendency of this application to Deposit Account No. 06-0916.

8. ☒ The prior application is assigned of record to: SUMITOMO DAINIPPON PHARMA CO., LTD., by virtue of a change of name submission recorded in the U.S. Patent and Trademark Office (USPTO) at Reel 033905, Frame 0778. The prior application was assigned to DAINIPPON SUMITOMO PHARMA CO., LTD. by virtue of an assignment from the inventor recorded in the U.S. Patent and Trademark Office (USPTO) at Reel 020124, Frame 0821. A corrective assignment was recorded in the USPTO at Reel 021008, Frame 0209, to correct the address of the assignee.

9. ☒ The power of attorney in the prior application is to FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Customer No. 22,852.

10. ☒ Please address all correspondence to FINNEGAN, HENDERSON, FARABOW, GARRETT and DUNNER, L.L.P., **Customer Number 22,852**.

11. ☐ A new power of attorney is enclosed.

12. ☐ Information Disclosure Statement is enclosed.

PETITION FOR EXTENSION. If any extension of time is necessary for the filing of this application, including any extension in parent Application No. 14/183,283, filed February 18, 2014, for the purpose of maintaining copendency between the parent application and this application, and such extension has not otherwise been requested, such an extension is hereby requested, and the Commissioner is authorized to charge necessary fees for such an extension to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 10, 2014

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11/919678
IAP05Rec'd PCT 31 OCT 2007

DESCRIPTION

PHARMACEUTICAL COMPOSITION

TECHNICAL FIELD

[0001]

The present invention relates to an oral preparation with a good disintegration which comprises as an active ingredient N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone). More particularly, the present invention relates to a preparation for oral administration, particularly a tablet, comprising lurasidone as an active ingredient, which has an equivalent dissolution profile of the active ingredient even though contents of the active ingredient therein are varied.

BACKGROUND ART

[0002]

Patent Document 1 discloses that a compound such as lurasidone can be orally administered and an oral preparation can be prepared by blending an active ingredient with a conventional carrier, excipient, binder, stabilizer and the like, but there is no disclosure of an oral preparation which shows a rapid dissolution and has an equivalent dissolution profile of the active ingredient even though contents of the active ingredient therein are varied in the wide range, particularly an oral preparation with increased contents of the active ingredient which has a similar dissolution profile to that of multiple tablets with a lower content of the active ingredient per tablet.

[0003]

For the purpose of securing the bioequivalence when

Par Pharm., Inc.
Exhibit 1013
Page 004

pharmaceutical preparations with different contents of the active ingredient were administered so as to be the same dose to each other, a guideline has been issued, i.e., "Guideline for Bioequivalence Studies of Oral Solid Dosage Forms with Different Content" (Notification No. 64 of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, promulgated on February 14, 2000) by which it has been required that pharmaceutical preparations with different contents should have an equivalent dissolution profile in each test solution such as buffers of pH1.2, 3.0 to 5.0 and 6.8 (which correspond to the pH values of stomach, intestine and oral cavity, respectively), water, and saline.

[0004]

Patent Document 2 discloses an oral preparation comprising lurasidone as an active ingredient, which shows a rapid dissolution and has an equivalent dissolution profile even though contents of the active ingredient therein are varied, particularly an oral preparation with increased contents of the active ingredient which has an equivalent dissolution profile to that of multiple tablets with a lower content of the active ingredient per tablet and can release a slightly water-soluble active ingredient therefrom at a desired concentration.

[0005]

Patent Document 2 further discloses an oral preparation, particularly a tablet, which shows a rapid dissolution of the active ingredient even though contents of the active ingredient therein are varied in the range of several mg to several tens of mg (e.g. in the range of 5 mg to 20 mg or in the range of 5 mg to 40 mg), and further has an equivalent dissolution profile in the same componential ratio. An oral preparation has been frequently required to be a preparation with higher contents of the active ingredient in order to get higher clinical effects, or a preparation which has an equivalent dissolution profile to

that of multiple tablets and can release the active ingredient therefrom at a desired concentration in wider ranges of contents in order to adjust clinical effects depending on conditions of patients. The art disclosed in Patent Document 2 may provide an oral preparation which has an equivalent dissolution profile in the range of 5 mg to 40 mg of lurasidone per tablet, as shown in Figure 1. However, as shown in Figure 2, when the content of the active ingredient per tablet was increased to double, i.e., 80 mg tablet, it could not have an equivalent dissolution profile. Hence, it remains in a state of administering multiple tablets at one time or using a tablet having a big size which is difficult to administer. Therefore, for such a slightly water-soluble active ingredient as lurasidone, it has been difficult to provide an oral preparation having an equivalent dissolution profile even in high content or in wider ranges of contents of the active ingredient.

[0006]

In Patent Document 2, a water-soluble polymer binder includes starch, but there is no description about a pregelatinized starch therein. The pregelatinized starch is known to remarkably improve a disintegration and a dissolution of a pharmaceutical composition as described, for example, in Patent Document 3, but it is often used, typically, in 10% or less of contents as also described in Non-patent Document 1.

[0007]

Patent Document 1: JP2800953

Patent Document 2: WO2002/024166

Patent Document 3: JP2000-26292

Non-patent Document 1: Handbook of Pharmaceutical Excipients, 2nd edition, 491, 1994, The Pharmaceutical Press

DISCLOSURE OF INVENTION

PROBLEMS TO BE RESOLVED BY THE INVENTION

[0008]

The present invention is directed to provide an oral preparation comprising lurasidone as an active ingredient which shows a rapid dissolution and has an equivalent dissolution profile even though contents of the active ingredient therein are varied in the wide range, particularly an oral preparation with increased contents of the active ingredient which has a similar dissolution profile to that of multiple tablets with a lower content of the active ingredient per tablet and can release the active ingredient therefrom at a desired concentration.

[0009]

The present invention is directed to provide a preparation for oral administration which comprises as an active ingredient N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (hereinafter referred to as lurasidone), which has an equivalent dissolution profile of the active ingredient even though contents of the active ingredient therein are varied.

MEANS OF SOLVING THE PROBLEMS

[0010]

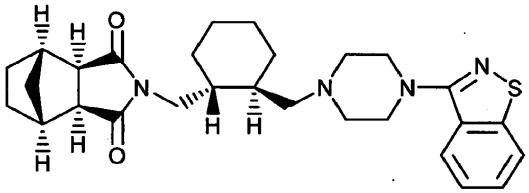
The present inventors have intensively studied in order to solve the above problems and found to solve said problems by means of the following methods.

[0011]

The present invention includes the following embodiments:

[0012]

(1) An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of the formula (1):



(1),

a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder.

(2) An oral preparation which is prepared by granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

(3) An oral preparation which is prepared by granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by a solution or dispersion of lurasidone and a water-soluble polymer binder.

(4) The oral preparation of any one of (1) to (3) wherein the water-soluble excipient is mannitol or lactose.

(5) A method of granulation of a powder mixture which comprises granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

(6) A method of granulation of a powder mixture which comprises granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by using a solution or dispersion of lurasidone and a water-soluble polymer binder.

(7) The method of granulation of (5) wherein the water-soluble excipient is mannitol or lactose.

(8) The oral preparation of any one of (1) to (4) wherein the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation.

(9) The oral preparation of any one of (1) to (4) wherein the

pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation.

(10) The oral preparation of any one of (1) to (4) wherein a content of lurasidone in the preparation is 20 to 45% (wt/wt).

(11) The oral preparation of any one of (1) to (4) wherein a content of lurasidone in the preparation is 25 to 40% (wt/wt).

(12) The oral preparation of any one of (1) to (4) wherein a content of lurasidone per tablet is 10 to 160 mg.

(13) The oral preparation of any one of (1) to (4) wherein a content of lurasidone per tablet is 20 to 120 mg.

(14) The oral preparation of any one of (1) to (4) wherein a content of lurasidone per tablet is 40 to 120 mg.

(15) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose and the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation.

(16) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

(17) The oral preparation of any one of (1) to (4) wherein the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

(18) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

(19) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is

incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

(20) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 40 to 120 mg.

(21) The oral preparation of any one of (1) to (4) wherein a pregelatinizing ratio of the pregelatinized starch is 50 to 95%.

(22) The oral preparation of any one of (1) to (4) wherein an average particle size of lurasidone is 0.1 to 8 μm.

(23) The oral preparation of any one of (1) to (4) wherein the pregelatinized starch contains water soluble matter of 30% or less.

(24) The oral preparation of any one of (1) to (4) wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation, a content of lurasidone in the preparation is 25 to 40% (wt/wt) and a content of lurasidone per tablet is 20 to 120 mg.

EFFECTS OF INVENTION

[0013]

It has been confirmed in the art disclosed in Patent Document 2 that a pharmaceutical preparation with low contents of lurasidone up to 40 mg per tablet could provide an oral preparation having an equivalent dissolution profile. However, a pharmaceutical preparation with higher contents of lurasidone could not have an equivalent dissolution profile. Therefore, double amounts or more of the preparation with low contents should have been administered to a patient in need of high doses of lurasidone, which imposed increased burdens on the patient, and hence an improvement thereon has been required. The preparation of the present invention which comprises a pregelatinized starch can provide

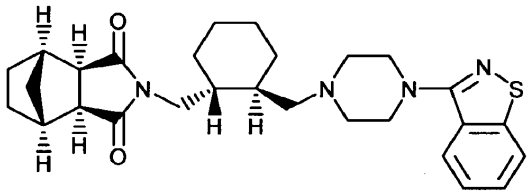
an oral preparation with higher contents of lurasidone which imposes less of burdens on a patient. Additionally, the present invention can provide an oral preparation with high contents of lurasidone, and a preparation for oral administration which has an equivalent dissolution profile even though contents of lurasidone therein are varied. Moreover, the preparations are excellent for a long-term conservation.

BEST MODE FOR CARRYING OUT THE INVENTION

[0014]

N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptane-dicarboxyimide hydrochloride (lurasidone) refers to a compound of the following formula:

[0015]



(1)

(see, for example, JP2800953). Lurasidone is known to exhibit a psychotropic effect, and it is useful as a therapeutic agent for schizophrenia, etc. Said compound is incorporated into the preparation, for example, in the range of 10 to 50% by weight, preferably in the range of 20 to 45% by weight, particularly in the range of 20 to 45% by weight on the basis of the total weight of a tablet. Additionally, the compound is preferably finely milled, for example, 90% by volume or more of particles have 27 μm or less of particle size, and average particle size in a volume ratio (i.e. 50% by volume particle size) includes, for example, in the range of 0.1 to 8 μm, preferably in the range of 1 to 4 μm. The contents of lurasidone are 10 to 160 mg, preferably 20 to

120 mg, more preferably 40 to 120 mg per tablet.

[0016]

The "pregelatinized starch" refers to those prepared by pregelatinizing various kinds of starch (e.g. corn starch, potato starch, wheat starch, rice starch, tapioca starch, etc.), and may include pregelatinized starch or partly pregelatinized starch described in Japanese Pharmaceutical Excipients. The pregelatinized starch has a pregelatinizing ratio, for example, in the range of 50 to 100%, preferably in the range of 50 to 95%, more preferably in the range of 80 to 95%. Additionally, the pregelatinized starch contains water soluble matter of, for example, 40% or less, more preferably 30% or less. Such a pregelatinized starch is typically used in a powder which average particle size is in the range of 1 to 1000 μm, preferably in the range of 1 to 500 μm, more preferably in the range of 10 to 100 μm. A commercially available pregelatinized starch suitable for the present invention includes, for example, partly pregelatinized starch such as PCS (brand name, manufactured by Asahi Kasei Corporation) or Starch 1500 (brand name, manufactured by Colorcon, Inc.), etc. Among the above pregelatinized starch, partly pregelatinized starch such as PCS (brand name, manufactured by Asahi Kasei Corporation) is preferably used. A pregelatinizing ratio of partly pregelatinized starch is preferably in the range of 50 to 95%, more preferably in the range of 80 to 95%. The pregelatinized starch used in the present invention is in the range of 10% to 50%, preferably in the range of 10% to 40%, particularly in the range of 20% to 30% by weight of the preparation.

[0017]

The "water-soluble excipient" includes, for example, mannitol, lactose, saccharose, sorbitol, D-sorbitol, erythritol, xylitol, etc. More preferable one includes mannitol and lactose. Further preferable one may include mannitol. Also, said water-soluble excipient may be used

alone, or two or more thereof may be used together. The water-soluble excipient is incorporated in an amount of, for example, the range of 30 to 80% by weight, preferably the range of 40 to 60% by weight on the basis of the total weight of a tablet. The average particle size of mannitol is, for example, in the range of 10 to 200 μm.

[0018]

The "water-soluble polymer binder" includes, for example, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, polyvinyl alcohol, etc. More preferable one includes hydroxypropylcellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone or polyvinyl alcohol. Said water-soluble polymer binder may be used alone, or two or more thereof may be used together. The water-soluble polymer binder is incorporated in an amount of, for example, the range of 0.5 to 10% by weight, preferably the range of 1 to 5% by weight on the basis of the total weight of a tablet.

The oral preparation in the form of a pharmaceutical composition of the present invention refers to a pharmaceutical preparation which is formulated into tablet, capsule, granule or fine granule. Said preparation may be formulated by a conventional method into tablet, capsule, granule or fine granule by using water-soluble excipient as well as water-insoluble excipient, binder, disintegrant, lubricant, etc. The following agents may be added thereto.

[0019]

The "water-insoluble excipient" includes, for example, corn starch, crystalline cellulose, etc. Said water-insoluble excipient may be used alone, or two or more thereof may be used together.

[0020]

The "disintegrant" includes, for example, corn starch, crystalline cellulose, low substituted hydroxypropylcellulose, carmellose, carmellose calcium, carmellose sodium, croscarmellose sodium,

carboxymethyl starch sodium, crospovidone, etc. Said disintegrant may be used alone, or two or more thereof may be used together. The disintegrant is used in an amount of, for example, the range of 0 to 10% by weight, preferably the range of 0.5 to 5% by weight on the basis of the total weight of a tablet.

[0021]

The "lubricant" includes, for example, magnesium stearate, talc, polyethylene glycol, silica, hydrogenated vegetable oil, etc.

[0022]

The oral preparation of the present invention may be prepared according to a conventional method depending on a desired dosage form.

(1) Preparation of an aqueous solution of water-soluble polymer binder:

A water-soluble polymer binder is dissolved in purified water. The amount of the water-soluble polymer binder is, for example, in the range of 1 to 20% by weight, preferably in the range of 2 to 8% by weight of purified water.

(2) Preparation of granule comprising lurasidone:

To a fluid bed granulator are charged excipient including lurasidone, mannitol and partly pregelatinized starch, and disintegrant, and thereto is sprayed the water-soluble polymer binder prepared in the above process (1) to be granulated.

[0023]

The apparatus for granulation includes, for example, one classified into fluid bed granulation, high share granulation, roto fluid bed granulation, etc., but it is not limited thereto.

(3) Drying of granule:

The above-obtained granule is dried either under reduced pressure or atmospheric pressure. The drying is carried out so that the loss on dry measured by infrared moisture meter is, for example, within

3% by weight, preferably 1 to 2% by weight.

(4) Blending of lubricant:

To the granule dried in the above (3) is added lubricant to be mixed. For mixing, for example, a blending machine classified into diffusion mixers [Tumble] is used. Specifically, tumble blender, V blenders, double cone, bin tumble, etc. are used, but it is not limited thereto.

(5) Compression:

The above mixture is compressed to give a tablet.

[0024]

The apparatus for compression includes, for example, one classified into tablet press, etc. The compression hardness is selected, for example, from the range of 30 to 200N.

(6) Film-coating is optionally carried out:

The above-obtained tablet may be optionally subjected to film-coating, if necessary. The apparatus for coating includes, for example, one classified into a coating pan. Preferable one includes one classified by perforated coating system.

[0025]

The coating agent includes, for example, a mixture of base material (e.g. hydroxypropyl methylcellulose, hydropropylcellulose, polyvinylpyrrolidone, polyvinyl alcohol, etc.) and plasticizer (e.g. polyethylene glycol, propylene glycol, triacetin, triethyl citrate, glycerin, glycerin fatty acid ester, polyethylene glycol, etc.). If necessary, an additive such as titanium oxide may be also added therein. After film-coating, carnauba wax, etc. may be also added as polishing agent therein.

(7) Drying:

The above-obtained tablet is dried. The drying is carried out either under reduced pressure or atmospheric pressure so that the loss

on dry measured by infrared moisture meter is, for example, within 3% by weight, preferably 1 to 2% by weight.

[0026]

Examples of the present invention are illustrated below. Said examples are intended to exemplify the present invention but not to limit the present invention thereto.

EXAMPLES

Example 1

[0027]

A. A film-coated tablet comprising 80 mg of lurasidone (Example 1)

Granules, uncoated tablets and FC tablets comprising the following components are sequentially prepared. The charging amounts shown in parentheses in the following description are an example for preparing the formulation shown in Example 1.

According to the preparation method, other examples may be also prepared in principle, provided that the charging amounts are needed to be changed depending on formulations.

[0028]

B. Preparation method

(1) Preparation of binding solution (5% aqueous hydroxypropyl methylcellulose solution):

Hydroxypropyl methylcellulose (32 g) as water-soluble polymer binder was dissolved in purified water (608 g) to give binding solution.

(2) Granulation:

Lurasidone (320 g), mannitol (576 g), partly pregelatinized starch (320 g) and croscarmellose sodium (16 g) were charged to a fluid bed granulator (Multiplex MP-01/manufactured by Powrex Corporation), and the mixture was granulated by spray granulation under the following conditions using the binding solution prepared in the above (1)

to give granule powder. To the obtained granule powder was added magnesium stearate to give a granule for compression having a formulation (b) after mixing (40 rpm, 5 minutes). Magnesium stearate was mixed in amounts calculated from a formulation on the basis of yields of granule powder.

Conditions for granulation

Temperature for supplying air: 60°C

Airflow: 50 to 65 m^3 /hr

Spray speed: 13 g/min

Diameter of spray nozzle: 1.2 mm

Spray pressure: 0.12MPa

Gun position: the middle stand

(3) Compression:

The granule for compression prepared in the above (2) was compressed by HT-AP12SS-II (manufactured by Hata Iron Works Co., Ltd.) to give a tablet.

Pestle size: φ10 mm 14R

Thickness: 4.20 to 4.30 mm

Compression pressure: 10 KN

(4) Coating:

The uncoated tablet prepared in the above (3) were coated by using High Coater HCT30N (manufactured by Freund Industrial Co., Ltd.) under the following conditions so as to control amounts of the coat to 5 mg, and thereto was added carnauba wax after coating to give a film-coated tablet.

FC conditions

Temperature for supplying air: 80°C

Airflow: 0.6 m^3 /min

Rotation rate of pan: 25 rpm

Spray pressure: 0.15MPa

Liquid flow rate: 5 g/min

The preparation obtained in the above method was evaluated a quality thereof according to the following methods, and the present invention has been achieved on the basis of the knowledge obtained therein.

[0029]

C. Quality evaluation

(1) Dissolution test

A manufactured preparation was subjected to the dissolution test according to the Japanese Pharmacopoeia, Dissolution test, Method 2. Measuring conditions are shown below.

Test solution: Diluted McIlvaine buffer, pH4.0

Rotation rate of paddle: 50 rpm

Test fluid: 900 ml

(2) Similarity of dissolution profiles

A similarity factor f2 shown in Scale-Up and Past-Approval Changes for Intermediate Release Products (SUPAC-IR) was used as an indicative for evaluating a similarity of dissolution profiles. The f2 value is calculated by the following equation. It was determined that each manufactured preparation had a similar dissolution profile in case that the f2 value calculated from dissolution ratio of each preparation by SUPAC-IR was in the range of $50 \leq f2 \leq 100$. Dissolution ratios at three time points such as 15 min, 30 min and 45 min after starting the test were used for a calculation of the f2 value.

[0030]

$$f2 = 50 \bullet LOG\left[\frac{100}{\sqrt{1+\frac{\sum_{i=1}^{n}(Ti-Ri)^2}{n}}}\right]$$

Ti and Ri are the percent dissolved at each point.

n is the number of points to be compared.

(3) Size distribution

A size distribution of lurasidone was measured according to a dry-spray method by Laser Diffraction Particle Size Analyzer (SLAD-3000/Shimadzu Corporation). Measuring conditions are shown below.

Amounts of sample: 2 g
Air pressure: 0.4MPa or more
Turntable rotation speed: 2
Parameter setting
Environmental setting

Monitoring average:	16	Measuring optimum range (Max):	1500
Dark measuring average:	2	(Min):	700
Light intensity display Max:	2000	(CH-1) baud rate (bps):	9600
Previous blank:	reading	Blank measurable Max:	300
Printer: monochrome		Blank measurable variation range:	20

Refractive parameter

Standard refraction:	1.70-0.20i

Measuring conditions setting

Measuring average:	1	Dry permissible Min:	300
Measuring interval (sec):	1	Max:	2500
Average:	64	Granule range for evaluation (Min):	0.1
Measured absorbance range (Max):	0.1	Granule range for evaluation (Max):	2000
(Min):	0.05	Start position of sensor usage:	1
Trigger mode:	OFF		
Dry threshold:	300		

[0031]

<Test 1>

In Examples 1, 2 and 3, tablets comprising specific pharmaceutical compositions comprising water-soluble excipient comprising 20 mg, 40 mg and 80 mg, respectively, of lurasidone per tablet, partly pregelatinized starch and water-soluble polymer binder were manufactured. In Comparative experiments 1 and 2, tablets comprising 40 mg and 80 mg, respectively, of lurasidone per tablet were manufactured on the basis of the formulation disclosed in Patent Document 2.

The manufactured preparations were subjected to the dissolution tests under conditions shown in (d) and (e), and similarities of dissolution profiles were evaluated. Additionally, preproductions in Comparative experiments 1 and 2 were shown in Test 8.

Results were shown in Tables 4 and 5. Temporal dissolution ratios in (d) were shown in Figures 2 and 3.

[0032]

(a) Formulations of granule powders

[0033]

Table 1

Unit: mg

Component	Example No.			Compar. Ex. No.	
	1	2	3	1	2
Lurasidone	80	40	20	40	80
Mannitol	144	72	36	188	148
Partly pregelatinized starch	80	40	20	-	-
Croscarmellose sodium	4	2	1	16	16
Hydroxypropyl methylcellulose	8	4	2	10	10

[0034]

(b) Formulations of granules for compression/uncoated tablets

[0035]

Table 2

Unit: mg

Component	Example No.			Compar. Ex. No.	
	1	1	1	1	2
Granules in the above (a)	316	158	79	254	254
Lactose	-	-	-	62	62
Magnesium stearate	4	2	1	4	4

[0036]

(c) Formulations of FC tablets

[0037]

Table 3

Unit: mg

Component	Example No.			Compar.Ex.No.	
	1	2	3	1	2
Uncoated tablets in the above (b)	320	160	80	320	320
Hydroxypropyl methylcellulose	3.25	1.95	1.3	2.6	2.6
Titanium oxide	1	0.6	0.4	0.8	0.8
Polyethylene glycol 6000	0.75	0.45	0.3	0.6	0.6
Carnauba wax	0.01	0.006	0.004	0.01	0.01

[0038]

(d) Dissolution test in the system comprising 80 mg of lurasidone in each vessel

Each film-coated tablet comprising 80 mg, 40 mg or 20 mg of lurasidone in the system comprising 80 mg of lurasidone in each vessel was subjected to the dissolution test, and a similarity of each dissolution profile was evaluated by f2 value.

[0039]

As evidenced by Table 4, f2 values in Examples 2 and 3 showed similarities to Example 1, but f2 value in Comparative experiment 2 did not show a similarity to Comparative experiment 1. In other words, as evidenced by Table 4 and Figure 3, in Examples 1 to 3, f2 values which represented similarities of dissolution profiles were in the range of

50≤f2≤100, and preparations which showed similarities of dissolution profiles without depending on contents in tablets (unit strength) even in preparations with different contents were obtained. On the other hand, as evidenced by Table 4 and Figure 2, dissolution of the formulation disclosed in Patent Document 2 in Comparative experiment 2 was apparently slower than that of two tablets of preparations in Comparative experiment 1, and a similarity of dissolution profile was not shown as detailed in Test 8.

[0040]

Table 4

Similarity factor	Example No.			Compar.Ex. No.	
	1	2	3	1	2
f2	-	88	97	-	37

[0041]

(e) Dissolution test in the system comprising 40 mg of lurasidone in each vessel

Each film-coated tablet comprising 40 mg or 20 mg of lurasidone in the system comprising 40 mg of lurasidone in each vessel was subjected to the dissolution test, and a similarity of each dissolution profile was evaluated by using f2 values in the similar manner.

[0042]

As evidenced by Table 5, f2 values in Example 3 and Comparative experiment 1 showed similarities to Example 2. In other words, f2 values were in the range of 50≤f2≤100 even in the system comprising 40 mg of lurasidone in each vessel, and similarities of dissolution profiles were shown without depending on contents in tablets (unit strength).

[0043]

Table 5

Similarity factor	Example No.		Compar. Ex. No.
	2	3	1
f2	-	88	97

[0044]

<Test 2>

Preparations comprising a pharmaceutical composition comprising water-soluble excipient and water-soluble polymer binder and partly pregelatinized starch were prepared in Examples 1 and 4. Preparations comprising a pharmaceutical composition comprising water-soluble excipient and water-soluble polymer binder and corn starch which was non-pregelatinized starch were prepared in Comparative experiments 3, 4 and 5. Each preparation was subjected to the dissolution test, and a similarity of each dissolution profile was evaluated by f2 value. Results were shown in Table 9.

(a) Formulations of granule powders

[0045]

Table 6

Unit: mg

Component	Example No.		Compar. Ex. No.		
	1	4	3	4	5
Lurasidone	80	80	80	80	80
Mannitol	144	176	108	108	-
Lactose	-	-	-	-	108
Partly pregelatinized starch	80	40	-	-	-
Corn starch	-	-	40	40	40
Croscarmellose sodium	4	8	16	16	16
Hydroxypropyl methylcellulose	8	12	10	10	10

[0046]

(b) Formulations of granules for compression/uncoated tablets

[0047]

Table 7

Unit: mg

Component	Example No.		Comparative Example No.		
	1	4	3	4	5
Granules in the above (a)	316	316	254	254	254
Mannitol	-	-	62	-	-
Magnesium stearate	4	4	4	4	4

[0048]

(c) Formulations of FC tablets

[0049]

Table 8

Unit: mg

Component	Example No.		Comparative Example No.		
	1	4	3	4	5
Uncoated tablets in the above (b)	320	320	320	258	258
Hydroxypropyl methylcellulose	3.25	-	2.6	2.6	2.6
Titanium oxide	1	-	0.8	0.8	0.8
Polyethylene glycol 6000	0.75	-	0.6	0.6	0.6

[0050]

(d) Dissolution test

As evidenced by Table 9, Example 4 showed a similarity to Example 1, but f2 values in Comparative experiments 3, 4 and 5 did not show similarities to Example 1. In other words, preparations containing corn starch in Comparative experiments 3, 4 and 5 showed different dissolution profiles and slow dissolutions compared to preparations containing partly pregelatinized starch in Examples 1 and 4.

[0051]

Table 9

Similarity factor	Example No.		Comparative Ex. No.		
	1	4	3	4	5
f2	-	67	44	29	26

[0052]

<Test 3>

Effects of blending quantities of partly pregelatinized starch in Examples 4, 5, 6 and 7 on dissolutions were evaluated. Results were shown in Table 13.

(a) Formulations of granule powders

[0053]

Table 10

Unit: mg

Component	Example No.				
	1	4	5	6	7
Lurasidone	80	80	80	80	80
Mannitol	144	176	116	136	156
Partly pregelatinized starch	80	40	100	80	60
Croscarmellose sodium	4	8	8	8	8
Hydroxypropyl methylcellulose	8	12	12	12	12

[0054]

(b) Formulations of granules for compression/uncoated tablets

[0055]

Table 11

Unit: mg

Component	Example No.				
	1	4	5	6	7
Granules in the above (a)	316	316	316	316	316
Magnesium stearate	4	4	4	4	4

[0056]

(c) Formulations of FC tablets

[0057]

Table 12

Unit: mg

Component	Example No.				
	1	4	5	6	7
Uncoated tablets in the above (b)	320	320	320	320	320
Hydroxypropyl methylcellulose	3.25	-	-	-	-
Titanium oxide	1	-	-	-	-
Polyethylene glycol 6000	0.75	-	-	-	-
Carnauba wax	0.01	-	-	-	-

[0058]

(d) Dissolution test

As evidenced by Table 13, f2 values in Examples 4, 5, 6 and 7 showed similarities to Example 1. In other words, a preparation comprising a pharmaceutical composition comprising 10% wt/wt or more of partly pregelatinized starch in preparation components showed a rapid dissolution and a similar dissolution profile.

[0059]

Table 13

Similarity factor	Example No.				
	1	4	5	6	7
f2	-	67	60	62	81

[0060]

<Test 4>

In Comparative experiment 6, a tablet was tried to be prepared with containing water-soluble excipient and partly pregelatinized starch but without water-soluble polymer binder. However, in a compression step, components could not be compressed due to capping and sticking, and no similar dissolution profile or even tablet was obtained. In Examples 8, 9, 10 and 11, preparations comprising pharmaceutical compositions with different blending quantities of water-soluble excipient and partly pregelatinized starch and water-soluble polymer binder were prepared. Results were shown in Table 17.

(a) Formulations of granule powders

[0061]

Table 14

Unit: mg

Component	Example No.					Compar.Ex.No.
	1	8	9	10	11	6
Lurasidone	80	80	80	80	80	80
Mannitol	144	136	138	140	142	148
Partly pregelatinized starch	80	80	80	80	80	80
Croscarmellose sodium	4	8	8	8	8	8
Hydroxypropyl methylcellulose	8	12	10	8	6	-

[0062]

(b) Formulations of granules for compression/uncoated tablets

[0063]

Table 15

Unit: mg

Component	Example No.					Compar. Ex. No.
	1	8	9	10	11	6
Granules in the above (a)	316	316	316	316	316	316
Magnesium stearate	4	4	4	4	4	4

[0064]

(c) Formulations of FC tablets

[0065]

Table 16

Unit: mg

Component	Example No.					Compar.Ex. No.
	1	8	9	10	11	6
Uncoated tablets in the above (b)	320	320	320	320	320	320
Hydroxypropyl methylcellulose	3.25	-	-	-	-	-
Titanium oxide	1	-	-	-	-	-
Polyethylene glycol 6000	0.75	-	-	-	-	-
Carnauba wax	0.01	-	-	-	-	-

[0066]

(d) Dissolution test

As evidenced by Table 17, f2 values in Examples 8, 9, 10 and 11 showed similarities to Example 1. In other words, preparations comprising pharmaceutical compositions comprising water-soluble polymer binder in the range of 1.8% wt/wt to 3.8% wt/wt showed rapid dissolutions and similar dissolution profiles.

[0067]

Table 17

Similarity factor	Example No.				
	1	8	9	10	11
f2	-	77	81	73	73

[0068]

<Test 5>

In Example 12, a preparation comprising a pharmaceutical composition comprising water-soluble polymer binder and partly pregelatinized starch was prepared by using lactose as water-soluble excipient. Results were shown in Table 21.

(a) Formulations of granule powders

[0069]

Table 18

Unit: mg

Component	Example No.		
	1	6	12
Lurasidone	80	80	80
Mannitol	144	136	-
Lactose	-	-	136
Partly pregelatinized starch	80	80	80
Croscarmellose sodium	4	8	8
Hydroxypropyl methylcellulose	8	12	12

[0070]

(b) Formulations of granules for compression/uncoated tablets

[0071]

Table 19

Unit: mg

Component	Example No.		
	1	6	12
Granules in the above (a)	316	316	316
Magnesium stearate	4	4	4

[0072]

(c) Formulations of FC tablets

[0073]

Table 20

Unit: mg

Component	Example No.		
	1	6	12
Uncoated tablets in the above (b)	320	320	320
Hydroxypropyl methylcellulose	3.25	-	-
Titanium oxide	1	-	-
Polyethylene glycol 6000	0.75	-	-
Carnauba wax	0.01	-	-

[0074]

(d) Dissolution test

As evidenced by Table 21, f2 values in Examples 6 and 12 showed similarities to Example 1. In other words, preparations containing mannitol and lactose as water-soluble excipient showed rapid dissolutions and similar dissolution profiles.

[0075]

Table 21

Similarity factor	Example No.		
	1	6	12
f2	-	62	66

[0076]

<Test 6>

In Examples 4, 13, 14 and 15, preparations comprising a specific pharmaceutical composition comprising water-soluble excipient and

water-soluble polymer binder and partly pregelatinized starch were prepared by using lurasidone bulk powders with different size distribution. Results were shown in Table 25.

(a) Size distribution of lurasidone bulk powders

D50 % (50% particle size) represents a particle size at a point where an integrated distribution calculated on the basis of volume is 50%, and D90 % (90% particle size) represents a particle size at a point where an integrated distribution calculated on the basis of volume is 90% (under sieving).

[0077]

Table 22

Unit: mg

Size distribution		Example No.			
		4	13	14	15
Particle size	D10 %	0.5	0.9	1.0	1.5
	D50 %	1.6	5.9	7.6	13.9
	D90 %	4.7	17.5	26.9	58.3

[0078]

(b) Formulations of granules for compression/uncoated tablets

[0079]

Table 23

Unit: mg

Component	Example No.			
	4	13	14	15
Lurasidone	80	80	80	80
Mannitol	176	144	144	144
Partly pregelatinized starch	40	80	80	80
Croscarmellose sodium	8	4	4	4
Hydroxypropyl methylcellulose	12	8	8	8
Magnesium stearate	4	4	4	4

[0080]

(c) Formulations of FC tablets

[0081]

Table 24

Unit: mg

Component	Example No.			
	4	13	14	15
Uncoated tablets in the above (b)	320	320	320	320
Hydroxypropyl methylcellulose	-	3.25	3.25	3.25
Titanium oxide	-	1	1	1
Polyethylene glycol 6000	-	0.75	0.75	0.75
Carnauba wax	-	0.01	0.01	0.01

[0082]

(d) Dissolution test

As evidenced by Table 25, f2 values in Examples 13, 14 and 15 showed similarities to Example 4. In other words, it was found that preparations prepared by using lurasidone bulk powders wherein 50% particle size is in the range of 1 to 8 μm and 90% particle size is 27 μm or less in size distribution showed similar dissolution profiles.

[0083]

Table 25

Similarity factor	Example No.			
	4	13	14	15
f2	-	56	56	46

[0084]

<Test 7>

Preparations wherein contents of lurasidone per tablet were 10 mg and 40 mg were manufactured by using the art disclosed in Patent Document 2, and were subjected to examination if they could provide preparations for oral administration with equivalent dissolution profiles in the range of 10 mg to 40 mg of lurasidone contents per tablet as disclosed in the document 2. Results were shown in Figure 1.

[0085]

As evidenced by Figure 1, dissolution profiles of preparations with different contents of lurasidone obtained by the art disclosed in Patent

Document 2 were shown by f2 values, and tablets with 10 mg and 40 mg of lurasidone per tablet could provide preparations for oral administration with equivalent dissolution profiles as described in Patent Document 2.

(a) Formulations of granules

[0086]

Table 26

Unit: mg

Component	10 mg tablet	40 mg tablet
Lurasidone	10	40
Mannitol	47	188
Croscarmellose sodium	4	16
Hydroxypropyl methylcellulose	2.5	10

(b) Formulations of uncoated tablets

[0087]

Table 27

Unit: mg

Component	10 mg tablet	40 mg tablet
Granules in (a)	63.5	254
Lactose	15.5	62
Magnesium stearate	1	4

(c) Formulations of FC tablets

[0088]

Table 28

Unit: mg

Component	10 mg tablet	40 mg tablet
Uncoated tablets in the above (b)	80	320
Hydroxypropyl methylcellulose	1.3	2.6
Titanium oxide	0.4	0.8
Polyethylene glycol 6000	0.3	0.6
Carnauba wax	0.006	0.01

[0089]

<Test 8>

It could be confirmed that a preparation with up to 40 mg of lurasidone per tablet could provide an oral preparation with equivalent dissolution profile in the art disclosed in Patent Document 2. A preparation wherein contents of lurasidone were 80 mg per tablet without containing partly pregelatinized starch was manufactured herein according to the art disclosed in Patent Document 2. The preparation was prepared by doubling a content ratio of the active ingredient so that a tablet weight thereof was the same as 40 mg tablet, in order to avoid an increased strain on a patient associated with growth of tablets in size. Results of Comparative experiments 1 and 2 were shown in Table 4 and Figure 2.

[0090]

As evidenced by Table 4 and Figure 2, 80 mg tablet with double content ratios of lurasidone without containing pregelatinized starch could not show equivalent dissolution to two tablets of 40 mg tablet as shown by f2 values in the art disclosed in Patent Document 2.

(a) Formulations of granules

[0091]

Table 29

Unit: mg

Component	40 mg tablet	80 mg tablet
Lurasidone	40	80
Mannitol	188	148
Croscarmellose sodium	16	16
Hydroxypropyl methylcellulose	10	10

(b) Formulations of uncoated tablets

[0092]

Table 30

Unit: mg

Component	40 mg tablet	80 mg tablet
Granules in (a)	254	254
Lactose	62	62
Magnesium stearate	4	4

(c) Formulations of FC tablets

[0093]

Table 31

Unit: mg

	40 mg tablet	80 mg tablet
Uncoated tablets in the above (b)	320	320
Hydroxypropyl methylcellulose	2.6	2.6
Titanium oxide	0.8	0.8
Polyethylene glycol 6000	0.6	0.6
Carnauba wax	0.01	0.01

[0094]

<Test 9>

Dissolutions of three kinds of preparations with different contents manufactured in Examples 1 to 3 of Test 1 were evaluated. Results were shown in Figure 3.

As evidenced by Figure 3, it was confirmed that preparations of the present invention which contained in the range of 20 mg to 80 mg of lurasidone per tablet showed equivalent dissolutions without depending on tablet contents (unit strength).

(a) Formulations of granule powders

[0095]

Table 32

Unit: mg

Component	80 mg tablet	40 mg tablet	20 mg tablet
Lurasidone	80	40	20
Mannitol	144	72	36
Partly pregelatinized starch	80	40	20
Croscarmellose sodium	4	2	1
Hydroxypropyl methylcellulose	8	4	2

(b) Formulations of granules for compression/uncoated tablets

[0096]

Table 33

Unit: mg

Component	80 mg tablet	40 mg tablet	20 mg tablet
Granules in the above (a)	316	158	79
Lactose	-	-	-
Magnesium stearate	4	2	1

(c) Formulations of FC tablets

[0097]

Table 34

Unit: mg

Component	80 mg tablet	40 mg tablet	20 mg tablet
Uncoated tablets in the above (b)	320	160	80
Hydroxypropyl methylcellulose	3.25	1.95	1.3
Titanium oxide	1	0.6	0.4
Polyethylene glycol 6000	0.75	0.45	0.3
Carnauba wax	0.01	0.006	0.004

[0098]

<Test 10>

Lurasidone 120 mg tablet preparations wherein each tablet weight was equal were prepared according to the art disclosed in the present invention as well as Patent Document 2, and dissolution profile of each preparation was evaluated.

(a) Experimental method

Lurasidone 120 mg tablet preparations were manufactured according to the preparation method of the present invention as well as Preparation method 2 in Patent Document 2 (described hereinafter) (Table 35). These manufactured preparations were subjected to the dissolution test on partly changed conditions described in C. Quality evaluation (1) dissolution test in the Example in the present specification.

The dissolution test was carried out by changing pH4.0 to pH3.8 in pH of the test solution diluted McIlvaine buffer.

[0099]

(b) Preparation method of the present invention

To a fluid bed granulator (Flow Coater FLF-30/manufactured by Freund Industrial Co., Ltd.) were charged lurasidone (8000 g), D-mannitol (14200 g), partly pregelatinized starch (8000 g) and croscarmellose sodium (400 g), and thereto was sprayed 5% hydroxypropyl methylcellulose solution previously prepared to be granulated on conditions that intake temperature was 80°C, intake airflow was 7 m^3/min, spray liquid flow rate was 200 mL/min and atomizing airflow was 200 L/min. The obtained granule was dried in the granulator on conditions that drying temperature was 80°C and drying time was 10 minutes, and it was confirmed by a halogen moisture analyzer that the loss on dry was within 2%. The obtained granule was sized by using a sizing machine (Fiore F-0 type). Then, the sized granule (18000 g) and magnesium stearate (228 g) were blended together by using a blending machine (container size 110 L) on conditions that rotation rate was 20 rpm and blending time was 5 minutes. Finally, the obtained mixture was compressed at a compressing pressure of 12.5 kN by using a compression apparatus (HT-AP12SS-II/manufactured by Hata Iron Works Co., Ltd.) to prepare

Par Pharm., Inc.
Exhibit 1013
Page 036

a lurasidone 120 mg uncoated tablet.

[0100]

(c) Preparation method 2 in Patent Document 2

To a fluid bed granulator (Multiplex MP-01/manufactured by Powrex Corporation) were charged lurasidone (160 g), D-mannitol (296 g) and croscarmellose sodium (32 g), and thereto was sprayed 5% hydroxypropyl methylcellulose solution previously prepared to be granulated on conditions that temperature for supplying air was 60°C and granulating time was 45 minutes. The obtained granule was dried in the granulator on conditions that drying temperature was 80°C and drying time was 5 minutes, and it was confirmed by a halogen moisture analyzer that the loss on dry was within 1%. Then, the obtained granule (254 g) and lactose (62 g) were blended together by using a blending machine (manufactured by Tsutsui Rikagaku Kikai Co., Ltd.) on conditions that rotation rate was 40 rpm and blending time was 30 minutes. After that, the resulting mixture (316 g) and magnesium stearate (4 g) were blended together by using a blending machine (manufactured by Tsutsui Rikagaku Kikai Co., Ltd.) on conditions that rotation rate was 40 rpm and blending time was 5 minutes. Finally, the obtained mixture was compressed at a compressing pressure of 12.5 kN by using a compression apparatus (HT-AP12SS-II/manufactured by Hata Iron Works Co., Ltd.) to prepare a lurasidone 120 mg uncoated tablet.

[0101]

(d) Results

Components of the manufactured preparations and results of the dissolution tests were shown below.

[0102]

Table 35

Components of tablets

Formulations	034-15-120-1000 (Disclosure of the present application)	RP-03323-120-1000 (Disclosure of Patent Document 2)
Lurasidone	120	120
Mannitol	213	222
Partly pregelatinized starch	120	-
Croscarmellose sodium	6	24
Tablettose 70	-	93
Hydroxypropyl methylcellulose	15	15
Magnesium stearate	6	6
Total	480	480

Dissolution profile

Time (min)	Dissolution rate (%)	
10	83	54
15	91	66
30	95	80
45	96	84
f2 value	-	37

As a result, it was confirmed that lurasidone 120 mg tablet manufactured according to the disclosure of the present application showed more rapid dissolution compared to lurasidone 120 mg tablet manufactured according to the disclosure of Patent Document 2.

[0103]

<Test 11>

Applied content ranges of drug substance of the present invention were evaluated on the basis of dissolution profiles of preparations.

(a) Experimental method

Lurasidone 80 mg tablets were manufactured according to the preparation method of the present invention (Table 36). These manufactured preparations were subjected to the dissolution test on conditions described in C. Quality evaluation (1) dissolution test in the Example in the present specification.

[0104]

(b) Preparation method

To a fluid bed granulator (Multiplex MP-01/manufactured by Powrex Corporation) were charged lurasidone, D-mannitol, partly pregelatinized starch and croscarmellose sodium, and thereto was sprayed 5% hydroxypropyl methylcellulose solution previously prepared to be granulated on conditions that temperature for supplying air was 60°C and granulating time was 45 minutes or 60 minutes. The obtained granule was dried in the granulator on conditions that drying temperature was 80°C and drying time was 5 minutes, and it was confirmed by a halogen moisture analyzer that the loss on dry was within 2%. Then, the obtained granule and magnesium stearate were blended together by using a blending machine (manufactured by Tsutsui Rikagaku Kikai Co., Ltd.) on conditions that rotation rate was 40 rpm and blending time was 5 minutes. Finally, the obtained mixture was compressed at a compressing pressure of 10 kN by using a compression apparatus (HT-AP12SS-II/manufactured by Hata Iron Works Co., Ltd.) to prepare a lurasidone 80 mg uncoated tablet.

[0105]

(c) Results

Components of manufactured preparations and results of dissolution tests were shown below.

[0106]

Table 36

Formulations	034-15-80-1000	RP-03320	RP-03321	RP-03322
Lurasidone	80	80	80	80
Mannitol	142	104	67	30
Partly pregelatinized starch	80	80	80	80
Croscarmellose sodium	4	4	4	4
Hydroxyproplyl methylcellulose	10	8	6	4
Magnesium stearate	4	4	3	2
Total	320	280	240	200

Dissolution profile

Time (min)	Dissolution ratio (%)			
10	85	73	71	68
15	89	80	80	81
30	93	88	88	89
45	94	90	91	91
f2 value	-	60	60	63

As a result, it could be confirmed that similar dissolution profiles were shown by components of preparations wherein lurasidone was contained in the range of 25 to 40%.

[0107]

<Test 12>

Dissolution profiles of preparations were evaluated for the water-soluble polymer binders of the present invention.

(a) Experimental method

Lurasidone 80 mg tablet was manufactured according to the preparation method of the present invention (Table 37). These manufactured preparations were subjected to the dissolution test on conditions described in C. Quality evaluation (1) dissolution test in Example in the present specification.

[0108]

(b) Preparation method

To a fluid bed granulator (Multiplex MP-01/manufactured by Powrex Corporation) were charged lurasidone (160 g), D-mannitol (284 g), partly pregelatinized starch (160 g) and croscarmellose sodium (8 g), and thereto was sprayed 5% water-soluble polymer binder solution previously prepared to be granulated on conditions that temperature for supplying air was 60°C and granulating time was 45 minutes. The obtained granule was dried in the granulator on conditions that drying temperature was 80°C and drying time was 5 minutes, and it was confirmed by a halogen moisture analyzer that the loss on dry was within 2%. Then, the obtained granule and magnesium stearate were blended together by using a blending machine (manufactured by Tsutsui Rikagaku Kikai Co., Ltd.) on conditions that rotation rate was 40 rpm and blending time was 5 minutes. Finally, the obtained mixture was compressed at a compressing pressure of 10 kN by using a compression apparatus (HT-AP12SS-II/manufactured by Hata Iron Works Co., Ltd.) to prepare a lurasidone 80 mg uncoated tablet.

[0109]

(c) Results

Components of manufactured preparations and results of dissolution tests were shown below.

[0110]

Table 37

Formulations	034-15-80-1000	RP-03326	RP-03327	RP-03328
Lurasidone	80	80	80	80
Mannitol	142	142	142	142
Partly pregelatinized starch	80	80	80	80
Croscarmellose sodium	4	4	4	4
Hydroxyproplyl methylcellulose	10	-	-	-
Polyvinylalcohol	-	10	-	-
Polyvinylpyrrolidone	-	-	10	-
Hydroxypropylcellulose	-	-	-	10
Magnesium stearate	4	4	4	4
Total	320	320	320	320

Dissolution profile

Time (min)	Dissolution ratio (%)			
10	83	59	78	80
15	91	76	82	87
30	95	94	88	91
45	96	96	90	92
f2 value	-	53	56	69

As a result, it was confirmed that preparations using as water-soluble polymer binder polyvinyl alcohol, polyvinylpyrrolidone or hydroxypropylcellulose met the standard of "C. Quality evaluation (2) Similarity of dissolution profiles" in the present specification (similar dissolution profiles).

[0111]

<Test 13>

Dissolution profiles of lurasidone 20, 40, 80 and 120 mg FC tablets prepared according to the art disclosed in the present invention were evaluated.

(a) Experimental method

Lurasidone 20, 40, 80 and 120 mg FC tablets were manufactured according to the preparation method of the present invention (Table 38).

[0112]

(b) Preparation method

To a fluid bed granulator (Flow Coater FLF-30/manufactured by Freund Industrial Co., Ltd.) were charged lurasidone (8000 g), D-mannitol (14200 g), partly pregelatinized starch (8000 g) and croscarmellose sodium (400 g), and thereto was sprayed 5% aqueous hydroxypropyl methylcellulose solution previously prepared to be granulated on conditions that intake temperature was 80°C, intake airflow was 7 m^3/min, spray liquid flow rate was 200 mL/min and atomizing airflow was 200 L/min. After spraying, the obtained granule was dried on conditions that drying temperature was 80°C and drying time was 10 minutes, and it was confirmed by a halogen moisture analyzer that the loss on dry was within 2%. The obtained granule powders were sized by using a sizing machine (Fiore F-0 type/manufactured by Tokuju Corporation). Then, the sized granule powders (18000 g) and magnesium stearate (228 g) were blended together by using a blending machine (container size 110 L/manufactured by Furukawa Altec Co., Ltd.) on conditions that rotation rate was 20 rpm and blending time was 5 minutes. The obtained powder mixtures were compressed at a compressing pressure of about 10 kN by using a compression apparatus (CLEANPRESS Correct 12HUK/manufactured by Kikusui Seisakusho Ltd. for a lurasidone 20, 40 or 80 uncoated tablet, HT-AP12SS-II/manufactured by Hata Iron Works Co., Ltd. for a lurasidone 120 mg uncoated tablet) to prepare a lurasidone 20, 40, 80 or 120 mg uncoated tablet. Then, an uncoated tablet was coated on conditions that temperature for supplying air was 80°C, airflow was 0.6 m^3/min, rotation rate of pan was 25 rpm, spray pressure was 0.15MPa and liquid flow rate was 5 g/min to give a lurasidone 20, 40, 80 or 120 mg FC tablet.

[0113]

Par Pharm., Inc.
Exhibit 1013
Page 043

(c) Dissolution test

Manufactured preparations were subjected to the dissolution test according to the Japanese Pharmacopoeia, Dissolution test, Method 2. Measuring conditions are shown below.

Test solution: Diluted McIlvaine buffer, pH3.8 and 4.0

Paddle rotation: 50 rpm

Test fluid: 900 ml

[0114]

(d) Results

Components of manufactured preparations and results of dissolution tests were shown below.

[0115]

Table 38

Components of tablets

Product name		Lurasidone 20 mg FC tablet	Lurasidone 40 mg FC tablet	Lurasidone 80 mg FC tablet	Lurasidone 120 mg FC tablet
Lot No.		034-15-20	034-15-40	034-15-80	034-15-120
Formulation	Lurasidone	20 mg	40 mg	80 mg	120 mg
	mannitol	35.5 mg	71 mg	142 mg	216mg
	Partly pregelatinized starch	20 mg	40 mg	80 mg	120 mg
	Croscarmellose sodium	1 mg	2 mg	4 mg	6 mg
	Hydroxypropyl methylcellulose	2.5 mg	5 mg	10 mg	15 mg
	Magnesium stearate	1 mg	2 mg	4 mg	6 mg
	Subtotal	80 mg	160 mg	320 mg	480 mg
	Hydroxypropyl methylcellulose	1.001 mg	1.690 mg	2.730 mg	1.100 mg
	Titanium oxide	0.308 mg	0.520 mg	0.840 mg	0.825 mg
	Macrogol 6000	0.231 mg	0.390 mg	0.630 mg	5.500 mg
	Carnauba wax	0.01 mg	0.01 mg	0.01 mg	0.01 mg
Total		81.55 mg	162.61 mg	324.21 mg	485.51 mg

Dissolution profile

Time (min)	Dissolution ratio (%)			
10	80	77	77	77
15	91	90	88	92
30	100	98	93	96
45	101	100	94	97
pH of test fluid	4.0	4.0	4.0	3.8

As a result, it was confirmed that lurasidone 20, 40, 80 and 120 mg FC tablets manufactured according to the disclosure of the present application showed rapid dissolutions.

[0116]

<Test 13>

Similarities of dissolution profiles were evaluated for 1 tablet of 40 mg FC tablet/2 tablets of 20 mg FC tablet, 1 tablet of 80 mg FC tablet/2

tablets of 40 mg FC tablet/4 tablets of 20 mg FC tablet, 1 tablet of 120 mg FC tablet/3 tablets of 40 mg FC tablet/6 tablets of 20 mg FC tablet.

(a) Experimental method

Preparation method and test method were abbreviated because they were similar to dissolution profiles in Test 12.

[0117]

(b) Results

Dissolution profiles of manufactured preparations and similarities thereof were shown below.

[0118]

Table 39

Tablet		40 mg tablet	20 mg tablet	80 mg tablet	40 mg tablet	20 mg tablet	120 mg tablet	40 mg tablet	20 mg tablet
Number of tablets		1 tablet	2 tablets	1 tablet	2 tablets	4 tablets	1 tablet	3 tablets	6 tablets
		Dissolution ratio (%)		Dissolution ratio (%)			Dissolution ratio (%)		
Time (min)	10	77	79	77	78	75	77	90	83
	15	90	90	88	86	84	92	94	90
	30	98	98	93	91	90	96	97	94
	45	100	100	94	93	92	97	98	95
f2 value		-	100	-	85	74	-	88	83

As a result, it was confirmed that all preparations met the standard of "C. Quality evaluation (2) Similarity of dissolution profiles" in the present specification.

INDUSTRIAL APPLICABILITY

[0119]

The present invention allows to provide a preparation for oral administration with a good disintegration which comprises as an active ingredient N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptane-dicarboxyimide hydrochloride (lurasidone), which has an equivalent dissolution profile of the active ingredient even though contents of the

11/919678
IAP05Rec'd PCT 31 OCT 2007

active ingredient therein are varied.

BRIEF DESCRIPTION OF DRAWINGS

[0120]

Figure 1 shows a comparison of dissolution profiles in preparations with different contents of lurasidone. Preparations wherein contents of lurasidone per tablet manufactured according to the art disclosed in Patent Document 2 were 10 mg (4 tablets) and 40 mg (1 tablet) were measured in dissolution profiles.

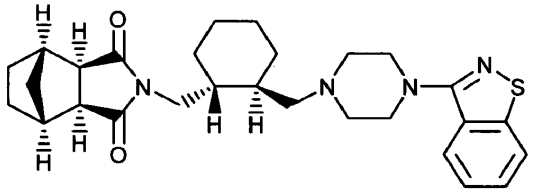
Figure 2 shows a comparison of dissolution profiles in preparations with different contents of lurasidone. Preparations wherein contents of lurasidone per tablet manufactured according to the art disclosed in Patent Document 2 were 40 mg (2 tablets) and 80 mg (1 tablet) were measured in dissolution profiles.

Figure 3 shows a comparison of dissolution profiles in preparations with different contents of lurasidone. Preparations wherein contents of lurasidone per tablet manufactured according to the present invention were 20 mg (4 tablets), 40 mg (2 tablets) and 80 mg (1 tablet) were measured in dissolution profiles.

Par Pharm., Inc.
Exhibit 1013
Page 047

CLAIMS

1. An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of the formula (1):



(1),

a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder.

2. An oral preparation which is prepared by granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

3. An oral preparation which is prepared by granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by a solution or dispersion of lurasidone and a water-soluble polymer binder.

4. The oral preparation of any one of claims 1 to 3 wherein the water-soluble excipient is mannitol or lactose.

5. A method of granulation of a powder mixture which comprises granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

6. A method of granulation of a powder mixture which comprises granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by using a solution or dispersion of lurasidone and a water-soluble polymer binder.

7. The method of granulation of claim 5 wherein the water-soluble excipient is mannitol or lactose.

8. The oral preparation of any one of claims 1 to 4 wherein the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation.

9. The oral preparation of any one of claims 1 to 4 wherein the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation.

10. The oral preparation of any one of claims 1 to 4 wherein a content of lurasidone in the preparation is 20 to 45% (wt/wt).

11. The oral preparation of any one of claims 1 to 4 wherein a content of lurasidone in the preparation is 25 to 40% (wt/wt).

12. The oral preparation of any one of claims 1 to 4 wherein a content of lurasidone per tablet is 10 to 160 mg.

13. The oral preparation of any one of claims 1 to 4 wherein a content of lurasidone per tablet is 20 to 120 mg.

14. The oral preparation of any one of claims 1 to 4 wherein a content of lurasidone per tablet is 40 to 120 mg.

15. The oral preparation of any one of claims 1 to 4 wherein the water-soluble excipient is mannitol or lactose and the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation.

16. The oral preparation of any one of claims 1 to 4 wherein the water-soluble excipient is mannitol or lactose and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

17. The oral preparation of any one of claims 1 to 4 wherein the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

18. The oral preparation of any one of claims 1 to 4 wherein the

water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

19. The oral preparation of any one of claims 1 to 4 wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation and a content of lurasidone in the preparation is 25 to 40% (wt/wt).

20. The oral preparation of any one of claims 1 to 4 wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 40 to 120 mg.

21. The oral preparation of any one of claims 1 to 4 wherein a pregelatinizing ratio of the pregelatinized starch is 50 to 95%.

22. The oral preparation of any one of claims 1 to 4 wherein an average particle size of lurasidone is 0.1 to 8 μm.

23. The oral preparation of any one of claims 1 to 4 wherein the pregelatinized starch contains water soluble matter of 30% or less.

24. The oral preparation of any one of claims 1 to 4 wherein the water-soluble excipient is mannitol or lactose, the pregelatinized starch is incorporated in an amount of 20 to 30% (wt/wt) based on the weight of the preparation, a content of lurasidone in the preparation is 25 to 40% (wt/wt) and a content of lurasidone per tablet is 20 to 120 mg.

ABSTRACT

A preparation for oral administration comprising: a pregelatinized starch comprising N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]-heptanedicarboxyimide hydrochloride (lurasidone) represented by the formula (1) as an active ingredient; a water-soluble excipient; and a water-soluble polymeric binder, the preparation exhibiting an invariant level of elution behavior even when the content of its active ingredient is varied.

Par Pharm., Inc.
Exhibit 1013
Page 051

Figure 1

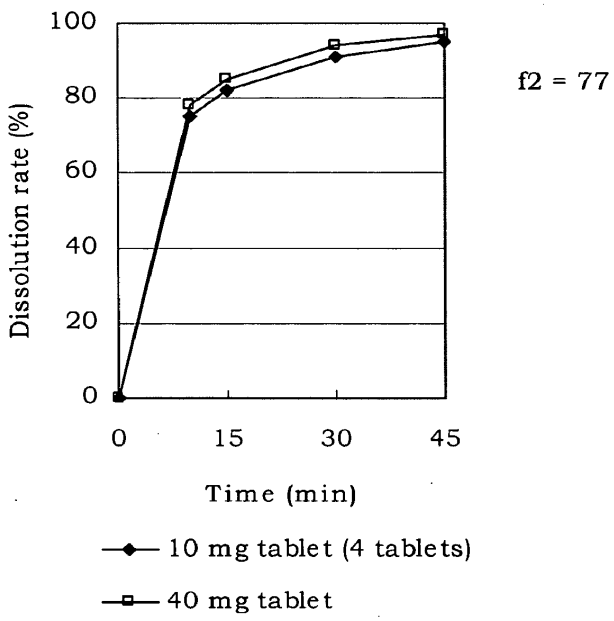

100
80
60
40
20
0
Dissolution rate (%)
0
15
30
45
Time (min)
f2 = 77
10 mg tablet (4 tablets)
40 mg tablet

Figure 2

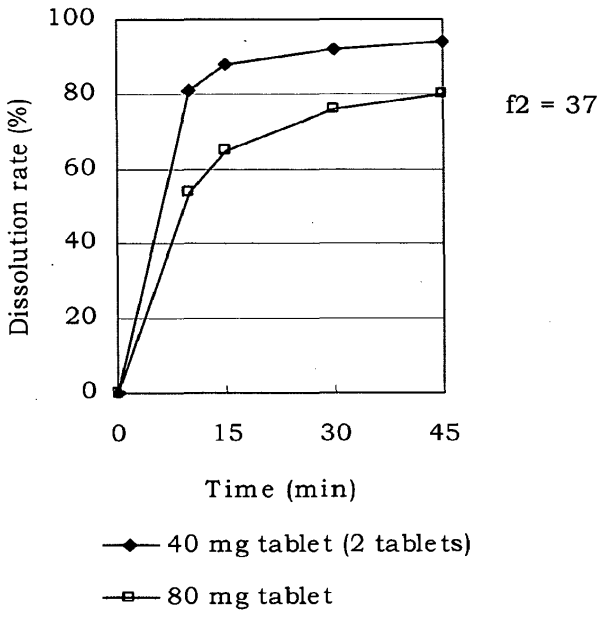
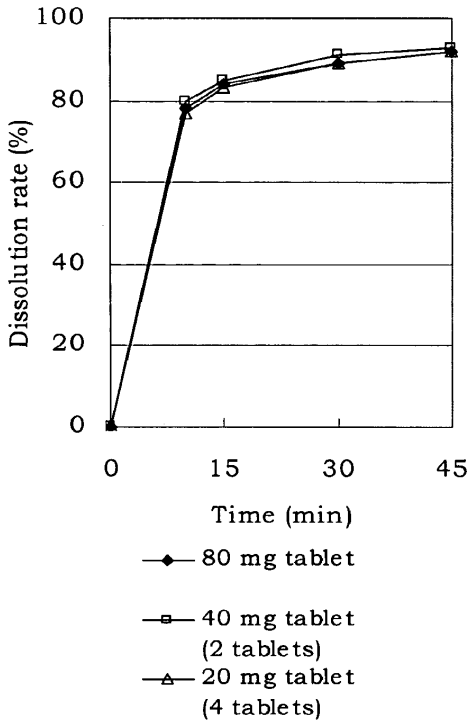

100
80
60
40
20
0
Dissolution rate (%)
0
15
30
45
Time (min)
f2 = 37
40 mg tablet (2 tablets)
80 mg tablet

Figure 3



f2 = 88
(2 tablets of 40 mg tablet for 80 mg tablet)

f2 = 97
(4 tablets of 20 mg tablet for 80 mg tablet)

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	05273.0147-02000
	Application Number	
Title of Invention	PHARMACEUTICAL COMPOSITION	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

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☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Kazuyuki		FUJIHARA	

Residence Information (Select One) ○ US Residency ◉ Non US Residency ○ Active US Military Service

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City	OSAKA	**State/Province**	
Postal Code	541-8524	**Country** [i]	JP

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

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For further information see 37 CFR 1.33(a).

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Title of the Invention	PHARMACEUTICAL COMPOSITION		
Attorney Docket Number	05273.0147-02000	**Small Entity Status Claimed**	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	3	**Suggested Figure for Publication (if any)**	

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For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

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Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	22852		

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When referring to the current application, please leave the application number blank.

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	Continuation of	14/183283	2014-02-18
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
14/183283	Continuation of	11/919678	2007-10-31

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Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
11/919678	a 371 of international	PCTJP2006/310571	2006-05-26	8729085	2014-05-20
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.					

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This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(d). When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(h)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)
2005-153508	JP	2005-05-26	
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Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Authorization to Permit Access:

☒ Authorization to Permit Access to the Instant Application by the Participating Offices

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	05273.0147-02000
	Application Number	
Title of Invention	PHARMACEUTICAL COMPOSITION	

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In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date o f filing this Authorization.

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Clear

◉ Assignee	○ Legal Representative under 35 U.S.C. 117	○ Joint Inventor
○ Person to whom the inventor is obligated to assign.	○ Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor :

If the Applicant is an Organization check here. ☒

Organization Name	SUMITOMO DAINIPPON PHARMA CO., LTD		
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Address 2			
City	OSAKA	**State/Province**	
Country	JP	Postal Code	541-8524
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	05273.0147-02000
	Application Number	
Title of Invention	PHARMACEUTICAL COMPOSITION	

Email Address	

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If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

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Address 2			
City		**State/Province**	
Country i		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.

Signature:

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Signature	Chuck Van Horn			Date (YYYY-MM-DD)	2014-10-10
First Name	Charles	Last Name	Van Horn	Registration Number	40266

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	05273.0147-02000
	Application Number	
Title of Invention	PHARMACEUTICAL COMPOSITION	

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1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent C o o p eration Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

AIA DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)			ATTORNEY DOCKET NUMBER	05273.0147-01000
			FIRST NAMED INVENTOR	KAZUYUKI FUJIHARA
			COMPLETE IF KNOWN	
☒ DECLARATION SUBMITTED WITH INITIAL FILING	OR	☐ DECLARATION SUBMITTED AFTER INITIAL FILING (SURCHARGE (37 CFR 1.16(F)) REQUIRED	APPLICATION NUMBER	UNASSIGNED
			FILING DATE	UNASSIGNED
			ART UNIT	UNASSIGNED
			EXAMINER NAME	UNASSIGNED

PHARMACEUTICAL COMPOSITION

(Title of the Invention)

As a below named inventor, I hereby declare that: (1) This declaration is directed to the application which ☒ is attached and/or ☐ was filed on February __, 2014, as United States Application No. _____ (Confirmation No. ____), or PCT International Application No. [Text] ; (2) the application was made or authorized to be made by me; (3) my residence and mailing address are as stated below next to my name; and (4) I believe I am the original inventor or an original joint inventor of a claimed invention in the application.

As a below named inventor, I have reviewed and understand the contents of the application, including the claims, and am aware of the duty to disclose to the USPTO all information known to me to be material to patentability as defined in 37C.F.R. § 1.56.

Authorization To Permit Access To Application by Participating Offices:

☒ If checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the World Intellectual Property Office (WIPO), and any other intellectual property offices in which a foreign application claiming priority to the above-identified patent application is filed access to the above-identified patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the Applicant does not wish the EPO, JPO, KIPO, WIPO, or other intellectual property office in which a foreign application claiming priority to the above-identified application is filed to have access to the above identified patent application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the above-identified patent application with respect to: 1) the above-identified patent application-as-filed; 2) any foreign application to which the above-identified patent application claims priority under 35 U.S.C. 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the above-identified patent application; and 3) any U.S. application-as-filed from which benefit is sought in the above-identified patent application.

In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date of filing the Authorization to Permit Access to Application by Participating Offices.

I hereby acknowledge that any willful false statements made in this declaration are punishable by fine or imprisonment of not more than five (5) years, or both, under section 1001 of Title 18 of the United States Code.

Legal Name of First Inventor **Kazuyuki Fujihara**	Signature Kazuyuki Fujihara	Date Feb. 12, 2014
Residence **Suzuka-shi, Mie-ken, Japan**		
Mailing Address **c/o DAINIPPON SUMITOMO PHARMA CO., LTD., 6-8, DOSHO-MACHI 2-CHOME, CHUO-KU, OSAKA-SHI, OSAKA, JP 541-8524**		

Legal Name of Second Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Third Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Fourth Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Fifth Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Sixth Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Seventh Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Eighth Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		
Legal Name of Ninth Inventor [Text]	Signature	Date
Residence [Text]		
Mailing Address [Text]		

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Filer:	Jennifer R. Gupta/Pat Welch
Attorney Docket Number:	05273.0147-02000

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Utility application filing	1011	1	280	280
Utility Search Fee	1111	1	600	600
Utility Examination Fee	1311	1	720	720
Pages:				
Claims:				
Claims in Excess of 20	1202	15	80	1200
Independent claims in excess of 3	1201	1	420	420
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Late Filing Fee for Oath or Declaration	1051	1	140	140
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**3360**

Electronic Acknowledgement Receipt	
EFS ID:	20390941
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	10-OCT-2014
Filing Date:	
Time Stamp:	18:18:56
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$3360
RAM confirmation Number	4537
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Transmittal of New Application	TransmittalOfContAppln.pdf	113336 4e444a90b6708f0cff2ec2f05cc9771a772f5dc5	no	3
Warnings:					
Information:					
2		OrigSpecAndDrawings.pdf	1659961 3600b693568142e0c07da87f3686cb0db83c8441	yes	51
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Specification		1	44	
	Claims		45	47	
	Abstract		48	48	
	Drawings-only black and white line drawings		49	51	
Warnings:					
Information:					
3	Application Data Sheet	ApplnDataSheet.pdf	380121 e8673a6ecf391fd348e202b9c74694aa1c8994ae	no	7
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
4	Oath or Declaration filed	AIA-Declaration-PriorAppln14183283.pdf	247847 e6113bf63e9c76507cb2b2f6a067ea076a1a31d1	no	2
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	39797 0ef7f5057cdf4513969501dc2808a84b74b2e8a2	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2441062		

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Kazuyuki FUJIHARA	)	Parent Group Art Unit: 1627
	)	
Application No.: 14/512,189	)	Parent Examiner: Sarah Pihonak
	)	
Filed: October 10, 2014	)	
	)	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	)	
	)	
	)	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

PRELIMINARY AMENDMENT

Prior to the examination of the above application, please amend this application as follows:

Amendments to the Specification begin at page 2 of this paper.

Amendments to the Claims begin at page 3 of this paper.

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Page 1, line 1, insert the following new paragraph:

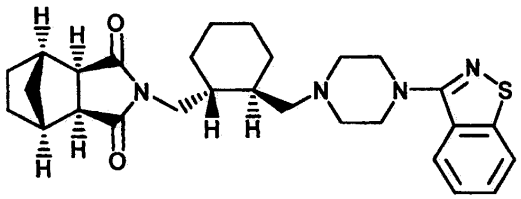
This is a continuation of prior Application No. 14/183,283, filed February 18, 2014, which is a continuation of Application No. 11/919,678, filed October 31, 2007, which issued on May 20, 2014, as U.S. Patent No. 8,729,085, which is a National Stage Entry of International Application No. PCT/JP2006/310571, filed May 26, 2006, which claims priority to Japanese Patent Application No. 2005-153508, filed May 26, 2005.

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1-24. (Canceled).

25. (New) An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of the formula (1):



(1),

a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder; wherein the content of lurasidone in the preparation is 20 to 45% (wt/wt), and the content of the pregelatinized starch in the preparation is 10 to 50% (wt/wt).

26. (New) The oral preparation of claim 25, wherein the oral preparation is prepared by the process which comprises granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

27. (New) The oral preparation of claim 25, wherein the oral preparation is prepared by the process which comprises granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by a solution or dispersion of lurasidone and a water-soluble polymer binder.

28. (New) The oral preparation of claim 25, wherein the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation.

29. (New) The oral preparation of claim 25, wherein the pregelatinized starch is incorporated in an amount of 10 to 30% (wt/wt) based on the weight of the preparation.

30. (New) The oral preparation of claim 25, wherein a content of lurasidone in the preparation is 20 to 40% (wt/wt).

31. (New) The oral preparation of claim 25, wherein the water-soluble excipient is one or more selected from the group of mannitol, lactose, saccharose, sorbitol, D-sorbitol, erythritol and xylitol.

32. (New) The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose.

33. (New) The oral preparation of claim 25, wherein a content of the water-soluble excipient per tablet is 30 to 60% (wt/wt).

34. (New) The oral preparation of claim 25, wherein the water-soluble polymer binder is hydroxypropyl methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone or hydroxypropylcellulose.

35. (New) The oral preparation of claim 25, wherein a content of the water-soluble polymer binder per tablet is 0.5 to 10% (wt/wt).

36. (New) The oral preparation of claim 25, wherein a content of lurasidone per tablet is 10 to 160 mg.

37. (New) The oral preparation of claim 25, wherein a content of lurasidone per tablet is 20 to 120 mg.

38. (New) The oral preparation of claim 25, wherein a content of lurasidone per tablet is 20 to 160 mg.

39. (New) The oral preparation of claim 25, wherein a content of lurasidone per tablet is 40 to 120 mg.

40. (New) The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40% (wt/wt) and the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation.

41. (New) The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40%, the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 20 to 120 mg.

42. (New) The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40%, the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 40 to 120 mg.

43. (New) The oral preparation of claim 25, wherein a pregelatinizing ratio of the pregelatinized starch is 50 to 95%.

44. (New) The oral preparation of claim 25, wherein a 50% by volume particle size of lurasidone is 0.1 to 8 μm.

45. (New) The oral preparation of claim 25, wherein the pregelatinized starch contains water soluble matter of 30% or less.

46. (New) The oral preparation of claim 25, further comprising a disintegrant wherein a content of the disintegrant per tablet is 0.5 to 5% (wt/wt).

47. (New) The oral preparation of claim 25, further comprising a disintegrant wherein

a content of the disintegrant per tablet is 0.5 to 5% (wt/wt);

a content of lurasidone in the preparation is 20 to 40%;

the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation;

a content of lurasidone per tablet is 40 to 120 mg;

a pregelatinizing ratio of the pregelatinized starch is 50 to 95%;

50% by volume particle size of lurasidone is 0.1 to 8 μm;

the pregelatinized starch contains water soluble matter of 30% or less;

the water-soluble excipient is mannitol or lactose, and a content of the water-soluble excipient per tablet is 30 to 60% (wt/wt);

the water-soluble polymer binder is hydroxypropyl methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone or hydroxypropylcellulose; and

a content of the water-soluble polymer binder per tablet is 0.5 to 10% (wt/wt).

48. (New) The oral preparation of either one of claim 46 or 47, wherein the disintegrant is one or more selected from the group of com starch, crystalline cellulose, low substituted hydroxypropylcellulose, carmellose, carmellose calcium, carmellose sodium, croscarmellose sodium, carboxymethyl starch sodium and crospovidone.

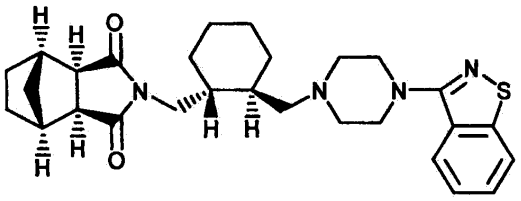
49. (New) The oral preparation of claim 25, wherein a similarity factor f2 of each preparation is in the range of $50 \leq f2 \leq 100$ when a content of lurasidone per tablet changes over a range of 20 to 120 mg.

50. (New) The oral preparation of claim 25, further comprising a lubricant, wherein a content of the lubricant per tablet is 1.0% (wt/wt) to 1.43% (wt/wt).

51. (New) The oral preparation of claim 50, wherein the lubricant is selected from the group of magnesium stearate, talc, polyethylene glycol, silica and hydrogenated vegetable oil.

52. (New) The oral preparation of claim 25, wherein the oral preparation is a tablet.

53. (New) An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of the formula (1):



(1),

a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder, wherein the oral preparation contains 20 to 45% (wt/wt) of lurasidone, the oral preparation contains 20 mg to 120 mg of lurasidone, the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the oral preparation, and the oral preparation exhibits an equivalent dissolution profile across the range of lurasidone per oral preparation.

54. (New) An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone), a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder, wherein a content of lurasidone in the preparation is 20 to 40% (wt/wt),

the content of pregelatinized starch in the preparation is 10 to 40% (wt/wt),

the water-soluble excipient is mannitol or lactose, and

the water-soluble polymer binder is one or more agents selected from the group of hydroxypropylcellulose, hydroxypropylmethylcellulose, polyvinylpyrrolidone and polyvinyl alcohol.

55. (New) An oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone), a pregelatinized starch, a water-soluble excipient and a water-soluble polymer binder, and further comprises a disintegrant and a lubricant, wherein the content of lurasidone in the preparation is 20 to 40% (wt/wt),

the content of pregelatinized starch in the preparation is 10 to 30% (wt/wt),

the water-soluble excipient is mannitol,

the water-soluble polymer binder is hydroxypropylmethylcellulose, and

the oral preparation is a tablet.

56. (New) A method for preparing of the oral preparation of claim 25, wherein the method comprises granulation of a powder mixture which comprises granulating a

powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by using a solution of a water-soluble polymer binder.

57. (New) A method for preparing of the oral preparation of claim 25, wherein the method comprises granulation of a powder mixture which comprises granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by using a solution or dispersion of lurasidone and a water-soluble polymer binder.

58. (New) A method of treating psychosis, comprising administering the oral preparation of claim 25, to a patient suffering from psychosis.

59. (New) A method of treating schizophrenia, comprising administering the oral preparation of claim 25, to a patient suffering from schizophrenia.

Par Pharm., Inc.
Exhibit 1013
Page 077

REMARKS

I. Status of Claims

Following entry of the Amendment, claims 25-59 will be pending. Original claims 1-24 are canceled, and claims 25-59 are added herein. The specification, *e.g.*, ¶¶ [0040] to [0043], [0044], [0046], [0047], [0098], [0149] (formulations RP-03320 and RP-03322), and [0150] of U.S. Patent Application Publication No. 2009/0143404 A1 ("the '404 publication"), which is the publication of the present application, and original claims 2-8, 10, 12-14, 35, and 36, provide written description support for the new claims. Specifically, the lower limit, i.e. 1.0%, of new claim 50 is calculated from formulation RP-03322 in Table 36 in paragraph [0149] of the '404 publication, where the formulation contains 2 mg of magnesium stearate and the total amount of the formulation is 200 mg (2 mg/200 mg x 100 = 1.0%); similarly, the upper limit, i.e. 1.43% of new claim 50, is calculated from formulation RP-03320 in Table 36 in paragraph [0149] of the '404 publication, where the formulation contains 4 mg of magnesium stearate and the total amount of the formulation is 280 mg (4 mg/280 mg x 100 = 1.43%). Accordingly, no new matter is added by the amendments provided herein. Entry of the amendments is respectfully requested.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: October 14, 2014

By: Charles E Van Horn

Charles E. Van Horn
Reg. No. 40,266
(202) 408-4000

Electronic Acknowledgement Receipt	
EFS ID:	20410225
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	14-OCT-2014
Filing Date:	
Time Stamp:	15:57:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		PreliminaryAmendment.pdf	305000 c8607ab63941ea893e4aa90255b6d16852ef3dd9	yes	11

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Preliminary Amendment	1	1
	Specification	2	2
	Claims	3	9
	Applicant Arguments/Remarks Made in an Amendment	10	11
Warnings:			
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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/512,189	Filing Date 10/10/2014	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)		
	10/14/2014	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
AMENDMENT	Total (37 CFR 1.16(i))	* 36	Minus	** 36	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 4	Minus	***4	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	**0**

		(Column 1)		(Column 2)	(Column 3)		
		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
AMENDMENT	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/BRENDA HINES/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

MULTIPLE DEPENDENT CLAIM FEE CALCULATION SHEET

Substitute for Form PTO-1360
(For use with Form PTO/SB/06)

Application Number	Filing Date
14512189	

Applicant(s) Kazuyuki FUJIHARA

* May be used for additional claims or amendments

CLAIMS	AS FILED		AFTER FIRST AMENDMENT		AFTER SECOND AMENDMENT	
	Indep	Depend	Indep	Depend	Indep	Depend
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48				2		
49				1		
50				1		
Total Indep	0		4		0	
Total Depend	0	↵	32	↵	0	↵
Total Claims	0		36		0	

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	Indep	Depend	Indep	Depend	Indep	Depend
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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
14/512,189	10/10/2014	1615	4220	05273.0147-02000	35	4

CONFIRMATION NO. 5575

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

FILING RECEIPT

OC000000071411317

Date Mailed: 10/20/2014

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Kazuyuki FUJIHARA, Suzuka-shi, JAPAN;

Applicant(s)

SUMITOMO DAINIPPON PHARMA CO., LTD, Osaka, JAPAN

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/183,283 02/18/2014
which is a CON of 11/919,678 10/31/2007 PAT 8729085
which is a 371 of PCT/JP2006/310571 05/26/2006

Foreign Applications (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.)
JAPAN 2005-153508 05/26/2005

Permission to Access - A proper **Authorization to Permit Access to Application by Participating Offices** (PTO/SB/39 or its equivalent) has been received by the USPTO.

Request to Retrieve - This application either claims priority to one or more applications filed in an intellectual property Office that participates in the Priority Document Exchange (PDX) program or contains a proper **Request to Retrieve Electronic Priority Application(s)** (PTO/SB/38 or its equivalent). Consequently, the USPTO will attempt to electronically retrieve these priority documents.

If Required, Foreign Filing License Granted: 10/16/2014

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/512,189**

Projected Publication Date: To Be Determined - pending completion of Corrected Papers

Non-Publication Request: No

Early Publication Request: No
Title

PHARMACEUTICAL COMPOSITION

Preliminary Class

424

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

Par Pharm., Inc.
Exhibit 1013
Page 087

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 14/512,189

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	280
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	600
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	720
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	* 16			OR	x 80 =	1280
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1				x 420 =	420
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							780
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	4080

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000

CONFIRMATION NO. 5575

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

FORMALITIES LETTER

OC000000071411318

Date Mailed: 10/20/2014

NOTICE TO FILE CORRECTED APPLICATION PAPERS

Filing Date Granted

An application number and filing date have been accorded to this application. The application is informal since it does not comply with the regulations for the reason(s) indicated below. Applicant is given TWO MONTHS from the date of this Notice within which to correct the informalities indicated below. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
  - The drawings must be reasonably free from erasures and must be free from alterations, overwriting, interlineations, folds, and copy marks. See Figure(s) 3.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

Par Pharm., Inc.
Exhibit 1013
Page 090

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice". https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

/mgabre/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Par Pharm., Inc.
Exhibit 1013
Page 091

MULTIPLE DEPENDENT CLAIM FEE CALCULATION SHEET

Substitute for Form PTO-1360
(For use with Form PTO/SB/06)

Application Number	Filing Date
14512189	

Applicant(s) Kazuyuki FUJIHARA

* May be used for additional claims or amendments

CLAIMS	AS FILED		AFTER FIRST AMENDMENT		AFTER SECOND AMENDMENT	
	Indep	Depend	Indep	Depend	Indep	Depend
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50				1		
Total Indep	0		4		0	
Total Depend	0	↵	32	↵	0	↵
Total Claims	0		36		0	

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	Indep	Depend	Indep	Depend	Indep	Depend
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PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Kazuyuki FUJIHARA	Group Art Unit: 1615
Application No.: 14/512,189	Examiner: *To Be Assigned*
Filed: October 10, 2014	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicant brings to the attention of the Examiner the documents on the attached listing. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

The listed documents are of record in prior Application No. 14/183,283, filing date February 18, 2014, upon which Applicant relies for the benefits provided in 35 U.S.C. § 120. Accordingly copies are not enclosed.

Applicant respectfully requests that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicant determines that the cited document(s) do not constitute

"prior art" under United States law, Applicant reserves the right to present to the U.S. Patent and Trademark Office the relevant facts and law regarding the appropriate status of such documents.

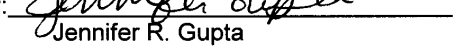
Applicant further reserves the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 12, 2014

By: 
Jennifer R. Gupta
Reg. No. 54,257
(202) 408-4000

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1615
				Examiner Name	To Be Assigned
Sheet	1	of	2	Attorney Docket Number	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-4,600,579	07-15-1986	Salpekar et al.	
		US-5,532,372	07-02-1996	Saji et al.	
		US-2004/0028741 A1	02-12-2004	Fujihara	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] Number[4] Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[6]
		EP 1327440 A1	07-16-2003	Sumitomo Pharmaceuticals Company, Limited		
		JP 08-325146	12-10-1996	Kyowa Hakko Kogyo Co. Ltd.		Abs
		JP 2000-26292	01-25-2000	Kissei Pharmaceutical Co., Ltd.		Abs
		WO 2004/078173 A1	09-16-2004	Shionogi & Co., Ltd.		Abs
		WO 01/76557 A1	10-18-2001	Sumitomo Pharma et al.		
		WO 02/24166 A1	03-28-2002	Sumitomo Pharmaceuticals Company, Limited		Abs

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[6]
		Request for Invalidation from invalidity proceedings in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation), August 5, 2012.	Yes
		Bi Dianzhou, Pharmaceutics, Edition 4, Beijing: People's Medical Publishing House, February 2003.	Yes
		"Application and Effect of Pregelatinized Starch in Tablets," Chinese Pharmaceutical Information, Vol.16, Issue 7, 2000, published in 2000	Yes
		"Use of Pregelatinized Starch in Tablet Manufacturing," Chinese Pharmaceutical Journal, Vol. 29, Issue 4, April 1994, published in April 1994.	Yes
		"Application of the Pregelatinized Starch in Capsules," Chinese Journal of Modern Applied Pharmacy, Vol. 8, Issue 1, February 1991, published in February 1991	Yes
		"*In Vitro* Dissolution and Bioavailability of Acyclovir Capsules Formulated with Pregelatinized Starch," Chinese Journal of Pharmaceuticals, 1998, 29(5), published on May 20, 1998.	Yes
		Dissolution of Drug Solid Preparation, "Factors Influencing Dissolution Rates," Wu Guangchen, Yue Zhiwei, People's Medical Publishing House, published in October 1994.	Yes
		Reply Brief from invalidity proceedings in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation),	Yes

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1615
				Examiner Name	To Be Assigned
Sheet	2	of	2	*Attorney Docket Number*	05273.0147-02000

NONPATENT LITERATURE DOCUMENTS			
		October 25, 2012.	
		Examination Decision on the Request for Invalidation in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation), April 26, 2013.	Yes
		EPO Communication dated Feb.1, 2012, with enclosed Supplemental Search Report, in EPO Appln. 11181100.6	
		Kibbe, Handbook of Pharmaceutical Excipients, Chapter 7, pp. 528-530 (2000)	
		Handbook of Pharmaceutical Excipients, 2nd edition, Vol. 491, The Pharmaceutical Press, 1994.	
		Chueshov, V. 1., et al., "Manufacturing Technologies of Drugs," Promyshlennaya Technologiya Lekarstv, Vol. 2, pp 10-11 (1999).	partial
		Russian Official Action (2009).	partial
		Makino, T., et al., "Importance of Gelatinization Degree of Starch Past Binder in Hardness and Disintegration Time of Tablets," Chem. Pharm. Bull., Vol. 43, No 3, pp 514-116 (1995).	

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PTO Notes regarding this form:

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[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.
[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).
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[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
[6] Applicant is to place a check mark here if English language Translation is attached.

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Electronic Acknowledgement Receipt	
EFS ID:	20678644
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	12-NOV-2014
Filing Date:	10-OCT-2014
Time Stamp:	16:49:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	RspnsToNotToFileCorrApplnPprs.pdf	35594 e7bdc6f3970a37da5fc30580a22f296e3db2891d	no	1
Warnings:					
Information:					

2	Drawings-only black and white line drawings	ReplacementSheets.pdf	1170033 6b5a73caa9f21dd5795f96b815fb6566278e198b	no	3
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	IDS-SB08.pdf	188837 a6a39daa6efb0aab9e858841e77c1d9b7fbbf09e	no	5
Warnings:					
Information:					
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			Total Files Size (in bytes):	1394464	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)
Kazuyuki FUJIHARA	) Group Art Unit: 1615
Application No.: 14/512,189	) Examiner: *To Be Assigned*
Filed: October 10, 2014	)
For: PHARMACEUTICAL COMPOSITION	) Confirmation No.: 5575
	) **VIA EFS-WEB**

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

RESPONSE TO NOTICE TO FILE CORRECTED APPLICATION PAPERS

In response to the Notice to File Corrected Application Papers mailed October 20, 2014, Applicant submits herewith Replacement Sheets consisting of clean drawings (3 sheets, Figures 1-3), in compliance with 37 C.F.R. §§ 1.84 and 1.121(d).

Please replace the drawings with the attached Replacement Sheets, grant any extensions of time required to enter this response, and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 12, 2014

By: Jennifer Gupta
Jennifer R. Gupta
Reg. No. 54,257
202-408-4000

Figure 1

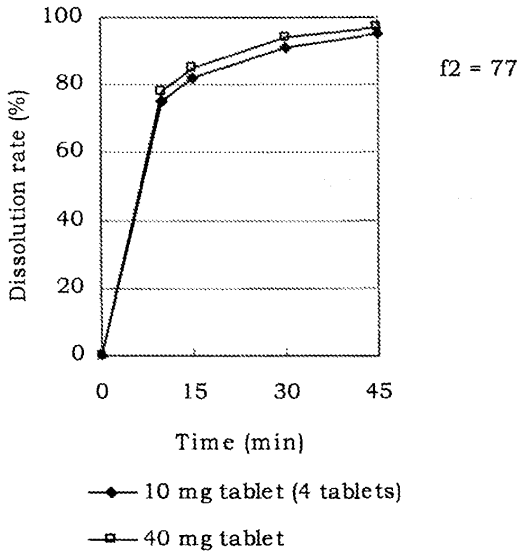

100
80
60
40
20
0
Dissolution rate (%)
0
15
30
45
Time (min)
f2 = 77
10 mg tablet (4 tablets)
40 mg tablet

Figure 2

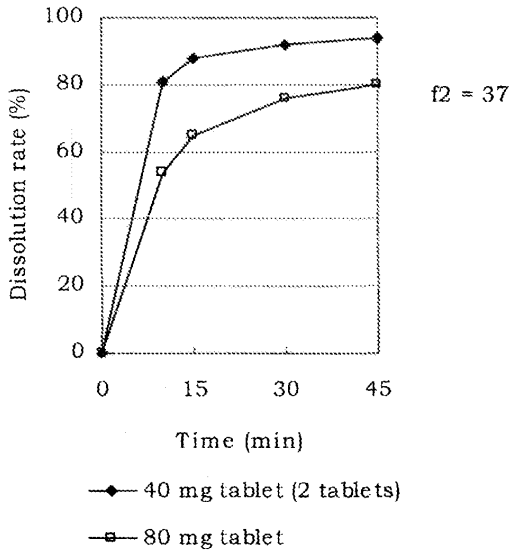
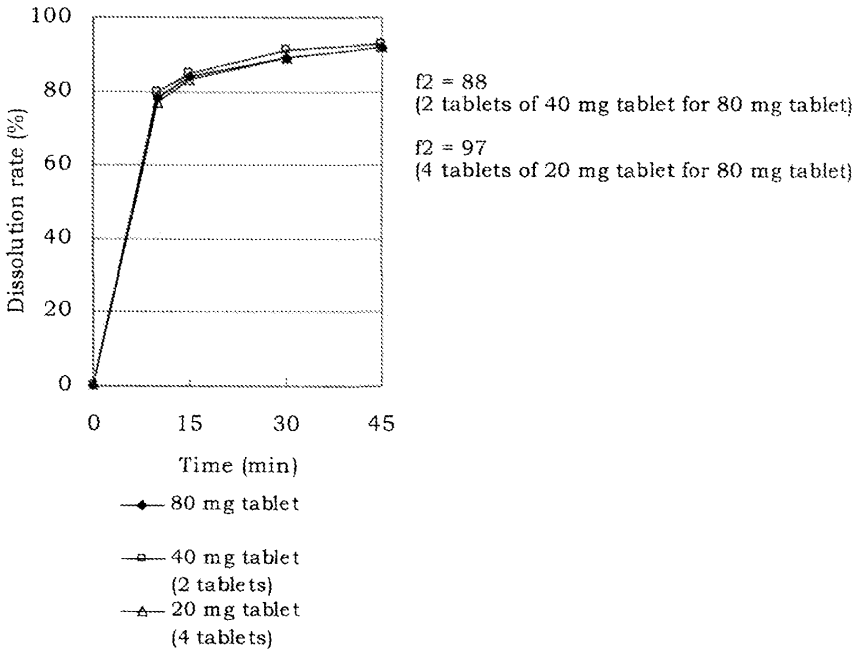

100
80
60
40
20
0
Dissolution rate (%)
0
15
30
45
Time (min)
f2 = 37
40 mg tablet (2 tablets)
80 mg tablet

Figure 3


100
80
60
40
20
0
Dissolution rate (%)
0
15
30
45
Time (min)
80 mg tablet
40 mg tablet
(2 tablets)
20 mg tablet
(4 tablets)
f2 = 88
(2 tablets of 40 mg tablet for 80 mg tablet)
f2 = 97
(4 tablets of 20 mg tablet for 80 mg tablet)

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
14/512,189	10/10/2014	1615	4220	05273.0147-02000	35	4

CONFIRMATION NO. 5575

UPDATED FILING RECEIPT

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

OC00000071904071

Date Mailed: 11/20/2014

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Kazuyuki FUJIHARA, Suzuka-shi, JAPAN;

Applicant(s)

SUMITOMO DAINIPPON PHARMA CO., LTD, Osaka, JAPAN

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/183,283 02/18/2014 PAT 8883794
which is a CON of 11/919,678 10/31/2007 PAT 8729085
which is a 371 of PCT/JP2006/310571 05/26/2006

Foreign Applications (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.)
JAPAN 2005-153508 05/26/2005

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If Required, Foreign Filing License Granted: 10/16/2014

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/512,189**

Projected Publication Date: 02/26/2015

Non-Publication Request: No

Early Publication Request: No
Title

PHARMACEUTICAL COMPOSITION

Preliminary Class

424

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 14/512,189

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	280
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	600
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	720
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	* 16			OR	x 80 =	1280
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1				x 420 =	420
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							780
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	4080

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
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出 願 年 月 日 Date of Application:	２００５年　５月２６日
出 願 番 号 Application Number:	特願２００５－１５３５０８
パリ条約による外国への出願に用いる優先権の主張の基礎となる出願の国コードと出願番号 The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is	ＪＰ２００５－１５３５０８
出 願 人 Applicant(s):	大日本住友製薬株式会社

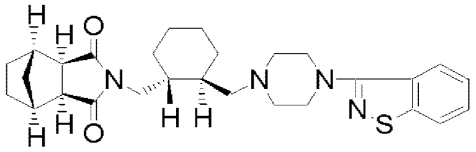
２０１４年１１月２５日

特許庁長官
Commissioner,
Japan Patent Office

伊藤 仁

【書類名】　特許願
【整理番号】　133348
【あて先】　特許庁長官殿
【国際特許分類】　A61K 31/495
【発明者】
　【住所又は居所】　大阪府茨木市蔵垣内１丁目３番４５号　住友製薬株式会社内
　【氏名】　富士原　和之
【特許出願人】
　【識別番号】　000183370
　【氏名又は名称】　住友製薬株式会社
【代理人】
　【識別番号】　100121588
　【弁理士】
　【氏名又は名称】　五十部　穣
　【電話番号】　06-6466-5214
【手数料の表示】
　【予納台帳番号】　056546
　【納付金額】　16,000円
【提出物件の目録】
　【物件名】　特許請求の範囲　1
　【物件名】　明細書　1
　【物件名】　図面　1
　【物件名】　要約書　1
　【包括委任状番号】　0205876

【書類名】特許請求の範囲
【請求項１】
式（１）
【化１】



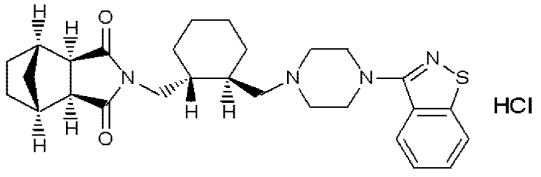
・HCl　(1)

で表されるＮ－[４－〔４－(１,２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ,３Ｒ)－２,３－テトラメチレン－ブチル]－(１'Ｒ,２'Ｓ,３'Ｒ,４'Ｓ)－２,３－ビシクロ〔２,２,１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）、アルファ化デンプン類、水溶性賦形剤、水溶性高分子結合剤を含有する経口製剤。
【請求項２】
ルラシドン・塩酸塩、アルファ化デンプン類及び水溶性賦形剤を含む混合末を、水溶性高分子結合剤を溶解した溶液を用いて造粒した経口製剤。
【請求項３】
アルファ化デンプン類及び水溶性賦形剤を含む混合末を、ルラシドン・塩酸塩及び水溶性高分子結合剤を溶解又は分散した液により、造粒した経口製剤。
【請求項４】
水溶性賦形剤がマンニトールもしくは乳糖である請求項１～３いずれか記載の経口製剤。
【請求項５】
ルラシドン・塩酸塩、アルファ化デンプン類及び水溶性賦形剤を含む混合末を、水溶性高分子結合剤を溶解した溶液を用いることにより造粒する方法。
【請求項６】
アルファ化デンプン類及び水溶性賦形剤を含む混合末を、ルラシドン・塩酸塩及び水溶性高分子結合剤を溶解又は分散した液を用いることにより造粒する方法。
【請求項７】
水溶性賦形剤がマンニトールもしくは乳糖である請求項５記載の造粒方法。
【請求項８】
アルファ化デンプン類の配合量が製剤重量に対して１０～５０％（ｗｔ／ｗｔ）である請求項１から４記載の経口製剤。
【請求項９】
アルファ化デンプン類の配合量が製剤重量に対して２０～３０％（ｗｔ／ｗｔ）である請求項１から４記載の経口製剤。
【請求項１０】
製剤中のルラシドン・塩酸塩含有量が、２０～４０％（ｗｔ／ｗｔ）である請求項１から４いずれか記載の経口製剤。
【請求項１１】
ルラシドン・塩酸塩の１錠中の含量が、１０～１２０㎎である請求項１から４いずれか記載の経口製剤。
【請求項１２】
アルファ化デンプン類のアルファ化率が５０～９５％である請求項１から４いずれか記載の経口製剤。
【請求項１３】
ルラシドン・塩酸塩の平均粒子径が０．１～８μｍである請求項１から４いずれか記載の経口製剤。
【請求項１４】
アルファ化デンプン類中の水可溶分が、２０％以下である請求項１から４いずれか記載の

経口製剤

【書類名】明細書
【発明の名称】医薬品組成物
【技術分野】
【０００１】
本発明は、Ｎ－［４－〔４－(１，２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ，３Ｒ)－２，３－テトラメチレン－ブチル]－(１’Ｒ，２’Ｓ，３’Ｒ，４’Ｓ)－２，３－ビシクロ〔２，２，１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）を有効成分とする崩壊性が良好な経口製剤に関する。詳しくはルラシドン・塩酸塩を有効成分とする経口製剤において、有効成分の含量が変動しても、同等の溶出挙動を示す経口投与用製剤、特に錠剤に関する。
【背景技術】
【０００２】
特許文献１には、ルラシドン・塩酸塩等の化合物について、経口的に投与することができること、また通常の担体・賦形剤・結合剤・安定剤等と有効成分とを配合することにより製造できることの記載はあるが、該有効成分の含量が広い範囲で異なっても速溶解性を示し、かつ、同等の溶出挙動を示す経口用の製剤、とくに有効成分の含量を増大した場合に低含量の製剤の複数錠と同様の溶出挙動を示す経口製剤に関する記載はない。
【０００３】
含量が異なる製剤を同一用量服用したときの生物学的同等性を保証することを目的として医薬審第６４号(平成１２年２月１４日公布)にて『含量が異なる経口固形製剤の生物学的同等性試験ガイドライン』が示され、含量が異なる製剤において、胃、腸および口腔内の各ｐＨ値に対応するｐＨ１．２、３．０～５．０および６．８の緩衝液、水、生理食塩水などの各試験液で同等の溶出挙動を示すことが求められるようになった。
【０００４】
ルラシドン・塩酸塩を有効成分とする薬剤について、該有効成分の含量が異なっても速溶解性を示し、かつ、同等の溶出挙動を示す経口製剤、とくに有効成分の含量を増大した場合に低含量の製剤の複数錠と同様の溶出挙動を示し、水難溶性の有効成分を所望の濃度に放出し得る経口製剤については特許文献２に開示されている。
【０００５】
特許文献２には有効成分の含量が数ｍｇ～数十ｍｇの範囲、例えば５ｍｇ～２０ｍｇまたは５ｍｇ～４０ｍｇの範囲、で変動しても、速溶解性を示し、かつ、同一組成比において同等の溶出挙動を示す経口製剤、特に錠剤が開示されている。経口製剤においては、より高い臨床効果を得るためにさらに高い含量の製剤、又は患者の症状に応じて臨床効果を調節するためにより広い含量範囲で、複数錠と同様の挙動を示し、有効成分を所望の濃度に放出し得る製剤が必要とされる場合が多い。特許文献２の開示技術では図１に示すようにルラシドン・塩酸塩が１錠あたり５ｍｇから４０ｍｇまでは同等の溶出挙動を示す経口製剤を提供することができる。しかしながら、図２に示すように、製剤中の有効成分の含有率を２倍にすることにより一錠中の有効成分の含有量を増やした場合、８０ｍｇ錠では同等の溶出挙動を示すことができなかった。従って、複数錠を一度に服用するか、服用に困難な大きさの錠剤にせざるを得ない状況であった。よって、水難溶性の有効成分であるルラシドン・塩酸塩については、高含量の経口製剤あるいはさらに広い範囲で溶出挙動が同等な経口製剤の提供は困難であった。
【０００６】
また、特許文献２には水溶性高分子結合剤としてデンプンが挙げられているが、アルファ化デンプンについての記載はない。アルファ化デンプンは、例えば、特許文献３に記載されているように、医薬品組成物の崩壊性及び溶出性が顕著に改善することが知られているが、医薬品に採用されることは必ずしも多くはない。崩壊剤として使用される場合、非特許文献１の中でも記述されるように通常、１０％以下の含有量で用いられることが多い。
【０００７】

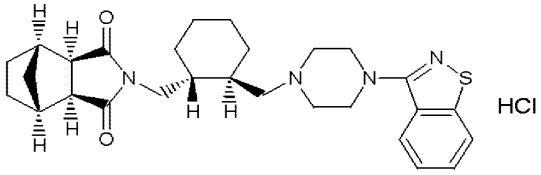
【特許文献１】特許第２８００９５３
【特許文献２】ＷＯ２００２／０２４１６６
【特許文献３】特開２０００－２６２９２
【非特許文献１】Handbook of Pharmaceutical Excipients, 2nd edition, 491, 1994, The Pharmaceutical Press
【発明の開示】
【発明が解決しようとする課題】
【０００８】
本発明の目的は、ルラシドン・塩酸塩を有効成分とし、該有効成分の含量が広い範囲で異なっても速溶解性を示し、かつ、同等の溶出挙動を示す経口用の製剤、とくに有効成分の含量を増大した場合に低含量の製剤の複数錠と同様の溶出挙動を示し、有効成分を所望の濃度に放出し得る経口製剤を提供することにある。
【０００９】
Ｎ－[４－〔４－(１,２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ,３Ｒ)－２,３－テトラメチレン－ブチル]－(１'Ｒ,２'Ｓ,３'Ｒ,４'Ｓ)－２,３－ビシクロ〔２,２,１〕ヘプタンジカルボキシイミド・塩酸塩（以下、ルラシドン・塩酸塩）を有効成分とする経口製剤において、有効成分の含量が変動しても、同等の溶出挙動を示す経口投与用製剤の提供することを目的とする。
【課題を解決するための手段】
【００１０】
本発明者らは、前記課題を解決するために鋭意検討したところ、以下の手段により当該課題を解決することを見いだすに至った。
【００１１】
すなわち、本発明は、以下の通りである。
（１）式（１）
【００１２】
【化１】



(1)

で表されるＮ－[４－〔４－(１,２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ,３Ｒ)－２,３－テトラメチレン－ブチル]－(１'Ｒ,２'Ｓ,３'Ｒ,４'Ｓ)－２,３－ビシクロ〔２,２,１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）、アルファ化デンプン類、水溶性賦形剤、水溶性高分子結合剤を含有する経口製剤。
（２）ルラシドン・塩酸塩、アルファ化デンプン類及び水溶性賦形剤を含む混合末を、水溶性高分子結合剤を溶解した溶液を用いて造粒した経口製剤。
（３）アルファ化デンプン類及び水溶性賦形剤を含む混合末を、ルラシドン・塩酸塩及び水溶性高分子結合剤を溶解又は分散した液により、造粒した経口製剤。
（４）水溶性賦形剤がマンニトールもしくは乳糖である（１）～（３）いずれか記載の経口製剤。
（５）ルラシドン・塩酸塩、アルファ化デンプン類及び水溶性賦形剤を含む混合末を、水溶性高分子結合剤を溶解した溶液を用いることにより造粒する方法。
（６）アルファ化デンプン類及び水溶性賦形剤を含む混合末を、ルラシドン・塩酸塩及び水溶性高分子結合剤を溶解又は分散した液を用いることにより造粒する方法。
（７）水溶性賦形剤がマンニトールもしくは乳糖である（５）記載の造粒方法。
（８）アルファ化デンプン類の配合量が製剤重量に対して１０～５０％（ｗｔ／ｗｔ）である（１）から（４）いずれか記載の経口製剤。

（９）アルファ化デンプン類の配合量が製剤重量に対して２０～３０％（ｗｔ／ｗｔ）である（１）から（４）いずれか記載の経口製剤。
（１０）製剤中のルラシドン・塩酸塩含有量が、２０～４０％（ｗｔ／ｗｔ）である（１）から（４）いずれか記載の経口製剤。
（１１）ルラシドン・塩酸塩の１錠中の含量が、１０～１２０mgである（１）から（４）いずれか記載の経口製剤。
（１２）アルファ化デンプン類のアルファ化率が５０～９５％である（１）から（４）いずれか記載の経口製剤。
（１３）ルラシドン・塩酸塩の平均粒子径が０．１～８μｍである（１）から（４）いずれか記載の経口製剤。
（１４）アルファ化デンプン類中の水可溶分が、２０％以下である（１）から（４）いずれか記載の経口製剤
【発明の効果】
【００１３】
本発明によりルラシドン・塩酸塩を有効成分とする崩壊性が良好な経口製剤において、ルラシドン・塩酸塩を高含有量含む経口製剤の提供が、また有効成分の含量が変動しても同等の溶出挙動を示す経口投与用製剤を提供することが可能となった。また、配合変化を起こさず、長期保存性にも優れている。
【発明を実施するための最良の形態】
【００１４】
Ｎ－[４－〔４－(１,２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ,３Ｒ)－２,３－テトラメチレン－ブチル]－(１'Ｒ,２'Ｓ,３'Ｒ,４'Ｓ)－２,３－ビシクロ〔２,２,１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）は下記式：
【００１５】
【化２】



(1)

で示される化合物である(特許第２８００９５３号参照)。ルラシドン・塩酸塩は向精神病作用を持つことが知られており、統合失調症等の治療薬として有効である。本化合物の配合量としては、錠剤全重量に基づいて、例えば、１０～５０重量%の範囲、好ましくは２０～４０重量%の範囲から選択される。更に、微粉砕されていることが好ましく、例えば体積比９０％以上の粒子が２７μm以下であり、体積比による平均粒子径としては例えば、０.１～８μｍの範囲が挙げられる。好ましくは、１～６μｍの範囲が挙げられる。１錠中に含まれるルラシドン・塩酸塩の含量としては、１０－１２０ｍｇ、好ましくは２０－８０ｍｇが挙げられる。
【００１６】
「アルファ化デンプン類」とは例えばトウモロコシデンプン、バレイショデンプン、コムギデンプン、コメデンプン、タピオカデンプン等各種デンプン類をアルファ化したものであり、このようなものとしては例えば医薬品添加物規格にあるアルファ化デンプン（英語名：Pregelatinized Starch）又は部分アルファ化デンプン（英語名：Partly Pregelatinized Starch）等を挙げることができる。アルファ化デンプン類のアルファ化率は、例えば５０～１００％、好ましくは５０～９５％、さらに好ましくは８０～９５％である。更に、アルファ化デンプン類中の水可溶分は、例えば２０％以下、より好ましくは５％以下である。これらアルファ化デンプン類は、通常、平均粒径が１～１０００μｍ、好ましくは１～５００μｍ、さらに好ましくは１０～１００μｍの粉末が用いられる。本発明に

適する市販のアルファ化デンプン類としては、例えばＰＣＳ（商品名、旭化成工業株式会社製）又はスターチ１５００（商品名、カラコン）等の部分アルファ化デンプンが挙げられる。上記アルファ化デンプン類の中でも部分アルファ化デンプン、例えばＰＣＳ（商品名、旭化成工業株式会社製）が好ましく用いられる。部分アルファ化デンプンのアルファ化率は、好ましくは５０～９５％、さらに好ましくは８０～９５％である。本発明において用いられるアルファ化デンプン類は、製剤重量に対して１０％以上５０％以下であり、好ましくは１０％以上３０％以下であり、特に好ましくは、２０％以上３０％以下である。

【００１７】

「水溶性賦形剤」としては、例えばマンニトール、乳糖、白糖、ソルビトール、Ｄ－ソルビトール、エリスリトール、キシリトール等が挙げられる。より好ましいものとしてはマンニトール及び乳糖が挙げられる。さらに好ましくはマンニトールを挙げることができる。また、該水溶性賦形剤は、１種または同時に２種以上を使用することができる。水溶性賦形剤の配合量としては、錠剤全重量に基づいて、例えば、３０～８０重量％の範囲、好ましくは４０～６０重量％の範囲から選択される。また、マンニトールの平均粒子径としては、例えば１０～２００μｍの範囲が挙げられる。

【００１８】

「水溶性高分子結合剤」としては、例えば、ヒドロキシプロピルセルロース、ヒドロキシプロピルメチルセルロース、ポリビニルピロリドン、ポリビニルアルコール等が挙げられる。より好ましいものとしては、ヒドロキシプロピルセルロース、ヒドロキシプロピルメチルセルロース、ポリビニルピロリドン、ポリビニルアルコールが挙げられる。該水溶性高分子結合剤は、これらの１種または同時に２種類以上を用いることができる。水溶性高分子結合剤の配合量としては錠剤全重量に基づいて、例えば、０．５～１０重量％の範囲、好ましくは１～５重量％の範囲から選択される。

本発明の医薬品組成物から成る経口製剤は、錠剤、カプセル剤、顆粒剤、細粒剤に製剤化されるものをいう。慣用手段によって、水溶性賦形剤に加えて非水溶性賦形剤、結合剤、崩壊剤、滑沢剤、等を使用して、錠剤、カプセル剤、顆粒剤、細粒剤に製剤化されるものであってもよい。また、以下のものを加えることもできる。

【００１９】

「非水溶性賦形剤」としては、例えばコーンスターチ、結晶セルロース等が挙げられる。また、１種または同時に２種以上を使用することができる。

【００２０】

「崩壊剤」としては、例えば、コーンスターチ、結晶セルロース、低置換度ヒドロキシプロピルセルロース、カルメロース、カルメロースカルシウム、カルメロースナトリウム、クロスカルメロースナトリウム、カルボキシメチルスターチナトリウム、クロスポビドン等が挙げられる。該崩壊剤は、１種または同時に２種以上を使用することができる。該崩壊剤の平均粒子径としては、例えば、５～７５μｍの範囲のものが挙げられ、好ましくは５～７５μｍの範囲の平均粒子径を有し、７５μｍを越える粒子が全体の５％以下であることが望ましい。崩壊剤の配合量としては、錠剤全重量に基づいて、例えば、０～１０重量％の範囲、好ましくは０．５～５重量％の範囲が挙げられる。

【００２１】

「滑沢剤」としては、例えばステアリン酸マグネシウム、タルク、ポリエチレングリコール、シリカ、硬化植物油等が挙げられる。

【００２２】

本発明の経口製剤の調製は、所望の剤形により異なるが、常法にしたがって所望の剤形にすることができる。

(１)水溶性高分子結合剤の水溶液の調製：

水溶性高分子結合剤を精製水に溶解する。その際の温度としては、例えば、２０℃から９０℃の範囲から選択され、好ましくは、２０℃から７０℃の範囲から選択される。水溶性高分子結合剤の量としては、精製水の量に対し、例えば１～２０重量％の範囲、好まし

くは２～８重量％の範囲から選択される。
（２）ルラシドン・塩酸塩含有造粒物の調製：
ルラシドン・塩酸塩、マンニトール、部分アルファ化デンプンを含む賦形剤および崩壊剤を仕込んだ流動層造粒機に、上記（１）の工程で調製された水溶性高分子結合剤を散布しながら造粒する。

【００２３】
造粒装置としては、例えば、流動層造粒(Fluid Bed Granulation)、高速攪拌造粒(High share granulation)、転動型流動層造粒(Roto Fluid Bed Granulation)等に分類される造粒装置が挙げられる。但し、これらに限定されるものではない。
（３）造粒物の乾燥：
上記造粒物を、減圧または常圧にて乾燥する。この乾燥は、赤外線水分計にて測定される乾燥減量値が、例えば、３重量％以内、好ましくは１～２重量％以内になるように行う。
（４）滑沢剤の配合：
上記（３）で乾燥した造粒物に滑沢剤を加えて混合する。混合は、例えば、攪拌ミキサー[タンブル](Diffusion mixers [Tumble])に分類される混合機が用いられる。具体的には、タンブラーブレンダー(Tumble Blender)、Ｖブレンダー(V Blenders)、ダブルコーン(Double Cone)、ビンタンブラー(Bin Tumble)等が挙げられる。但し、これらに限定されるものではない。
（５）打錠：
上記混合物を打錠して錠剤を調製する。
【００２４】
打錠装置としては、例えば、錠剤プレス(Tablet Press)に分類される打錠機等が挙げられる。打錠硬度としては、例えば３０～２００Ｎ範囲から選択される。
（６）所望によりフィルムコーティングを施す：
上記錠剤には、必要に応じてフィルムコーティングしてもよい。コーティング装置としては、例えばコーティングパンに分類される装置が挙げられる。好ましくは、通気式コーティングシステム(Perforated Coating System)で分類される装置が挙げられる。
【００２５】
コーティング剤としては、例えば、ヒドロキシプロピルメチルセルロース、ヒドロキシプロピルセルロース、ポリビニルピロリドン、ポリビニルアルコール等の基剤と、例えば、ポリエチレングリコール、プロピレングリコール、トリアセチン、クエン酸トリエチル、グリセリン、グリセリン脂肪酸エステル、ポリエチレングリコール等の可塑剤を組み合わせたものが挙げられる。また、必要に応じて、酸化チタン等の添加剤を加え調製することもできる。また、フィルムコーティング後に、光沢化剤としてカルナバロウ等を加えることもできる。
（７）乾燥：
上記のようにして得られた錠剤を乾燥する。乾燥は減圧または常圧で行い、赤外線水分計にて測定される乾燥減量値が、例えば、３重量％以内、好ましくは１～２重量％以内になるように行う。
【００２６】
以下に本発明の実施例を挙げるが、本実施例は本発明を説明するためのものであって、本発明をなんら限定するものではない。
【実施例１】
【００２７】
Ａ．ルラシドン・塩酸塩を８０ｍｇ含有するフィルムコート錠（実施例１）
下記組成からなる顆粒、裸錠およびＦＣ錠を順次調製する。尚、説明文中の括弧内に示す仕込み量は実施例１に示す処方の製剤を調製するための一例を示すものである。
原則としてこの製造方法に準じれば、その他に示す実施例についても調製できる。但し、

仕込み量は処方に基づき変更する必要がある。
【００２８】
Ｂ．製造方法
(１)結合液の調製（５％　ヒドロキシプロピルメチルセルロース水溶液）：
水溶性高分子結合剤のヒドロキシプロピルメチルセルロース(３２ｇ)を精製水(６４０ｇ)に溶解し、これを結合液とした。
(２)造粒：
ルラシドン・塩酸塩（３２０ｇ）、マンニトール(５７６ｇ)、部分アルファ化デンプン（３２０ｇ）、クロスカルメロースナトリウム(１６ｇ)を流動層造粒機(マルチプレックスＭＰ－０１／パウレック製)に仕込み、上記(１)で調製した結合液を用いて、下記条件でスプレー造粒し造粒末を得た。得られた造粒末にステアリン酸マグネシウムを加えて混合後(４０ｒｐｍ、５分)に、処方(ｂ)を有する打錠用顆粒を得た。尚、ステアリン酸マグネシウムの仕込み量は造粒末の収量に基づき処方から算出される量を混合した。
造粒条件
給気温度：６０℃
風量：５０－６５m^3／ｈｒ
スプレー速度：１３ｇ／分
スプレーノズル径：１.２ｍｍ
スプレー圧力：０．１２ＭＰａ
ガン位置：中段
(３)打錠：
上記(２)で調製した打錠用顆粒をHT-AP12SS-II(畑鉄工所)を用いて錠剤を成形した。
杵サイズ：φ１０ｍｍ１４Ｒ
厚み：４．２０～４．３０ｍｍ
打錠圧縮圧力：１０ＫＮ
(４)コーティング：
上記(３)で調製した裸錠をハイコーターＨＣＴ３０Ｎ(フロイント産業)で皮膜量が５ｍｇになるように下記条件でコーティングを行い、コーティング後にカルナバロウを添加しフィルムコート錠を得た。
ＦＣ条件
給気温度　：８０℃
風量　　：０.６m^3／分
パン回転数：２５ｒｐｍ
スプレー圧：０.１５ＭＰａ
液速　　：５ｇ／分
上述の方法により得られた製剤は以下の方法により品質を評価し、そこで得られた知見をもとに本発明を見出すに至った。
【００２９】
Ｃ．品質評価
（１）溶出試験
日本薬局方溶出試験法第２法に従い、試作した製剤の溶出試験を実施した。以下に測定条件を示す。
試験溶液：希釈マックイルベイン緩衝液(diluted McIlvaine buffer、ｐＨ４.０)
パドル回転数：５０ｒｐｍ
試験液：９００ｍｌ
（２）溶出プロファイルの類似性
溶出プロファイルの類似性を評価するための指標としてScale-Up and Past-Approval Changes for Intermediate Release Products(SUPAC-IR)に示される類似因子f2を用いた。f2は以下の式により算出される。SUPAC-IRにより各製剤の溶出率から算出されるf2値が５０≦f2≦１００の範囲にある場合、試作した各製剤は類似の溶出プロファイルであると判

定した。また、f2値の算出に当っては試験開始後１５分、３０分および４５分の３ポイントの時点での溶出率を用いた。

【００３０】

【数１】

$$f2 = 50 \cdot LOG\left[\frac{100}{\sqrt{1+\frac{\sum_{i=1}^{n}(Ti-Ri)^2}{n}}}\right]$$

Ti and Ri are the percent dissolved at each point.
n is the number of points to be compared.

（３）粒度分布

レーザー回折粒度分布測定装置（SLAD-3000/島津製作所）の乾式噴射法にてルラシドン・塩酸塩の粒度分布を測定した。以下に測定条件を示す。

試料量：2g
エアー圧：0.4MPa以上
ターンテーブル回転スピード：2
パラメータ設定
環境設定
モニター平均回数：16
暗測定平均回数　：2
光強度表示最大値：2000
前回のブランク値：読み込み
プリンター：モノクロ
屈折率パラメーター
標準屈折率：1.70-0.20i
測定条件設定
測定回数：1
測定間隔（秒）：1
平均回数：64
測定吸光度範囲（最大値）：0.1
（最小値）：0.05
トリガーモード：OFF
乾式しきい：300
測定最適範囲（最大）　：1500
（最小）　：700
（CH-1）ボーレート(bps)：9600
ブランク測定許容最大値　：300
ブランク測定許容変動範囲：20
乾式許容最小値：300
最大値：2500
評価対象粒子範囲（最小値）：0.1
評価対象粒子範囲（最大値）：2000
センサ使用開始位置：1

【００３１】

＜試験１＞

実施例１、２，３で、１錠中にルラシドン・塩酸塩を２０ｍｇ、４０ｍｇおよび８０ｍｇ含有する水溶性賦形剤、部分アルファ化デンプンおよび水溶性高分子結合剤から成る特定の医薬品組成物を含む錠剤を試作した。また、比較例１、２で、特許文献２の開示処方に基づき１錠中にルラシドン・塩酸塩を４０ｍｇおよび８０ｍｇ含有する錠剤を試作した。

試作した製剤を（ｄ）および（ｅ）に示す条件で溶出試験を実施し、溶出プロファイルの類似性を評価した。なお、比較例１、２の試作については試験８にて示した。

結果は、表４，５に示した。なお、（ｄ）については経時的な溶出率についても図２，３で示した。

【００３２】

（ａ）造粒末の処方

【００３３】

【表１】

単位：ｍｇ

成分	実施例番号			比較例番号	
	1	2	3	1	2
ルラシドン・塩酸塩	80	40	20	40	80
マンニトール	144	72	36	188	148
部分アルファ化デンプン	80	40	20	−	−
クロスカルメロースナトリウム	4	2	1	16	16
ヒドロキシプロピルメチルセルロース	8	4	2	10	10

【００３４】

（ｂ）打錠用顆粒/裸錠の処方

【００３５】

【表２】

単位：ｍｇ

成分	実施例番号			比較例番号	
	1	1	1	1	2
上記（ａ）の顆粒	316	158	79	254	254
乳糖	−	−	−	62	62
ステアリン酸マグネシム	4	2	1	4	4

【００３６】

（ｃ）ＦＣ錠の処方

【００３７】

【表３】

単位：ｍｇ

成分	実施例番号			比較例番号	
	1	2	3	1	2
上記(ｂ)の裸錠	320	160	80	320	320
ヒドロキシプロピルメチルセルロース	3.25	1.95	1.3	2.6	2.6
酸化チタン	1	0.6	0.4	0.8	0.8
ポリエチレングリコール６０００	0.75	0.45	0.3	0.6	0.6
カルナバロウ	0.01	0.006	0.004	0.01	0.01

【００３８】

（ｄ）１ベッセル当りルラシドン・塩酸塩が８０ｍｇとなる系での溶出試験

１ベッセル当りルラシドン・塩酸塩が８０ｍｇとなる系でルラシドン・塩酸塩を８０ｍｇ、４０ｍｇおよび２０ｍｇを含有する各フィルムコート錠の溶出試験を実施し、それぞれの溶出プロファイルの類似性をｆ２値により評価した。

【００３９】

表４から明らかなように、実施例２，３のｆ２値は実施例1に対する類似性を示したが、比較例２のｆ２値は比較例1に対する類似性を示さなかった。即ち、表４，図３から明らかなように、実施例１乃至３は溶出プロファイルの類似性を示すｆ２値が５０≦ｆ２≦１００の範囲となり、含量の異なる製剤においても、錠剤の含量（力価）に依存することなく溶出プロファイルの類似性を示す製剤が得られた。一方、表４，図２から明らかにように、詳細を試験８に記載したが、特許文献２開示処方の比較例２は比較例１からなる製剤２錠の溶出よりも明らかに遅く、溶出プロファイルの類似性は示さなかった。

【００４０】

【表４】

類似因子	実施例番号			比較例番号	
	1	2	3	1	2
ｆ２	－	８８	９７	－	３７

【００４１】

（ｅ）１ベッセル当りルラシドン・塩酸塩が４０ｍｇとなる系での溶出試験

１ベッセル当りルラシドン・塩酸塩が４０ｍｇとなる系でルラシドン・塩酸塩を４０ｍｇおよび２０ｍｇを含有する各フィルムコート錠の溶出試験を実施し、それぞれの溶出プロファイルの類似性を同様にｆ２値を用いて評価した。

【００４２】

表５から明らかなように、実施例３,比較例１のｆ２値は実施例２に対する類似性を示した。即ち、１ベッセル当りルラシドン・塩酸塩が４０ｍｇである系においても、ｆ２値は５０≦ｆ２≦１００の範囲となり、錠剤の含量（力価）に依存することなく溶出プロファイルの類似性が示された。

【００４３】

【表５】

類似因子	実施例番号		比較例番号
	2	3	1
ｆ２	－	８８	９７

【００４４】

＜試験２＞

実施例１および４で、水溶性賦形剤と水溶性高分子結合剤および部分アルファ化デンプンから成る医薬品組成物を含む製剤を調製した。また、比較例３，４および５で、水溶性賦形剤と水溶性高分子結合剤およびアルファ化していないデンプンであるコーンスターチから成る医薬品組成物を含む製剤を調製した。各製剤の溶出試験を実施し、溶出プロファイルの類似性をｆ２値により評価した。結果は、表９に示した。

（ａ）造粒末の処方

【００４５】

【表６】

単位：ｍｇ

成分	実施例番号		比較例番号		
	1	4	3	4	5
ルラシドン・塩酸塩	80	80	80	80	80
マンニトール	144	176	108	108	–
乳糖	–	–	–	–	108
部分アルファ化デンプン	80	40	–	–	–
コーンスターチ	–	–	40	40	40
クロスカルメロースナトリウム	4	8	16	16	16
ヒドロキシプロピルメチルセルロース	8	12	10	10	10

【００４６】

（ｂ）打錠用顆粒/裸錠の処方

【００４７】

【表７】

単位：ｍｇ

成分	実施例番号		比較例番号		
	1	4	3	4	5
上記（ａ）の顆粒	316	316	254	254	254
マンニトール	−	−	62	−	−
ステアリン酸マグネシム	4	4	4	4	4

【００４８】

（ｃ）ＦＣ錠の処方

【００４９】

【表８】

単位：ｍｇ

成分	実施例番号		比較例番号		
	1	4	3	4	5
上記(ｂ)の裸錠	320	320	320	258	258
ヒドロキシプロピルメチルセルロース	3.25	−	2.6	2.6	2.6
酸化チタン	1	−	0.8	0.8	0.8
ポリエチレングリコール６０００	0.75	−	0.6	0.6	0.6

【００５０】

（ｄ）溶出試験

表９から明らかなように、実施例４は実施例１に対する類似性を示したが、比較例３、４、５のｆ２値は実施例１に対して類似性を示さなかった。即ち、比較例３，４および５のコーンスターチを含む製剤は、実施例１および４の部分アルファ化デンプンを含む製剤と比較して、溶出プロファイルが異なり、溶出の遅い製剤であった。

【００５１】

【表９】

類似因子	実施例番号		比較例番号		
	1	4	3	4	5
ｆ２	−	６７	４４	２９	２６

【００５２】

＜試験３＞

実施例４，５，６，７で、部分アルファ化デンプンの配合量の溶出性に及ぼす影響を評価した。結果は表１３に示した。

（ａ）造粒末の処方

【００５３】

【表１０】

単位：ｍｇ

成分	実施例番号				
	1	4	5	6	7
ルラシドン・塩酸塩	80	80	80	80	80
マンニトール	144	176	116	136	156
部分アルファ化デンプン	80	40	100	80	60
クロスカルメロースナトリウム	4	8	8	8	8
ヒドロキシプロピルメチルセルロース	8	12	12	12	12

【００５４】

（ｂ）打錠用顆粒/裸錠の処方

【００５５】
【表１１】

単位：ｍｇ

成分	実施例番号				
	1	4	5	6	7
上記（ａ）の顆粒	316	316	316	316	316
ステアリン酸マグネシム	4	4	4	4	4

【００５６】
（ｃ）ＦＣ錠の処方
【００５７】
【表１２】

単位：ｍｇ

成分	実施例番号				
	1	4	5	6	7
上記（ｂ）の裸錠	320	320	320	320	320
ヒドロキシプロピルメチルセルロース	3.25	−	−	−	−
酸化チタン	1	−	−	−	−
ポリエチレングリコール６０００	0.75	−	−	−	−
カルナバロウ	0.01	−	−	−	−

【００５８】
（ｄ）溶出試験
表１３から明らかなように、実施例４、５、６、７のｆ２値は実施例１に対する類似性を示した。即ち、部分アルファ化デンプンを製剤組成中の１０％wt/wt以上含有する医薬品組成物から成る製剤は、速溶解性を示し、かつ、類似の溶出プロファイルを示した。
【００５９】
【表１３】

類似因子	実施例番号				
	1	4	5	6	7
ｆ２	−	６７	６０	６２	８１

【００６０】
＜試験４＞
比較例６で、水溶性賦形剤と部分アルファ化デンプンを含むが、水溶性高分子結合剤を含まない錠剤の製剤化を試みたが、打錠工程において、キャッピングとスティッキングが発生し打錠できず、類似の溶出プロファイルを得るどころか錠剤すら得られなかった。実施例８，９，１０および１１で、水溶性賦形剤および部分アルファ化デンプンと水溶性高分子結合剤の配合量の異なる医薬品組成物を含む製剤を調製した。結果は、表１７に示した。
（ａ）造粒末の処方
【００６１】

【表１４】

単位：ｍｇ

成分	実施例番号				比較例番号	
	1	8	9	10	11	6
ルラシドン・塩酸塩	80	80	80	80	80	80
マンニトール	144	136	138	140	142	148
部分アルファ化デンプン	80	80	80	80	80	80
クロスカルメロースナトリウム	4	8	8	8	8	8
ヒドロキシプロピルメチルセルロース	8	12	10	8	6	－

【００６２】

（ｂ）打錠用顆粒/裸錠の処方

【００６３】

【表１５】

単位：ｍｇ

成分	実施例番号					比較例番号
	1	8	9	10	11	6
上記（ａ）の顆粒	316	316	316	316	316	316
ステアリン酸マグネシム	4	4	4	4	4	4

【００６４】

（ｃ）ＦＣ錠の処方

【００６５】

【表１６】

単位：ｍｇ

成分	実施例番号					比較例番号
	1	8	9	10	11	6
上記（ｂ）の裸錠	320	320	320	320	320	320
ヒドロキシプロピルメチルセルロース	3.25	－	－	－	－	－
酸化チタン	1	－	－	－	－	－
ポリエチレングリコール６０００	0.75	－	－	－	－	－
カルナバロウ	0.01	－	－	－	－	－

【００６６】

（ｄ）溶出試験

表１７から明らかなように、実施例８，９、１０、１１のｆ２値は実施例1に対する類似性を示した。即ち、水溶性高分子結合剤を１．８％wt/wtから３．８％wt/wtの範囲において含有する医薬品組成物から成る製剤は、速溶解性を示し、かつ、類似の溶出プロファイルを示した。

【００６７】

【表１７】

類似因子	実施例番号				
	1	8	9	10	11
ｆ２	－	７７	８１	７３	７３

【００６８】

＜試験５＞

実施例１２で、水溶性賦形剤として乳糖を用い、水溶性高分子結合剤および部分カルファー化デンプンから成る医薬品組成物を含む製剤を調製した。結果は、表２１に示した。

（ａ）造粒末の処方

【００６９】
【表１８】

単位：ｍｇ

成分	実施例番号		
	1	6	12
ルラシドン・塩酸塩	80	80	80
マンニトール	144	136	-
乳糖	-	-	136
部分アルファ化デンプン	80	80	80
クロスカルメロースナトリウム	4	8	8
ヒドロキシプロピルメチルセルロース	8	12	12

【００７０】
（ｂ）打錠用顆粒/裸錠の処方
【００７１】
【表１９】

単位：ｍｇ

成分	実施例番号		
	1	6	12
上記（ａ）の顆粒	316	316	316
ステアリン酸マグネシム	4	4	4

【００７２】
（ｃ）ＦＣ錠の処方
【００７３】
【表２０】

単位：ｍｇ

成分	実施例番号		
	1	6	12
上記(ｂ)の裸錠	320	320	320
ヒドロキシプロピルメチルセルロース	3.25	-	-
酸化チタン	1	-	-
ポリエチレングリコール６０００	0.75	-	-
カルナバロウ	0.01	-	-

【００７４】
（ｄ）溶出試験
表２１から明らかなように、実施例６および１２のｆ２値は実施例１に対する類似性を示した。即ち、水溶性賦形剤としてマンニトールおよび乳糖にて速溶解性を示し、かつ、類似の溶出プロファイルを示した。
【００７５】
【表２１】

類似因子	実施例番号		
	1	6	12
ｆ２	－	６２	６６

【００７６】
＜試験６＞
実施例４，１３，１４および１５で、粒度分布の異なるルラシドン・塩酸塩原末を用いて、水溶性賦形剤と水溶性高分子結合剤および部分アルファ化デンプンから成る特定の医

薬品組成物を含む製剤を調製した。結果は、表２５に示した。
（ａ）ルラシドン・塩酸塩原末の粒度分布
D50 %（５０%粒子径）とは体積基準により算出される積算分布が５０%となるポイントでの粒子径を示し、D90 %（９０%粒子径）とは、体積基準により算出される積算分布が９０%（ふるい下）となるポイントでの粒子径を表す。
【００７７】
【表２２】

単位：ｍｇ

粒度分布		実施例番号			
		4	13	14	15
粒子径	D10 %	0.5	0.9	1.0	1.5
	D50 %	1.6	5.9	7.6	13.9
	D90 %	4.7	17.5	26.9	58.3

【００７８】
（ｂ）打錠用顆粒/裸錠の処方
【００７９】
【表２３】

単位：ｍｇ

成分	実施例番号			
	4	13	14	15
ルラシドン・塩酸塩	80	80	80	80
マンニトール	176	144	144	144
部分アルファ化デンプン	40	80	80	80
クロスカルメロースナトリウム	8	4	4	4
ヒドロキシプロピルメチルセルロース	12	8	8	8
ステアリン酸マグネシウム	4	4	4	4

【００８０】
（ｃ）ＦＣ錠の処方
【００８１】
【表２４】

単位：ｍｇ

成分	実施例番号			
	4	13	14	15
上記（ｂ）の裸錠	320	320	320	320
ヒドロキシプロピルメチルセルロース	–	3.25	3.25	3.25
酸化チタン	–	1	1	1
ポリエチレングリコール６０００	–	0.75	0.75	0.75
カルナバロウ	–	0.01	0.01	0.01

【００８２】
（ｄ）溶出試験
表２５から明らかなように、実施例１３，１４、１５のｆ２値は実施例４に対する類似性を示した。即ち、５０%粒子径が１～８μｍの範囲、９０%粒子径が２７μｍ以下の粒度分布のルラシドン・塩酸塩原末を用いて調製した製剤で類似の溶出プロファイルが得られることを見出した。
【００８３】

【表２５】

類似因子	実施例番号			
	4	13	14	15
ｆ２	－	５６	５６	４６

【００８４】

＜試験７＞

特許文献２の開示技術を用いて１錠中のルラシドン・塩酸塩の含有量が１０ｍｇと４０ｍｇとなる製剤を試作し、開示文献２の通り、１錠中のルラシドン・塩酸塩含量が１０ｍｇから４０ｍｇまでは同等の溶出挙動を示す経口製剤を提供できるかどうか検証した。結果は、図１に示した。

【００８５】

図１から明らかなように、特許文献２の開示技術により得られるルラシドン・塩酸塩を異なる含有量を有する製剤の溶出プロファイルは、ｆ２の値から明らかなように、１錠中にルラシドン・塩酸塩を１０ｍｇ含有する錠剤と４０ｍｇ含有する製剤は、特許文献２のとおり同等の溶出挙動を示す経口製剤を提供できた。

（ａ）顆粒の処方

単位：ｍｇ

成分	10mg錠	40mg錠
ルラシドン・塩酸塩	10	40
マンニトール	47	188
クロスカルメロースナトリウム	4	16
ヒドロキシプロピルメチルセルロース	2.5	10

【００８６】

（ｂ）裸錠の処方

ｃ

単位：ｍｇ

成分	10mg錠	40mg錠
（ａ）の顆粒	63.5	254
マンニトール	15.5	62
ステアリン酸マグネシウム	1	4

【００８７】

（ｃ）ＦＣ錠の処方

単位：ｍｇ

成分	10mg錠	40mg錠
上記（ｂ）の裸錠	80	320
ヒドロキシプロピルメチルセルロース	1.3	2.6
酸化チタン	0.4	0.8
ポリエチレングリコール６０００	0.3	0.6
カルナバロウ	0.006	0.01

【００８８】

＜試験８＞

特許文献２の開示技術では１錠中にルラシドン・塩酸塩を４０ｍｇまで含有する製剤では同等の溶出挙動を示す経口製剤を提供できることを確認できた。ここでは、特許文献２の開示技術を用いて、部分アルファー化デンプンを含まない１錠中のルラシドン・塩酸塩含有量が８０ｍｇとなる製剤を試作した。錠剤の大型化は患者への負担を大きくするため、４０ｍｇ錠と同じ錠剤重量となるように、有効成分の含有率を２倍にすることにより製した。比較例１および２の結果は表４および図２に示した。

【００８９】
表４および図２から明らかなように、特許文献２の開示技術では、ｆ２の値から明らかなように、ルラシドン・塩酸塩の含有率を２倍にしたアルファ化デンプンを含まない８０ｍｇ錠では４０ｍｇ錠２錠と同等の溶出性を示すことはできなかった。
（ａ）顆粒の処方

単位：ｍｇ

成分	40mg錠	80mg錠
ルラシドン・塩酸塩	40	80
マンニトール	188	148
クロスカルメロースナトリウム	16	16
ヒドロキシプロピルメチルセルロース	10	10

【００９０】
（ｂ）裸錠の処方

単位：ｍｇ

成分	40mg錠	80mg錠
（ａ）の顆粒	254	254
マンニトール	62	62
ステアリン酸マグネシウム	4	4

【００９１】

（ｃ）ＦＣ錠の処方

単位：ｍｇ

成分	40mg錠	80mg錠
上記（ｂ）の裸錠	320	320
ヒドロキシプロピルメチルセルロース	2.6	2.6
酸化チタン	0.8	0.8
ポリエチレングリコール６０００	0.6	0.6
カルナバロウ	0.01	0.01

【００９２】
＜試験９＞
試験１の実施例１～３にて試作した含量の異なる３種類の製剤の溶出性を評価した。結果は、図３に示した。
図３から明らかなように、本発明により１錠中にルラシドン・塩酸塩を２０ｍｇから８０ｍｇを含有する製剤においても、錠剤の含量（力価）に依存しない同等の溶出性が確認された。
（ａ）造粒末の処方
【００９３】
【表２６】

単位：ｍｇ

成分	80mg錠	40mg錠	20mg錠
ルラシドン・塩酸塩	80	40	20
マンニトール	144	72	36
部分アルファ化デンプン	80	40	20
クロスカルメロースナトリウム	4	2	1
ヒドロキシプロピルメチルセルロース	8	4	2

【００９４】

（ｂ）打錠用顆粒/裸錠の処方

単位：ｍｇ

成分	80mg錠	40mg錠	20mg錠
上記（ａ）の顆粒	316	158	79
乳糖	−	−	−
ステアリン酸マグネシム	4	2	1

【００９５】

（ｃ）ＦＣ錠の処方

単位：ｍｇ

成分	80mg錠	40mg錠	20mg錠
上記(ｂ)の裸錠	320	160	80
ヒドロキシプロピルメチルセルロース	3.25	1.95	1.3
酸化チタン	1	0.6	0.4
ポリエチレングリコール６０００	0.75	0.45	0.3
カルナバロウ	0.01	0.006	0.004

【産業上の利用可能性】

【００９６】

本発明によりＮ−［４−〔４−(１，２−ベンズイソチアゾール−３−イル)−１−ピペラジニル〕−(２Ｒ，３Ｒ)−２，３−テトラメチレン−ブチル］−(１’Ｒ，２’Ｓ，３’Ｒ，４’Ｓ)−２，３−ビシクロ〔２，２，１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）を有効成分とする崩壊性が良好な経口製剤において、有効成分の含量が変動しても、同等の溶出挙動を示す経口投与用製剤を提供することが可能となった。

【図面の簡単な説明】

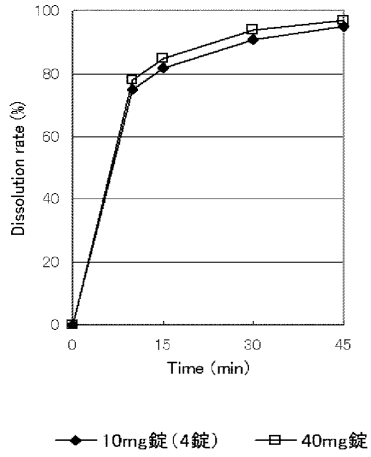
【００９７】

【図１】図1はルラシドン・塩酸塩を異なる含有量を有する製剤の溶出プロファイルの比較を示したものである。特許文献２の開示技術を用いて試作した１錠中のルラシドン・塩酸塩の含有量が１０ｍｇ（４錠）と４０ｍｇ（１錠）の製剤について溶出プロファイルを測定した。

【図２】図２は、ルラシドン・塩酸塩を異なる含有量を有する製剤の溶出プロファイルの比較を示したものである。特許文献２の開示技術を用いて試作した１錠中のルラシドン・塩酸塩の含有量が４０ｍｇ（２錠）と８０ｍｇ（１錠）の製剤について溶出プロファイルを測定した。

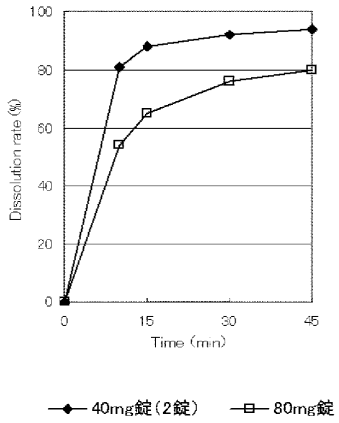
【図３】図３は、ルラシドン・塩酸塩を異なる含有量を有する製剤の溶出プロファイルの比較を示したものである。本発明の技術を用いて試作した１錠中のルラシドン・塩酸塩の含有量が２０ｍｇ（４錠）、４０ｍｇ（２錠）と８０ｍｇ（１錠）の製剤について溶出プロファイルを測定した。

【書類名】図面
【図１】



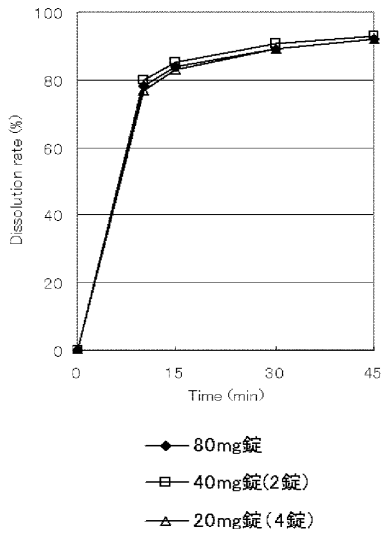
f2＝77

【図２】



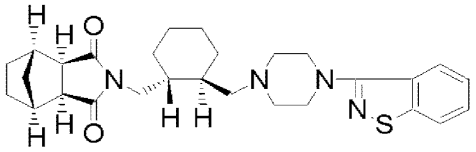
f2＝37

【図３】



f2＝88　(80 錠に対して 40mg 錠 2 錠)
f2＝97　(80 錠に対して 20mg 錠 4 錠)

【書類名】要約書
【要約】
【課題】　式（１）
【化１】



・HCl　(1)

で表されるＮ－[４－〔４－(１,２－ベンズイソチアゾール－３－イル)－１－ピペラジニル〕－(２Ｒ,３Ｒ)－２,３－テトラメチレン－ブチル]－(１'Ｒ,２'Ｓ,３'Ｒ,４'Ｓ)－２,３－ビシクロ〔２,２,１〕ヘプタンジカルボキシイミド・塩酸塩（ルラシドン・塩酸塩）を有効成分とする経口製剤において、有効成分の含量が変動しても、同等の溶出挙動を示す経口投与用製剤の提供。
【解決手段】　アルファ化デンプン類を含むことを特徴とする、ルラシドン・塩酸塩と水溶性賦形剤、水溶性高分子結合剤を含有する経口製剤は、経口投与された場合に、消化管内での有効成分の溶出性に優れ、かつ有効成分の含量が異なる製剤間で同等の溶出挙動を示すことができ、個々の患者に応じて最も適した薬剤の選択を可能にし、臨床上極めて有用である。
【選択図】なし

【書類名】　出願人名義変更届（一般承継）
【提出日】　平成17年10月26日
【あて先】　特許庁長官殿
【事件の表示】
　【出願番号】　特願2005-153508
【承継人】
　【識別番号】　000002912
　【氏名又は名称】　大日本住友製薬株式会社
　【代表者】　宮武　健次郎
　【電話番号】　06-6466-5214
【提出物件の目録】
　【物件名】　権利の承継を証明する書面　1
　　【援用の表示】　なお、当該書面は、平成１７年１０月１９日付提出の平成１０年特許願第５４７９２７号の特許出願人名義変更届（一般承継）に添付した履歴事項全部証明書を援用し、省略する。

出願人履歴

０００１８３３７０

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新規登録

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大日本製薬株式会社

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20051003

名称変更

大阪府大阪市中央区道修町２丁目６番８号

大日本住友製薬株式会社

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000

CONFIRMATION NO. 5575

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

PUBLICATION NOTICE

Title:PHARMACEUTICAL COMPOSITION

Publication No.US-2015-0056284-A1
Publication Date:02/26/2015

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

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Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Doc Code: PA..
Document Description: Power of Attorney

PTO/AIA/82A (07-13)
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NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

Application Number	14/512,189
Filing Date	October 10, 2014
First Named Inventor	Kazuyuki FUJIHARA
Title	PHARMACEUTICAL COMPOSITION
Art Unit	1627
Examiner Name	Sarah PIHONAK
Attorney Docket Number	05273.0147-02000

SIGNATURE of Applicant or Patent Practitioner

Signature	Jennifer Gupta	Date (Optional)	3/4/15
Name	Jennifer R. Gupta	Registration Number	54,257
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.

☑ *Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Document Description: Power of Attorney

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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date
14/512,189	October 10, 2014

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 22,852

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

SUMITOMO DAINIPPON PHARMA CO., LTD., 6-8, Dosho-machi 2-chome, Chuo-ku, Osaka-shi, Osaka, 541-8524 Japan

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	2015/02/26
Name	Masayo TADA		
Title	Representative Director, President and Chief Executive Officer		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

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Electronic Acknowledgement Receipt	
EFS ID:	21675158
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	04-MAR-2015
Filing Date:	10-OCT-2014
Time Stamp:	16:31:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Power of Attorney	AIA-POA-82A-82B.pdf	128277 95056cf7eebc51d363dbce057a9cae8042e6d073	no	2

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Information:

Total Files Size (in bytes):	128277

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000

CONFIRMATION NO. 5575

POA ACCEPTANCE LETTER

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

OC000000073939052

Date Mailed: 03/12/2015

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 03/04/2015.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/hachristian/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Kazuyuki FUJIHARA	Group Art Unit: 1627
Application No.: 14/512,189	Examiner: Sarah, PIHONAK
Filed: October 10, 2014	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicant brings to the attention of the Examiner the documents on the attached form. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

A copy of each of the listed non patent literature documents is attached. A copy of the listed U.S. patent and U.S. patent publication is not enclosed pursuant to 37 C.F.R. § 1.98(a)(2)(ii).

Applicant respectfully requests that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicant determines that the cited document(s) do not constitute

"prior art" under United States law, Applicant reserves the right to present to the U.S. Patent and Trademark Office the relevant facts and law regarding the appropriate status of such documents.

Applicant further reserves the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: April 22, 2015

By: /Jennifer R. Gupta/
Jennifer R. Gupta
Reg. No. 54,257
(202) 408-4000

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1627
				Examiner Name	Sarah PIHONAK
Sheet	1	of	1	Attorney Docket Number	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-6,150,366	11-21-2000	Arenson et al.	

U.S. PUBLISHED PATENT APPLICATIONS

Examiner Initials*	Cite No.[3]	Document Number Number-Kind Code[4] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-2004-0186105 A1	09-23-2004	Allenspach et al..	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[5] Number[6] Kind Code[7] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[8]

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[6]
		GHOSH, Tapash K. et al., "Theory and Practice of Contemporary Pharmaceutics," CRC Press, Chapter 10, pg. 279-331 (2005).	
		GENNARO, Alfonso R., "Remington: The Science and Practice of Pharmacy," 19th Edition, Mack Publishing Co., Chapter 92, Vol. II, pp. 1615-1620, [1995]	

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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[7] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
[8] Applicant is to place a check mark here if English language Translation is attached.
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**.

Electronic Acknowledgement Receipt	
EFS ID:	22138559
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	22-APR-2015
Filing Date:	10-OCT-2014
Time Stamp:	16:38:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	NPL-Ghosh.pdf	14261061 535374e89b66d8ad71643934551488881fc8612f9	no	54
Warnings:					
Information:					

2	Non Patent Literature	NPL-Gennaro.pdf	3485580 f6dd30da40374eef7842186018e5b4b2057b1c78	no	8
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	IDS-SB08_4-22-15.pdf	142498 c9702d9bc0ac78297f106341c492d4e87a7284e7	no	4
Warnings:					
Information:					
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			Total Files Size (in bytes):	17889139	

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<u>New Applications Under 35 U.S.C. 111</u>
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<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

<u>New International Application Filed with the USPTO as a Receiving Office</u>
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PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Kazuyuki FUJIHARA	)	Group Art Unit: 1627
	)	
Application No.: 14/512,189	)	Examiner: Sarah, PIHONAK
	)	
Filed: October 10, 2014	)	
	)	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	)	
	)	
	)	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the attention of the Examiner the document on the attached form. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

A copy of the listed non patent literature document is attached. A copy of each of the listed U.S. patent publications is not enclosed pursuant to 37 C.F.R. § 1.98(a)(2)(ii).

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making an appropriate notation on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that the listed document is material or constitutes "prior art." If the Examiner applies the document as prior art against any claim in the application and Applicants determine that the cited document does not constitute "prior art" under United

States law, Applicants reserve the right to present to the U.S. Patent and Trademark Office the relevant facts and law regarding the appropriate status of such document.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed document, should the document be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: July 15, 2015

By: Jennifer Gupta
Jennifer R. Gupta
Reg. No. 54,257

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1627
				Examiner Name	Sarah PIHONAK
Sheet	1	of	1	*Attorney Docket Number*	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] *(if known)*	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

U.S. PUBLISHED PATENT APPLICATIONS

Examiner Initials*	Cite No.[3]	Document Number Number-Kind Code[4] *(if known)*	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-2003/0203020 A1	10-30-2003	Ortyl et al.	
		US-2005/0147669 A1	07-07-2005	Lawrence et al.	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[5] Number[6] Kind Code[7] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[8]

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[8]
		GOHIL, Usha C. et al., "Investigations into the use of pregelatinised starch to deveop powder-filled hard capsules," International Journal of Pharmaceutics 285 (2004) pp. 51-63.	

Examiner Signature		Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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[3] Applicant's unique citation designation number (optional).
[4] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.
[5] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).
[6] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.
[7] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
[8] Applicant is to place a check mark here if English language Translation is attached.
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Electronic Acknowledgement Receipt	
EFS ID:	22929029
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	15-JUL-2015
Filing Date:	10-OCT-2014
Time Stamp:	17:11:34
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	IDS-SB08_7-15-15.pdf	138650 8902de38cdd7c6e6bfe82ac59b9749ca2c14e491	no	4
Warnings:					
Information:					

This is not an USPTO supplied IDS fillable form					
2	Non Patent Literature	NPL_Gohil-InvestigationsIntoTheUse2004 pp51-63.pdf	5452234 5ad562b77676b3c138a71fb29d9dad595e05902f	no	13
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			Total Files Size (in bytes):	5590884	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000	5575

22852 7590 11/03/2015

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
PIHONAK, SARAH	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
11/03/2015	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

regional-desk@finnegan.com

Office Action Summary	**Application No.** 14/512,189	**Applicant(s)** FUJIHARA, KAZUYUKI	
	Examiner SARAH PIHONAK	**Art Unit** 1627	**AIA (First Inventor to File) Status** No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) 25-59 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☐ Claim(s) _____ is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☒ Claim(s) 25-59 are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

1. The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 25-57, drawn to an oral preparation comprising lurasidone and a method for preparing the composition, classified in C07D417/14.

II. Claims 58-59, drawn to a method for treating psychosis and a method for treating schizophrenia, classified in A61K 31/428.

2. The inventions are independent or distinct, each from the other because:

3. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the oral preparation comprising lurasidone can be used for purposes other than treating psychosis or schizophrenia, such as for the treatment of anxiety disorder. As the product of invention I has utility outside of the methods of invention II, and the inventions are categorized in different searching classes, the inventions are independent and distinct from each other.

4. The examiner has required restriction between product or apparatus claims and process claims. Where applicant elects claims directed to the product/apparatus, and all

product/apparatus claims are subsequently found allowable, withdrawn process claims that include all the limitations of the allowable product/apparatus claims should be considered for rejoinder. All claims directed to a nonelected process invention must include all the limitations of an allowable product/apparatus claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product/apparatus claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product/apparatus are found allowable, an otherwise proper restriction requirement between product/apparatus claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product/apparatus claim will not be rejoined. See MPEP § 821.04. Additionally, in order for rejoinder to occur, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product/apparatus claims. **Failure to do so may result in no rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above

and there would be a serious search and/or examination burden if restriction were not required because one or more of the following reasons apply:

The product of invention I can be used for purposes other than the methods of invention II; additionally, the inventions are categorized in different searching classes. Therefore, a search for the product of invention I would not necessarily overlap in scope for the particular methods of invention II.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable

over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 or pre-AIA 35 U.S.C. 103(a) of the other invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Kazuyuki FUJIHARA	)	Group Art Unit: 1627
	)	
Application No.: 14/512,189	)	Examiner: Sarah Pihonak
	)	
Filed: October 10, 2014	)	
	)	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	)	
	)	
	)	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

RESPONSE TO RESTRICTION REQUIREMENT

In reply to the Office Action (Restriction Requirement) mailed November 3, 2015, the shortened statutory period ending January 3, 2016, Applicant respectfully requests reconsideration of this application in view of the following remarks.

REMARKS

In the Restriction Requirement, the Examiner required restriction under 35 U.S.C. § 121 between:

Group I - Claims 25-57, drawn to an oral preparation comprising lurasidone and a method for preparing the composition, classified in C07D417/14.

Group II - Claims 58-59, drawn to a method for treating psychosis and a method for treating schizophrenia, classified in A61K 31/428.

Applicant provisionally elects to prosecute Group I, claims 25-57, drawn to an oral preparation comprising lurasidone and a method for preparing the composition, with traverse.

According to MPEP 803, these are two requirements that must be met before a proper restriction requirement may be made: (1) the inventions must be independent or distinct as claimed; and (2) there must be a serious burden on the Office if restriction is not required. Applicant respectfully submits that the Office has failed to establish the second requirement set forth in MPEP 803. Automated search tools now relieve much of the burden associated with searching, so that separate classification is no longer an adequate reason for insisting our restriction.

Further, a proper search and examination of the subject matter covered by pending claims 25-57 would not be unduly burdensome on the Office since a search of the subject matter of Group I would overlap with a search of the subject matter of Group II. Specifically, a search of the subject matter of all of claims 1-59 would require the Office to search for at least one compound of formula (1). Thus, the search and examination of Group II would necessarily include a search of Group I claims.

Accordingly, it is unclear what burden is on the Office to examine the claims of Groups I and II together.

Accordingly, the Office is requested to reconsider and withdraw the requirement for restriction. In the event that restriction requirement is maintained, Applicant reserves the right to file a divisional application on the non-elected inventions and/or to request rejoinder of appropriate claims once the subject matter of claims 25-57 is found allowable.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 15, 2015

By: Charles E Van Horn
Charles E. Van Horn
Reg. No. 40,266

Electronic Acknowledgement Receipt	
EFS ID:	24366981
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Jennifer R. Gupta/Pat Welch
Filer Authorized By:	Jennifer R. Gupta
Attorney Docket Number:	05273.0147-02000
Receipt Date:	15-DEC-2015
Filing Date:	10-OCT-2014
Time Stamp:	15:54:38
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		ResponseToRestrReq.pdf	85516 8ac0296f346d39da25a8fae25e0f26d3de1bf961	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response to Election / Restriction Filed	1	1
	Applicant Arguments/Remarks Made in an Amendment	2	3
Warnings:			
Information:			
	Total Files Size (in bytes):	85516	

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000	5575

22852 7590 02/09/2016

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
PIHONAK, SARAH	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
02/09/2016	ELECTRONIC

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regional-desk@finnegan.com

Office Action Summary	Application No. 14/512,189	Applicant(s) FUJIHARA, KAZUYUKI	
	Examiner SARAH PIHONAK	Art Unit 1627	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

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- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/15/15*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *25-59* is/are pending in the application.

5a) Of the above claim(s) *58 and 59* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *25-57* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *10/10/14* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☒ All b)☐ Some** c)☐ None of the:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

1. The present application is being examined under the pre-AIA first to invent provisions.

Priority

This application, filed on 10/10/14, is a continuation of 14/183283, filed on 2/18/14. 14/183/283 is a continuation of 11/919678, filed on 10/31/2007. 11/919678 is a national stage entry of PCT/JP2006/310571. A claim for foreign priority is also made to 2005-153508, filed on 5/26/2005. A certified copy of the foreign priority document is on file.

Status of Claims and Response to Restriction Requirement

2. Claims 25-59 are currently pending as of the reply filed on 12/15/15. Claims 1-24 have been cancelled.

3. Applicant's election with traverse of the invention of Group I, claims 25-57 in the reply filed on 12/15/15 is acknowledged. The traversal is on the ground(s) that the Office has failed to establish that a serious burden would exist if restriction was not made between claims directed to a product and a process of use. Applicants have further argued that a search of both inventions I and II would not be unduly burdensome since a search of the subject matter of Group I would overlap with a search of the subject matter of Group II. This is not found persuasive because inventions directed to a product and a process of using that product can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be

used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the oral preparation comprising lurasidone can be used for purposes other than treating psychosis or schizophrenia, such as for the treatment of anxiety disorder. Furthermore, the inventions are categorized in different CPC searching classes and subclasses; different inventive classes are required for searching the claimed product and method.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 58-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/15/15.

5. Claims 25-57 were examined.

6. Claims 25-57 are rejected.

Claim Rejections-35 USC § 103

7. The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under pre-AIA 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 25-57 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Fujihara et. al., EP 1327440 (publ. date 7/16/2003; cited in an IDS), in view of Allenspach et. al., US Pat. Publ. 2004/0186105 (publ. date 9/23/2004, cited in an IDS), and Nakamura et. al., WO 2004/017973 (publ. date 3/4/2004). Nakamura et. al. was published in Japanese; for convenience, an English translation of this publication will be discussed.

The claims are directed to an oral preparation comprising N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of formula (1); a pregelatinized starch; a water soluble excipient; and a water soluble polymer binder; wherein the content of lurasidone in the preparation is 20-45% (wt/wt), and the content of the pregelatinized starch in the preparation is 10-50% (wt/wt).

Fujihara et. al. teaches an oral composition having favorable disintegration characteristics comprised of a slightly water soluble active ingredient, such as

lurasidone, along with a first disintegrant, a second disintegrant, and a water soluble polymer binder (Abstract; p. 4-5, paragraph [0008]). Fujihara et. al. teaches that the composition provides advantageous dissolution characteristics when ingested as well as rapid dissolution of the active ingredient even when the amount is varied in the range of several mg. to several tens of mg. (Abstract; p. 1, para [0001]). The first disintegrant is taught to include corn starch, microcrystalline cellulose, carmellose, carmellose calcium, carmellose sodium, croscarmellose sodium, carboxymethyl starch sodium and crospovidone (p. 4, lines 6-9; p. 5, paragraph [0011]; p. 22, paragraph [0152], table 28). The first disintegrant is taught to comprise from about 5-300% by weight to the weight of the slightly water soluble active agent (p. 4, item 33). For a tablet having a weight of 137.7 mg., comprising 40 mg. of lurasidone, 5% by weight of the first disintegrant to the weight of lurasidone would be equivalent to about 1.45% by total weight of the tablet (p. 29, paragraph [0194-0195], Tables 44-45), which meets the content of disintegrant per tablet recited in instant claim 46. It is taught that one of the water soluble excipients includes sugar alcohols such as mannitol or lactose, D-sorbitol, erythritol, or xylitol (p. 3, paragraph [0007], items (18) and (21); p. 5, paragraph [0014]). The other disintegrant is taught as including excipients such as microcrystalline cellulose, croscarmellose sodium, carmellose, carmellose calcium, carboxymethyl starch sodium, and crosspovidone (p. 5, paragraph [0011]), and the water soluble polymer binder includes polyvinylpyrrolidone, polyvinyl alcohol, hydroxypropyl methylcellulose, and hydroxypropylcellulose (p. 4, lines 10-12; p. 5, paragraph [0010]). It is taught that the amount of lurasidone present in the oral composition is 40 mg., which is within the

range instantly claimed (p. 5, paragraph [0015]; p. 22, paragraph [0152], Table 28), and that the average particle size of lurasidone is between 0.5 to 5 µm (p. 6, paragraph [0021]). It is taught that for a tablet of a weight of 137.7 mg., the amount of lurasidone present is 40 mg., which is approximately 29 % of the weight of the composition (p. 29, paragraph [0194-0195], Tables 44-45). The water soluble polymer binder is taught to comprise from about 1 to 10% by weight of the preparation (p. 4, lines 39-40), and water soluble excipients such as mannitol or lactose are taught to comprise from 200 to 2000 % by weight to the weight of lurasidone (p. 9, paragraph [0066]). Fujihara et. al. provides an example wherein lurasidone comprises 40 mg. of the tablet, while mannitol comprises 132 mg., of a total mass of 250 mg. for the tablet (p. 23, paragraph [0159], Table 32, Ex. 24). Thus, Fujihara teaches a water soluble excipient such as D-mannitol or lactose to comprise about 53% of the tablet (p. 23, paragraph [0159], Ex. 24 of Table 32; 132 mg./250 mg. is about 53%), which is within the content range of water soluble excipient cited in instant claims 33 and 47. Fujihara teaches the composition to comprise a lubricant selected from magnesium stearate, talc, or hydrogenated oil, in the range of 0.3 to 3% by weight to the total tablet weight (p. 7, paragraphs [0032-0033]). Fujihara provides an example formulation wherein the amount of the disintegrant crosscarmellose sodium is 4.8 % of the tablet weight (12 mg. for a 250 mg. tablet; p. 23, paragraph [0159], Table 32); therefore, the limitation of claim 47 is met. It is taught that the oral preparation comprises a granule, which is prepared by granulating the water-soluble polymer binder with the powdery mixture consisting of the active agent (lurasidone), a water soluble excipient, and another disintegrant (p. 3, paragraph [0007],

items (11-13); p. 4, paragraph [0007], item (40)). Fujihara et. al. teaches that the preparation can be formulated as pills, granules, fine granules, capsules, tablets, etc. (p. 5, paragraph [0016]). Fujihara teaches preparing the composition comprising combining a water soluble polymer binder to a powder mixture consisting of a water soluble excipient, a first excipient, and a slightly water soluble active agent; preparation of granules is also taught to involve combining the excipient and the active ingredients in an aqueous suspension, as well in aqueous solution ([p. 3, paragraph [0007], items (4) and (10); p. 4, items (37) to (40)).

Fujihara does not explicitly teach the composition to comprise lurasidone at a content of greater than 40 mg. or pregelatinized starch. It is not explicitly taught that the similarity factor f2 of the composition is in the range of $50 \leq f2 \leq 100$ when a content of lurasidone per tablet changes over a range of 20 to 120 mg.

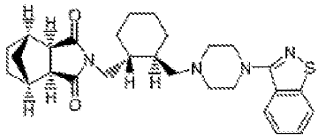
Allenspach et. al. teaches an oral composition comprising a drug of low water solubility and pregelatinized starch having low viscosity and/or exhibiting a multimodal particle size distribution (Abstract; p. 4, para [0044]). Allenspach teaches the composition to be suitable for a wide variety of drugs having low or slight water solubility (p. 2, para [0022]-p. 3, para [0023]). Starch 1500 is exemplified as a low viscosity pregelatinized starch; the composition is taught to comprise from about 1-50%, preferably about 2.5 to 30% by weight pregelatinized starch (p. 4, paragraphs [0045-0046]). Starch 1500 is included as a pregelatinized starch containing water soluble matter of 30% or less as well as having a pregelatinizing ratio of pregelatinized starch in the range of 50 to 95% (see the instant specification, paragraph [0016]); therefore, the

teaching of Starch 1500 by Allenspach meets the limitations of instant claims 43 and 45. Allenspach teaches that the incorporation of low viscosity pregelatinized starch into the composition improves the dissolution rate (p. 2, paragraphs [0013-0014]; p. 9, paragraph [0110]). Tablets are taught (p. 2, paragraphs [0015] and [0020]). Allenspach teaches the low water solubility active drug and pregelatinized starch can be combined with any other desired excipients by blending the components as a powder or granules together to prepare a tablet (p. 5, paragraph [0063]).

Fujihara et. al. teaches an oral tablet composition comprising an active agent of low water solubility, of which lurasidone is exemplified, as well as the recited water soluble excipients, water soluble polymer binders, and lubricants recited in the instant claims. Allenspach teaches improving the dissolution rate of a tablet comprising a low water solubility active agent via the incorporation of a low viscosity pregelatinized starch, from about 1-50% by weight of the composition. One of ordinary skill in the art would have found it prima facie obvious to have incorporated a low viscosity pregelatinized starch, such as Starch 1500, into the tablet composition taught by Fujihara, since lurasidone is an active agent having low water solubility, and Allenspach teaches the addition of a low viscosity pregelatinized starch to improve the dissolution rate of an oral composition comprising a low water solubility drug. As Allenspach teaches the amount of pregelatinized starch to range from 1-50% by weight of the composition, it would have been obvious to have incorporated pregelatinized starch into the Fujihara composition, in a content of 10-50% by weight, as recited in the instant claims.

Fujihara does not explicitly teach the composition to comprise lurasidone at a content of greater than 40 mg.

Nakamura et. al. teaches the daily dose of the active compound, (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptane dicarboxyimide or its pharmaceutically acceptable salt for oral administration to range from 5 to 120 mg for the treatment of schizophrenia (see Abstract; p. 3 of 35, see 1st paragraph):



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. Oral administration once a day is taught, as well as tablet compositions (see p. 3 of 35, 1st paragraph; see p. 4 of 35, 2nd paragraph).

Although Fujihara teaches the oral composition to comprise from 5-40 mg. lurasidone, it would have been routine and obvious for a person of ordinary skill in the art to have adjusted the dose of lurasidone and to have increased the amount of this drug in the composition, as Nakamura teaches a daily dose of lurasidone in an oral composition, including a tablet, to range from 5-120 mg. One of ordinary skill in the art would have been motivated to have increased the amount of lurasidone in the composition of Fujihara up to 120 mg., as Nakamura teaches this dosage to be acceptable for oral preparations, including tablets. Furthermore, it would have been considered routine and obvious for one of ordinary skill in the art, at the time of the invention, to have established an optimum dose range for lurasidone and to have arrived at a dose of 160 mg., as Fujihara and Nakamura teach the dose of lurasidone to vary. Additionally, MPEP 2144.05 states “Generally, differences in concentration or

temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical". Also see *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The instantly claimed composition comprising lurasidone from 20-45% by weight, a water soluble excipient, a water soluble polymer binder, and pregelatinized starch from 10-50% by weight exhibits a similarity factor f2 in the range of 50≤f2≤100 when a content of lurasidone per tablet changes over a range of 20 to 120 mg.; therefore, it would have been prima facie obvious that the prior art composition comprising lurasidone and pregelatinized starch within the claimed ratio content, a water soluble excipient, and a water soluble polymer binder from the combined teachings of Fujihara, Allenspach, and Nakamura would have exhibited the same characteristic. Fujihara teaches preparing an oral lurasidone preparation via the steps of instant claims 27 and 56-57, with the exception of the pregelatinized starch; Allenspach teaches combining the pregelatinized starch with the low water solubility active agent and additional excipients. Thus, it would have been prima facie obvious to have arrived at the steps of instant claims 27 and 56-57 by granulating a powder mixture of lurasidone, pregelatinized starch, water soluble excipient and water soluble polymer binder via a solution or suspension.

Claim Rejections-Obviousness Type Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit http://www.uspto.gov/forms/. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more

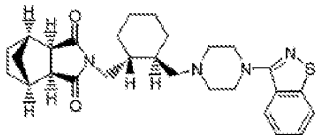
information about eTerminal Disclaimers, refer to

http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

11. Claims 25-57 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 8,729,085 (USP '085). The instant claims are directed to an oral preparation comprising 20-160 mg. of N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 10-50 weight % of pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. The claims of USP 8,729,085 (USP '085) are directed to an oral preparation which comprises N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 20-50 weight % of pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. Both the instant claims and the claims of USP '085 are directed to an oral preparation comprising lurasidone and pregelatinized starch in overlapping weight percentages, along with the additional components including a water soluble excipient and water soluble polymer binder; the claims are thus not patentably distinguishable from each other.

12. Claims 25-57 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 7,727,553 (USP '553), in view of Nakamura et. al., WO 2004/017973 (publ. date 3/4/2004; cited in the IDS), and Allenspach et. al., US Pat. Publ. 2004/0186105. The instant claims are directed to an oral preparation comprising 20-160 mg. of N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 10-50 weight % of pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. The claims of USP '553 are directed to an oral preparation comprising 5-40 mg. of N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride; a water soluble excipient selected from mannitol or lactose; a first disintegrant selected from corn starch, carmellose, carmellose sodium, croscarmellose sodium, crosspovidone, and carboxylmethyl starch sodium; a water soluble polymer binder selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, and polyvinylpyrrolidone in an amount of 1-5% by weight of the composition; a second disintegrant selected from lactose, crosspovidone, carmellose sodium; wherein the first disintegrant is present from 5-300% by weight of the active agent; and the water soluble excipient is present in an amount of 200-2000% by weight of the active ingredient. For a 160 mg. preparation, 40 mg. of lurasidone would be equivalent to 40% by weight of the composition; 5% of first distintegrant by weight of lurasidone (40 mg.) would be 2 mg., and 2 mg. of corn

starch, carmellose, carmellose sodium, croscarmellose sodium, crosspovidone, and carboxylmethyl starch sodium would be equivalent to about 1.25 % of a 160 mg. preparation. 200% of lactose or mannitol of 40 mg. of lurasidone would be equivalent to 80 mg. of lactose or mannitol, which would be equivalent to 50% of a 160 mg. preparation. Therefore, the content of mannitol or lactose; water soluble excipient; water soluble polymer binder and lurasidone recited in the claims of USP '553 overlaps with the content ranges recited in the instant claims. While the claims of USP '553 do not recite pregelatinized starch, it would have been prima facie obvious to have incorporated this starch into the composition claimed in the '553 patent in view of Allenspach. Allenspach teaches incorporating a low viscosity pregelatinized starch, from about 1-50% by weight of the composition, improves the dissolution characteristics for a low water solubility active agent (Abstract; p. 2, paragraphs [0013-0014]; p. 4, para [0044] and [0046]; p. 9, paragraph [0110]). Therefore, it would have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, to have incorporated a pregelatinized starch, a water soluble excipient, a disintegrant, and a lubricant to the tablet composition claims of USP '553, at the content ratios recited in the instant claims. Although the claims of USP '553 do not recite lurasidone in an concentration greater than 40 mg., Nakamura et. al. teaches the daily dose of the active compound, (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptane dicarboxyimide or its pharmaceutically acceptable salt for oral administration to range from 5 to 120 mg for the treatment of schizophrenia (see Abstract; p. 3 of 35, see 1st paragraph):



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. Oral administration once a day is taught, as well as tablet compositions (see p. 3 of 35, 1st paragraph; see p. 4 of 35, 2nd paragraph). Therefore, it would have been prima facie obvious to have incorporated up to 120 mg. of lurasidone into the composition claimed in USP '553, Nakamura teaches an oral composition comprising this amount of the drug. The instantly claimed composition comprising lurasidone from 20-45% by weight, a water soluble excipient, a water soluble polymer binder, and pregelatinized starch from 10-50% by weight exhibits a similarity factor f2 in the range of 50≤f2≤100 when a content of lurasidone per tablet changes over a range of 20 to 120 mg.; therefore, it would have been prima facie obvious that the composition claimed in USP '553 further comprising pregelatinized starch, as it is comprised of the same components, would have exhibited the same characteristic. The instant claims and the claims of USP '553 are therefore obvious variants of each other.

13. Claims 25-57 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 8,883,794 (USP '794). The instant claims are directed to an oral preparation comprising 20-160 mg. of N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 10-50 weight % of

pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. The claims of USP 8,883,794 (USP '794) are directed to an oral preparation which comprises 20-120 mg. N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 20-30 weight % of pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. Both the instant claims and the claims of USP '085 are directed to an oral preparation comprising lurasidone and pregelatinized starch in overlapping weight percentages, along with the additional components including a water soluble excipient and water soluble polymer binder; the claims are thus not patentably distinguishable from each other.

14. Claims 25-57 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 25-50 of copending Application No. 14/733204 (reference application), in view of Fujihara et. al., EP 1327440 (publ. date 7/16/2003; cited in an IDS), and Allenspach et. al., US Pat. Publ. 2004/0186105. The instant claims are directed to an oral preparation comprising 20-160 mg. of N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone); a water soluble excipient; a water-soluble polymer binder; a disintegrant; and from 10-50 weight % of pregelatinized starch, wherein the content of lurasidone in the preparation is 20-45 weight %. The co-pending claims are directed to an oral tablet comprising from 20-120

mg. of lurasidone, a pregelatinized starch, a water soluble excipient, a disintegrant, and a lubricant, wherein the tablet has a dissolution rate of at least more than 8-% at 30 minutes as measured according to Japanese Pharmacopoeia. The co-pending claims further recite the content ratio of lurasidone in the tablet to range from 20-45% by weight (see claim 26). Although the co-pending claims do not explicitly recite the content of water soluble excipient, water soluble polymer binder, disintegrant, lubricant, and pregelatinized starch, it would have been prima facie obvious to one of ordinary skill in the art to have arrived at the content ratio of these components that overlap or are included in the contents recited in the instantly claimed composition, in consideration of the teachings of Fujihara and Allenspach. Fujihara teaches an oral composition having favorable disintegration characteristics comprised of a slightly water soluble active ingredient, such as lurasidone, along with a first disintegrant, a second disintegrant, and a water soluble polymer binder (Abstract; p. 4-5, paragraph [0008]). Fujihara et. al. teaches that the composition provides advantageous dissolution characteristics when ingested as well as rapid dissolution of the active ingredient even when the amount is varied in the range of several mg. to several tens of mg. (Abstract; p. 1, para [0001]). The compound N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) is taught as a slightly water soluble active agent in the oral preparation (p. 3, para [0007], item (41); pp. 4-5, para [0008]). The first disintegrant is taught to include corn starch, microcrystalline cellulose, carmellose, carmellose calcium, carmellose sodium, croscarmellose sodium, carboxymethyl starch sodium and

crospovidone (p. 4, lines 6-9; p. 5, paragraph [0011]; p. 22, paragraph [0152], Ex. 28). The first disintegrant is taught to comprise from about 5-300% by weight to the weight of the slightly water soluble active agent (p. 4, item 33). For a tablet having a weight of 137.7 mg., comprising 40 mg. of lurasidone, 5% by weight of the first disintegrant to the weight of lurasidone would be equivalent to about 1.45% by total weight of the tablet (p. 29, paragraph [0194], Table 44). It is taught that one of the water soluble excipients includes sugar alcohols such as mannitol or lactose, D-sorbitol, erythritol, or xylitol (p. 3, paragraph [0017], items (18) and (21); p. 5, paragraph [0014]). The other disintegrant is taught as including excipients such as microcrystalline cellulose, croscarmellose sodium, carmellose, carmellose calcium, carboxymethyl starch sodium, and crosspovidone (p. 5, paragraph [0011]), and the water soluble polymer binder includes polyvinylpyrrolidone, polyvinyl alcohol, hydroxypropyl methylcellulose, and hydroxypropylcellulose (p. 4, lines 10-12; p. 5, paragraph [0010]). It is taught that the amount of lurasidone present in the oral composition is 40 mg. (p. 5, paragraph [0015]; p. 22, paragraph [0152], Table 28), and that the average particle size of lurasidone is between 0.5 to 5 µm (p. 6, paragraph [0021]). It is taught that for a tablet of a weight of 137.7 mg., the amount of lurasidone present is 40 mg., which is approximately 29 % of the weight of the composition (p. 29, paragraph [0194], Table 44). The water soluble polymer binder is taught to comprise from about 1 to 10% by weight of the preparation (p. 4, lines 39-40), and water soluble excipients such as mannitol or lactose are taught to comprise from 200 to 2000 % by weight to the weight of lurasidone (p. 9, paragraph [0066]). Fujihara et. al. provides an example wherein lurasidone comprises 40 mg. of

the tablet, while mannitol comprises 132 mg., of a total mass of 250 mg. for the tablet (p. 23, paragraph [0159], Table 32, Ex. 24). Thus, Fujihara teaches a water soluble excipient such as D-mannitol or lactose to comprise about 53% of the tablet (p. 23, paragraph [0159], Ex. 24 of Table 32; 132 mg./250 mg. is about 53%). Fujihara teachtes the composition to comprise a lubricant selected from magnesium stearate, talc, or hydrogenated oil, in the range of 0.3 to 3% by weight to the total tablet weight (p. 7, paragraphs [0032-0033]). Furthermore, Allenspach teaches incorporating a low viscosity pregelatinized starch, from about 1-50% by weight of the composition, improves the dissolution characteristics for a low water solubility active agent (Abstract; p. 2, paragraphs [0013-0014]; p. 4, para [0044] and [0046]; p. 9, paragraph [0110]). Therefore, it would have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, to have incorporated a pregelatinized starch, a water soluble excipient, a disintegrant, and a lubricant to the tablet composition claimed in appl. '204, at the content ratios recited in the instant claims. Although the instant claims do not recite a process of preparing the oral tablet, and the co-pending claims recite a method of preparing the oral lurasidone tablet, since the product of the instant claims is an obvious variation of the product recited in the co-pending claims, it would have been obvious that that one of ordinary skill in the art would have arrived at the instantly claimed product by practicing the method claimed in the co-pending application. The instant claims and the co-pending claims are therefore not patentably distinct.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Information Disclosure Statements

15. The information disclosure statements (IDS) submitted on 11/12/14; 4/22/15; and 7/15/15 were filed and are of record. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Conclusion

16. Claims 25-57 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

Notice of References Cited	Application/Control No. 14/512,189	Applicant(s)/Patent Under Reexamination FUJIHARA, KAZUYUKI	
	Examiner SARAH PIHONAK	Art Unit 1627	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
	A	US-				
	B	US-				
	C	US-				
	D	US-				
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N	WO 2004017973 A1	03-2004	JP	SAMI SHUNSUKE	A61K31/496
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1627
				Examiner Name	Sarah PIHONAK
Sheet	1	of	1	Attorney Docket Number	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-6,150,366	11-21-2000	Arenson et al.	

U.S. PUBLISHED PATENT APPLICATIONS

Examiner Initials*	Cite No.[3]	Document Number Number-Kind Code[4] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-2004-0186105 A1	09-23-2004	Allenspach et al..	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[5] Number[6] Kind Code[7] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[8]

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[6]
		GHOSH, Tapash K. et al., "Theory and Practice of Contemporary Pharmaceutics," CRC Press, Chapter 10, pg. 279-331 (2005).	
		GENNARO, Alfonso R., "Remington: The Science and Practice of Pharmacy," 19th Edition, Mack Publishing Co., Chapter 92, Vol. II, pp. 1615-1620, [1995]	

Examiner Signature	/SARAH PIHONAK/	Date Considered	02/04/2016

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.P/

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[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.

[3] Applicant's unique citation designation number (optional).
[4] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.
[5] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).
[6] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.
[7] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
[8] Applicant is to place a check mark here if English language Translation is attached.
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**.

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www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 5575

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
14/512,189	10/10/2014 RULE	514	1627	05273.0147-02000

APPLICANTS
SUMITOMO DAINIPPON PHARMA CO., LTD, Osaka, JAPAN;

INVENTORS
Kazuyuki FUJIHARA, Suzuka-shi, JAPAN;

**** CONTINUING DATA ***************************
This application is a CON of 14/183,283 02/18/2014 PAT 8883794
which is a CON of 11/919,678 10/31/2007 PAT 8729085
which is a 371 of PCT/JP2006/310571 05/26/2006

**** FOREIGN APPLICATIONS ***************************
JAPAN 2005-153508 05/26/2005

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****
10/16/2014

Foreign Priority claimed	35 USC 119(a-d) conditions met	Verified and Acknowledged	Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
☑ Yes ☐ No	☑ Yes ☐ No	/SARAH PIHONAK/ Examiner's Signature	☐ Initials	JAPAN	3	35	4

ADDRESS

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER
LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413
UNITED STATES

TITLE

PHARMACEUTICAL COMPOSITION

FILING FEE RECEIVED		
4220	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

BIB (Rev. 05/07).

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	Art Unit
	SARAH PIHONAK	1627

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	02/04/2016								
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	4	-								
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	36	✓								

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	14512189	FUJIHARA, KAZUYUKI
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CLAIM		DATE								
Final	Original	02/04/2016								
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	40	✓								
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	56	✓								
	57	✓								
	58	N								
	59	N								

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	Art Unit
	SARAH PIHONAK	1627

CPC- SEARCHED		
Symbol	Date	Examiner
a61k31/496	2/4/16	s.p.
a61k9/0053,2009,2018,2027,2031,2054,2059,2095	2/4/16	s.p.
c07d417/12	2/4/16	s.p.

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
invention and claims search in stn, east	2/4/16	s.p.
inventor and assignee search in east, palm	2/4/16	s.p.

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

	/SARAH PIHONAK/ Primary Examiner.Art Unit 1627

PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Kazuyuki FUJIHARA	Group Art Unit: 1615
Application No.: 14/512,189	Examiner: *To Be Assigned*
Filed: October 10, 2014	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicant brings to the attention of the Examiner the documents on the attached listing. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

The listed documents are of record in prior Application No. 14/183,283, filing date February 18, 2014, upon which Applicant relies for the benefits provided in 35 U.S.C. § 120. Accordingly copies are not enclosed.

Applicant respectfully requests that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicant determines that the cited document(s) do not constitute

"prior art" under United States law, Applicant reserves the right to present to the U.S. Patent and Trademark Office the relevant facts and law regarding the appropriate status of such documents.

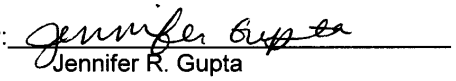
Applicant further reserves the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 12, 2014

By: 
Jennifer R. Gupta
Reg. No. 54,257
(202) 408-4000

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1615
				Examiner Name	To Be Assigned
Sheet	1	of	2	Attorney Docket Number	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-4,600,579	07-15-1986	Salpekar et al.	
		US-5,532,372	07-02-1996	Saji et al.	
		US-2004/0028741 A1	02-12-2004	Fujihara	

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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] Number[4] Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[6]
/S.P/		EP 1327440 A1	07-16-2003	Sumitomo Pharmaceuticals Company, Limited		
/S.P/		JP 08-325146	12-10-1996	Kyowa Hakko Kogyo Co. Ltd.		Abs
/S.P/		JP 2000-26292	01-25-2000	Kissei Pharmaceutical Co., Ltd.		Abs
/S.P/		WO 2004/078173 A1	09-16-2004	Shionogi & Co., Ltd.		Abs
/S.P/		WO 01/76557 A1	10-18-2001	Sumitomo Pharma et al.		
/S.P/		WO 02/24166 A1	03-28-2002	Sumitomo Pharmaceuticals Company, Limited		Abs

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[6]
/S.P/		Request for Invalidation from invalidity proceedings in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation), August 5, 2012.	Yes
/S.P/		Bi Dianzhou, Pharmaceutics, Edition 4, Beijing: People's Medical Publishing House, February 2003.	Yes
/S.P/		"Application and Effect of Pregelatinized Starch in Tablets," Chinese Pharmaceutical Information, Vol.16, Issue 7, 2000, published in 2000	Yes
/S.P/		"Use of Pregelatinized Starch in Tablet Manufacturing," Chinese Pharmaceutical Journal, Vol. 29, Issue 4, April 1994, published in April 1994.	Yes
/S.P/		"Application of the Pregelatinized Starch in Capsules," Chinese Journal of Modern Applied Pharmacy, Vol. 8, Issue 1, February 1991, published in February 1991	Yes
/S.P/		"*In Vitro* Dissolution and Bioavailability of Acyclovir Capsules Formulated with Pregelatinized Starch," Chinese Journal of Pharmaceuticals, 1998, 29(5), published on May 20, 1998.	Yes
/S.P/		Dissolution of Drug Solid Preparation, "Factors Influencing Dissolution Rates," Wu Guangchen, Yue Zhiwei, People's Medical Publishing House, published in October 1994.	Yes
/S.P/		Reply Brief from invalidity proceedings in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation), 2012	Yes

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1615
				Examiner Name	To Be Assigned
Sheet	2	of	2	Attorney Docket Number	05273.0147-02000

NONPATENT LITERATURE DOCUMENTS			
/S.P/		October 25, 2012. cont'd from previous page	
/S.P/		Examination Decision on the Request for Invalidation in corresponding Chinese Application No. 200680018223.4 (original Chinese version and English-language translation), April 26, 2013.	Yes
/S.P/		EPO Communication dated Feb.1, 2012, with enclosed Supplemental Search Report, in EPO Appln. 11181100.6	
/S.P/		Kibbe, Handbook of Pharmaceutical Excipients, Chapter 7, pp. 528-530 (2000)	
/S.P/		Handbook of Pharmaceutical Excipients, 2nd edition, Vol. 491, The Pharmaceutical Press, 1994.	
/S.P/		Chueshov, V. 1., et al., "Manufacturing Technologies of Drugs," Promyshlennaya Technologiya Lekarstv, Vol. 2, pp 10-11 (1999).	partial
/S.P/		Russian Official Action (2009).	partial
/S.P/		Makino, T., et al., "Importance of Gelatinization Degree of Starch Past Binder in Hardness and Disintegration Time of Tablets," Chem. Pharm. Bull., Vol. 43, No 3, pp 514-116 (1995).	

Examiner Signature	/SARAH PIHONAK/	Date Considered	02/04/2016

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
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EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
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L4	46	tablet$1 and l3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 14:23
L5	7	"1535616".PN.	EPO; JPO; DERWENT	OR	OFF	2016/02/04 14:27
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L11	3089	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) and l10	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:24

Par Pharm., Inc.
Exhibit 1013
Page 198

EAST Search History (Prior Art)

L12	0	(benzoisothiazol with piperazinyl with isoindole) and l11	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:26
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L14	23	lurasidone and l11	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:27
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Par Pharm., Inc.
Exhibit 1013
Page 199

EAST Search History (Prior Art)

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S8	2	("20030203020"|"20050147699").PN.	US-PGPUB; USPAT	OR	OFF	2016/02/04 10:12
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Par Pharm., Inc.
Exhibit 1013
Page 200

EAST Search History (Prior Art)

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S19	28	(pregelatin$7 near10 ratio) and S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:08
S20	13	S19 not S18	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:08
S21	4232	starch near2 ("1500")	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:11
S22	73	S15 and S21	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:11

```
Connecting via Winsock to STN at pto-stn on port 23



Welcome to STN International!  Enter x:X

LOGINID:ssptasmp1617

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1  JAN 29  Instructor-led and on-demand STN training options available
                  from CAS
 NEWS  2  JAN 11  STN Express 8.6 Now Available
 NEWS  3  MAR 23  Enhanced Coverage of Latin America (AR, MX) in Derwent World
                  Patent Index
 NEWS  4  APR 15  USPATFULL/USPAT2 Now Include Corporate Patent Applicant
                  Information
 NEWS  5  MAY 22  Country Coverage in Derwent World Patent Index Extended to
                  Include Turkey
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 NEWS  8  JUL 7   100 Millionth Small Molecule Added to CAS REGISTRY
 NEWS  9  SEP 15  New Version of Emtree Introduces over 800 New Terms to
                  Embase on Classic STN and New STN
 NEWS 10  NOV 25  Change to PI field in CAplus records
 NEWS 11  DEC 17  Latest Release of New STN Enhances Search Functionality,
                  Workflow, and Efficiency
 NEWS 12  JAN 11  PatentPak Now available to STN Express 8.6 and STN on the
                  Web customers
 NEWS 13  JAN 11  CAplus Family of Files Updated with New Data to Support
                  PatentPak in STN
 NEWS 14  JAN 14  The Derwent World Patents Index (DWPI): Latest Manual Code
                  Revision is now live

 NEWS EXPRESS 11 JAN 2016 CURRENT WINDOWS VERSION IS V8.6,
              AND CURRENT DISCOVER FILE IS DATED 11 JAN 2016.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *
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FILE 'HOME' ENTERED AT 10:33:21 ON 04 FEB 2016

=> d his

     (FILE 'HOME' ENTERED AT 10:33:21 ON 04 FEB 2016)

=> file caplus
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   0.27   0.27

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FILE COVERS 1907 - 4 Feb 2016 VOL 164 ISS 7
FILE LAST UPDATED: 3 Feb 2016 (20160203/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC)
reclassification data for the first quarter of 2016.

CAplus now includes the comprehensive Cooperative Patent Classification
(CPC). See HELP CPC for details.

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s us 20150056284/pn
L1   1 US 20150056284/PN
                (US20150056284/PN)

=> d l1 abs ibib it

L1   ANSWER 1 OF 1 CAPLUS COPYRIGHT 2016 ACS on STN
AB   A preparation for oral administration comprises a pregelatinized starch comprising N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone hydrochloride) as an active ingredient; a water-soluble excipient; and a water-soluble polymeric binder, where the preparation exhibits an invariant level of elution behavior even when the content of its active ingredient is varied. For example, tablets were formulated containing lurasidone 80, mannitol 144, pregelatinized starch 80,

croscarmellose sodium 4, hydroxypropyl Me cellulose 8, and Mg stearate 4 mg per tablet and film coated with a composition containing hydroxypropyl Me cellulose, titania, polyethylene glycol, and carnauba wax.

ACCESSION NUMBER: 2006:1252571 CAPLUS Full-text
DOCUMENT NUMBER: 146:13212
TITLE: Oral pharmaceutical compositions of lurasidone
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Dainippon Sumitomo Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126681	A1	20061130	WO 2006-JP310571	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006250340	A1	20061130	AU 2006-250340	20060526
AU 2006250340	B2	20120209		
CA 2606510	A1	20061130	CA 2006-2606510	20060526
CA 2606510	C	20140722		
EP 1884242	A1	20080206	EP 2006-746900	20060526
EP 1884242	B1	20130417		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
KR 2008012306	A	20080211	KR 2007-7027270	20060526
KR 1380088	B1	20140410		
CN 101184489	A	20080521	CN 2006-80018223	20060526
CN 101184489	B	20110119		
RU 2398586	C2	20100910	RU 2007-148997	20060526
BR 2006011409	A2	20101123	BR 2006-11409	20060526
CN 102048734	A	20110511	CN 2010-10564784	20060526
CN 102048734	B	20131120		
JP 4733120	B2	20110727	JP 2007-517921	20060526
EP 2422783	A1	20120229	EP 2011-181100	20060526
EP 2422783	B1	20150408		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PT 1884242	E	20130521	PT 2006-746900	20060526
ES 2408687	T3	20130621	ES 2006-746900	20060526
KR 2013122019	A	20131106	KR 2013-7027051	20060526
KR 1552033	B1	20150909		
ES 2535478	T3	20150512	ES 2011-181100	20060526
TW I359020	B	20120301	TW 2006-121223	20060614
US 20090143404	A1	20090604	US 2007-919678	20071031
US 8729085	B2	20140520		
MX 2007014872	A	20080215	MX 2007-14872	20071123
IN 2007CN05369	A	20080125	IN 2007-CN5369	20071126

```
     IN 267160            A1   20150703
     HK 1108379           A1   20130726    HK 2008-102367          20080303
     JP 2011126915        A    20110630    JP 2011-61211           20110318
     JP 5285105           B2   20130911
     US 20140235651       A1   20140821    US 2014-14183283        20140218
     US 8883794           B2   20141111
     US 20150056284       A1   20150226    US 2014-14512189        20141010 <--
     US 20150265611       A1   20150924    US 2015-14733204        20150608
PRIORITY APPLN. INFO.:                      JP 2005-153508       A  20050526
                                            CN 2006-80018223     A3 20060526
                                            EP 2006-746900       A3 20060526
                                            JP 2007-517921       A3 20060526
                                            KR 2007-7027270      A3 20060526
                                            WO 2006-JP310571     W  20060526
                                            US 2007-919678       A1 20071031
                                            US 2014-14183283     A1 20140218
                                            US 2014-14512189     A1 20141010
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IT   Dissolution
     Particle size
     Pharmaceutical coated tablets
     Pharmaceutical granules
     Pharmaceutical tablets
        (oral compns. of lurasidone with improved dissoln. profile)
IT   63-42-3, Lactose   69-65-8, D-Mannitol   9005-25-8D, Starch,
     pregelatinized   367514-87-2, Lurasidone   367514-88-3, Lurasidone
     hydrochloride
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (oral compns. of lurasidone with improved dissoln. profile)
OS.CITING REF COUNT:     2     THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
                               (3 CITINGS)
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> file registry
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     8.09       8.36

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DICTIONARY FILE UPDATES:   3 FEB 2016  HIGHEST RN 1859189-64-2

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```

predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/training/stn/database-specific

```
=> e lurasidone/cn
E1            1     LURAPRET TX-PMC 28/CN
E2            1     LURASAN/CN
E3            1 --> LURASIDONE/CN
E4            1     LURASIDONE HYDROCHLORIDE/CN
E5            1     LURATEX A 25/CN
E6            1     LURAZEPAM/CN
E7            1     LURAZOL BLACK BA/CN
E8            1     LURAZOL BLACK DFN/CN
E9            1     LURAZOL BLACK E/CN
E10           1     LURAZOL BLACK RS/CN
E11           1     LURAZOL BLACK SD/CN
E12           1     LURAZOL BLACK SN/CN

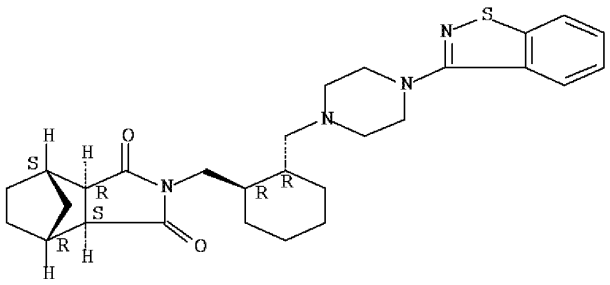
=> set expand continuous
SET COMMAND COMPLETED

=> s e3
L2            1 LURASIDONE/CN

=> d l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2016 ACS on STN
RN   367514-87-2  REGISTRY
ED   Entered STN:  07 Nov 2001
CN   4,7-Methano-1H-isoindole-1,3(2H)-dione,
     2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)-  (CA
     INDEX NAME)
OTHER NAMES:
CN   (3aR,4S,7R,7aS)-2-[[(1R,2R)-2-[[4-(1,2-Benzisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-4,7-methano-1H-isoindole-
     1,3(2H)-dione
CN   2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-
     1H-isoindole-1,3(2H)-dione
CN   Lurasidone
FS   STEREOSEARCH
MF   C28 H36 N4 O2 S
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, TOXCENTER, USPAT2,
       USPATFULL

Absolute stereochemistry.
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

228 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
241 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> s 367514-87-2/crn
L3          13 367514-87-2/CRN

=>  display set notice

SET PARAMETER CURRENT  PERMANENT LOGIN  DEFAULT
------------- -------  --------- ------ -------
NOTICE (USD)
  DISPLAY     'OFF'              'OFF'  '100'
  SEARCH      '1000'             '1000' '1000'

=> FIL REGISTRY

COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   10.25      18.61

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=> S 9005-25-8/RN

L4 1 9005-25-8/RN

=> SET NOTICE 1 DISPLAY

NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
SET COMMAND COMPLETED

=> D L4 SQIDE 1-

YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y
THE ESTIMATED COST FOR THIS REQUEST IS 8.75 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2016 ACS on STN
RN 9005-25-8 REGISTRY
CN Starch (CA INDEX NAME)
OTHER NAMES:
CN α-Starch
CN 1000Y (starch)
CN 75A
CN 75A (polysaccharide)
CN A 1FB004215
CN Absorbo HP
CN AccuGel
CN Ace P 320
CN ADM Clineo 716
CN Aeromyl 115
CN Agglofroid 009
CN Agglofroid 313E
CN Allbond 200
CN Alphajel KS 37
CN Alstar B
CN Alstar E
CN Alstar H
CN Amaizo 100
CN Amaizo 213
CN Amaizo 310
CN Amaizo 5
CN Amaizo 71
CN Amaizo 710
CN Amaizo W 13
CN Amalean I-A 2131
CN Amalean I-A 7081
CN Amerikor 818
CN Amicoa
CN Amidex 3001
CN Amidex 3005
CN Amidex 4001
CN Amido-STA 1500
CN Amidomax 4800

CN Amigel
CN Amigel 12014
CN Amigel 30076
CN Amijel VA 160
CN Amilofaks
CN Amilofax 00
CN Amilys 100
CN Amisol 3408
CN Amycol HF
CN Amycol K
CN Amycol W
CN Amylex 20/20
CN Amylofiber SH
CN Amylogel
CN Amylogel 03001
CN Amylogel 03003
CN Amylogel HB 450
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DEF A high-polymeric carbohydrate material primarily composed of amylopectin and amylose. It is usually derived from cereal grains such as corn, wheat and sorghum, and from roots and tubers such as potatoes and tapioca. It includes starch which has been pregelatinized by heating in the presence of water.
DR 9057-05-0, 42616-76-2, 53112-52-0, 53262-79-6, 60496-95-9, 67674-80-0, 75138-75-9, 75398-82-2, 85746-25-4, 118550-61-1, 131800-97-0, 152987-55-8, 154636-77-8, 730985-55-4, 730985-56-5, 730985-57-6, 955949-61-8, 1309960-29-9, 1374255-25-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
SR CA
LC STN Files: ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFIALL, IPA, MEDLINE, MSDS-OHS, NAPRALERT, PIRA, RTECS*, TOXCENTER, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); NANO (Nanomaterial); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); PRPH (Prophetic); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); NANO (Nanomaterial); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); PRPH (Prophetic); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); NANO (Nanomaterial); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); NANO (Nanomaterial); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or

```
       reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

          180930 REFERENCES IN FILE CA (1907 TO DATE)
           16059 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          185020 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> SET NOTICE OFF DISPLAY

NOTICE SET TO OFF  FOR DISPLAY COMMAND
SET COMMAND COMPLETED

=>

=> d his

     (FILE 'HOME' ENTERED AT 10:33:21 ON 04 FEB 2016)

     FILE 'CAPLUS' ENTERED AT 10:33:41 ON 04 FEB 2016
L1            1 S US 20150056284/PN

     FILE 'REGISTRY' ENTERED AT 10:34:20 ON 04 FEB 2016
                E LURASIDONE/CN
                SET EXPAND CONTINUOUS
L2            1 S E3
L3           13 S 367514-87-2/CRN

     FILE 'REGISTRY' ENTERED AT 10:34:57 ON 04 FEB 2016
L4            1 S 9005-25-8/RN
                SET NOTICE 1 DISPLAY
                SET NOTICE OFF DISPLAY

=> file caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   3.20      21.81

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FILE COVERS 1907 - 4 Feb 2016 VOL 164 ISS 7
FILE LAST UPDATED: 3 Feb 2016 (20160203/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2015
```

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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Dec 2015

CAplus includes complete International Patent Classification (IPC)
reclassification data for the first quarter of 2016.

CAplus now includes the comprehensive Cooperative Patent Classification
(CPC).  See HELP CPC for details.

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d his

     (FILE 'HOME' ENTERED AT 10:33:21 ON 04 FEB 2016)

     FILE 'CAPLUS' ENTERED AT 10:33:41 ON 04 FEB 2016
L1             1 S US 20150056284/PN

     FILE 'REGISTRY' ENTERED AT 10:34:20 ON 04 FEB 2016
                 E LURASIDONE/CN
                 SET EXPAND CONTINUOUS
L2             1 S E3
L3            13 S 367514-87-2/CRN

     FILE 'REGISTRY' ENTERED AT 10:34:57 ON 04 FEB 2016
L4             1 S 9005-25-8/RN
                 SET NOTICE 1 DISPLAY
                 SET NOTICE OFF DISPLAY

     FILE 'CAPLUS' ENTERED AT 10:35:15 ON 04 FEB 2016

=> s l2 or l3
            241 L2
            116 L3
L5          301 L2 OR L3

=> s l4
L6       185020 L4

=> s l5 and l6
L7           14 L5 AND L6

=> s l7 and (ay<=2006 or py<=2006 or pry<=2006)
        6029724 AY<=2006
       27662969 PY<=2006
        5523015 PRY<=2006
L8            2 L7 AND (AY<=2006 OR PY<=2006 OR PRY<=2006)

=> s l8 not l1
L9            1 L8 NOT L1

=> d l9 abs ibib hitind hitstr

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2016 ACS on STN
AB    Disclosed are oral compns. containing a hardly water-soluble active ingredient and
      having favorable disintegration characteristics which comprise a molded solid
```

article (for example, granules) obtained by mixing the hardly water-soluble active ingredient, a first disintegrating agent and a water-soluble filler with the use of a water-soluble polymer binder and then mixing this molded solid article with a second disintegrating agent, or a molded solid article obtained by mixing the hardly water-soluble active ingredient, a disintegrating agent and a sugar alc. with the use of a water-soluble polymer binder. When orally administered, these prepns. show excellent elution of the active ingredient in the digestive tract. Moreover, these prepns. can show the same elution behavior at different contents of the active ingredient and thus enable the selection of the most suitable drug for each patient, which makes these prepns. highly useful in clin. medicine. A film-coated tablet was prepared form granules containing N-[4-[4-(1,2-benzisothiazole-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride 10, lactose 50, sodium croscarmellose 6 mg, and polyvinyl alc. 1.2 mg, calcium hydrogen phosphate anhydride 35, crystalline cellulose 17, and magnesium stearate 0.8 mg, and a coating material containing hydroxypropyl Me cellulose 1.95, titanium oxide 0.6, concentrate glycerin 0.45 mg, and carnauba wax q.s.

ACCESSION NUMBER: 2002:240535 CAPLUS Full-text
DOCUMENT NUMBER: 136:268164
TITLE: Oral compositions with favorable disintegration characteristics
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024166	A1	20020328	WO 2001-JP7983	20010914 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 20040028741	A1	20040212	US 2003-381036		20030321 <--
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			WO 2001-JP7983	W	20010914 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

IPCI A61K0009-16 [ICM,7]; A61K0009-20 [ICS,7]; A61K0009-30 [ICS,7]; A61K0031-496 [ICS,7]; A61K0045-00 [ICS,7]; A61K0047-10 [ICS,7]; A61K0047-26 [ICS,7]; A61K0047-30 [ICS,7]

IPCR A61K0009-00 [I]; A61K0009-16 [I]; A61K0009-20 [I]; A61K0009-30 [I]; A61K0031-496 [I]

CC 63-6 (Pharmaceuticals)

IT 63-42-3, Lactose 69-65-8, D-Mannitol 557-04-0, Magnesium stearate 7757-93-9, Calcium hydrogen phosphate 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinyl pyrrolidone 9004-34-6, Crystalline cellulose, biological studies 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Corn starch, biological studies 74811-65-7, Sodium croscarmellose 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing hardly water-soluble active ingredients)

IT 9005-25-8, Corn starch, biological studies 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing hardly water-soluble active ingredients)

RN 9005-25-8 CAPLUS

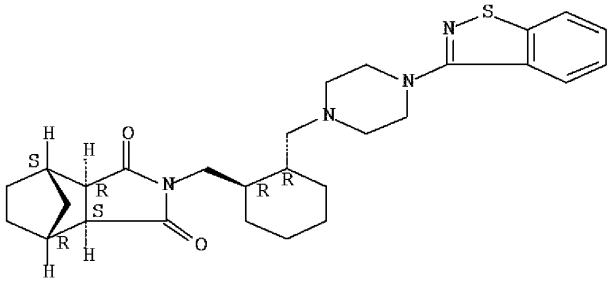
CN Starch (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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L6        185020 S L4
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L8             2 S L7 AND (AY<=2006 OR PY<=2006 OR PRY<=2006)
L9             1 S L8 NOT L1

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L10       3083 (STARCH (S) PREGELATIN?)

=> d his

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L9             1 SEA SPE=ON  ABB=ON  PLU=ON  L8 NOT L1
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Connecting via Winsock to STN at pto-stn on port 23



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LOGINID:ssptasmp1617

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1  JAN 29  Instructor-led and on-demand STN training options available
                  from CAS
 NEWS  2  JAN 11  STN Express 8.6 Now Available
 NEWS  3  MAR 23  Enhanced Coverage of Latin America (AR, MX) in Derwent World
                  Patent Index
 NEWS  4  APR 15  USPATFULL/USPAT2 Now Include Corporate Patent Applicant
                  Information
 NEWS  5  MAY 22  Country Coverage in Derwent World Patent Index Extended to
                  Include Turkey
 NEWS  6  MAY 28  Partner with CAS to help shape the future of CAS products!
 NEWS  7  JUL 2   Major Update to GBFULL Improves Quality of Full Text
 NEWS  8  JUL 7   100 Millionth Small Molecule Added to CAS REGISTRY
 NEWS  9  SEP 15  New Version of Emtree Introduces over 800 New Terms to
                  Embase on Classic STN and New STN
 NEWS 10  NOV 25  Change to PI field in CAplus records
 NEWS 11  DEC 17  Latest Release of New STN Enhances Search Functionality,
                  Workflow, and Efficiency
 NEWS 12  JAN 11  PatentPak Now available to STN Express 8.6 and STN on the
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 NEWS 13  JAN 11  CAplus Family of Files Updated with New Data to Support
                  PatentPak in STN
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 NEWS 14  JAN 14  The Derwent World Patents Index (DWPI): Latest Manual Code
                  Revision is now live

 NEWS EXPRESS 11 JAN 2016 CURRENT WINDOWS VERSION IS V8.6,
              AND CURRENT DISCOVER FILE IS DATED 11 JAN 2016.

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FULL ESTIMATED COST                                   0.27       0.27

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DICTIONARY FILE UPDATES:   3 FEB 2016  HIGHEST RN 1859189-64-2

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=> e lurasidone/cn
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ED   Entered STN:  07 Nov 2001
CN   4,7-Methano-1H-isoindole-1,3(2H)-dione,
     2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
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MF   C28 H36 N4 O2 S
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Absolute stereochemistry.
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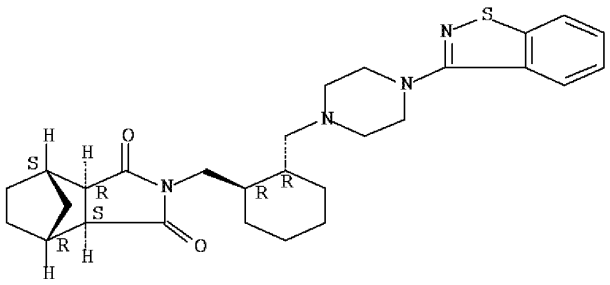

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

228 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
241 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	10.25	10.52

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FILE COVERS 1907 - 4 Feb 2016 VOL 164 ISS 7
FILE LAST UPDATED: 3 Feb 2016 (20160203/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC) reclassification data for the first quarter of 2016.

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L4   ANSWER 1 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB   The invention relates to articles and related devices and systems having surface topog. and/or surface elastic properties for providing nontoxic bioadhesion control. An article includes a first plurality of spaced features arranged in a plurality of groupings including repeat units. The spaced features within a grouping are spaced apart at an average distance of about 1 nm to about 500 μm, each feature having a surface that is substantially parallel to a surface on a neighboring feature separated from its neighboring feature. The groupings of features are arranged with respect to one another so as to define a tortuous pathway. The plurality of spaced features provide the article with an engineered roughness index of about 5 to about 20.
ACCESSION NUMBER: 2010:1127861 CAPLUS Full-text
DOCUMENT NUMBER: 153:440825
TITLE: Surface topographies for non-toxic bioadhesion control
INVENTOR(S):   Brennan, Anthony B.; Long, Christopher James; Bagan, Joseph W.; Schumacher, James Frederick; Spiecker, Mark M.
PATENT ASSIGNEE(S):   University of Florida, USA
SOURCE: U.S. Pat. Appl. Publ., 64pp., Cont.-in-part of U.S. Ser. No. 567,103.
                         CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20100226943	A1	20100909	US 2009-550870	20090831 <--
US 9016221	B2	20150428		
US 20050178286	A1	20050818	US 2004-780424	20040217 <--

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INCL 424400000; 428141000; 428143000
IPCI A61K0009-00 [I]; B32B0003-00 [I]; A61K0009-70 [I]; B63B0059-04 [I];
     B08B0017-02 [I]; B08B0017-06 [I]; A61F0002-02 [I]; A61L0027-00 [I];
     A41D0031-00 [I]; A61L0002-02 [I]; B64D0015-00 [I]; A61F0002-00 [N];
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NCL  424/400.000; 428/141.000; 428/143.000; 114/067.000R; 114/222.000
CC   63-7 (Pharmaceuticals)
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IT   195883-06-8, Omtriptolide   196597-26-9, Ramelteon   196612-93-8,
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     197509-46-9, Laniquidar   198022-65-0, Icofungipen   198283-73-7,
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557795-19-4, Sunitinib 566906-50-1, Beminafil 569351-91-3, Dasantafil
641571-10-0, Nilotinib 677017-23-1, Berubicin 678160-57-1, Zoticasone
679809-58-6, Enoxaparin 698387-09-6, Neratinib 715646-49-4,
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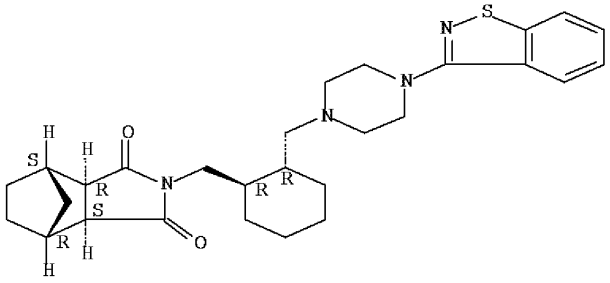
Gadobutrol
RL: PRP (Properties); TEM (Technical or engineered material use); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(surface topogs. for nontoxic bioadhesion control)

IT 367514-87-2, Lurasidone
RL: PRP (Properties); TEM (Technical or engineered material use); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(surface topogs. for nontoxic bioadhesion control)

RN 367514-87-2 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA
INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB It is intended to provide a granular preparation which scarcely undergoes caking during preservation, namely, a granular preparation characterized by containing an active ingredient other than a biguanide-type drug, a sugar or a sugar alc., an organic acid and a specific water-soluble polysaccharide and being prevented from caking; and a method of preventing a granular preparation from caking which comprises adding a specific water-soluble polysaccharide to the active ingredient as described above, a sugar or a sugar alc. and an organic acid. For example, mosapride citrate dihydrate, mannitol, and malic acid were extrusion granulated and pullulan was added; after 4 day storage at 40°, no agglutination was observed

ACCESSION NUMBER: 2008:529939 CAPLUS Full-text
DOCUMENT NUMBER: 148:503185
TITLE: Granular preparation prevented from caking
INVENTOR(S): Matsui, Yasuhiro; Ikeda, Yuki; Ochiai, Yasushi
PATENT ASSIGNEE(S): Dainippon Sumitomo Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008050847	A1	20080502	WO 2007-JP70854	20071025 <--

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KR 2009081407 A 20090728 KR 2009-7010551 20071025 <--
EP 2095812 A1 20090902 EP 2007-830588 20071025 <--
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CN 101541311 A 20090923 CN 2007-80044336 20071025 <--
CN 101541311 B 20130123
JP 5315056 B2 20131016 JP 2008-541029 20071025 <--
US 20100093875 A1 20100415 US 2009-446783 20090602 <--
PRIORITY APPLN. INFO.: JP 2006-290561 A 20061025 <--
WO 2007-JP70854 W 20071025

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

IPCI A61K0009-14 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-26 [I]; A61K0047-36 [I]

IPCR A61K0009-14 [I]; A61K0047-10 [I]; A61K0047-12 [I]; A61K0047-26 [I]; A61K0047-36 [I]

CC 63-6 (Pharmaceuticals)

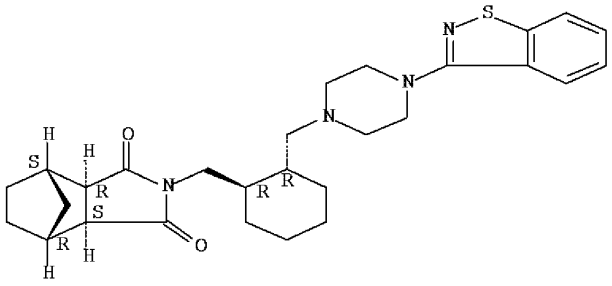
IT 50-70-4, Sorbitol, biological studies 50-81-7, L-Ascorbic acid, biological studies 69-65-8, D-Mannitol 77-92-9, Citric acid, biological studies 87-69-4, Tartaric acid, biological studies 87-99-0, Xylitol 99-20-7, Trehalose 103-90-2, Acetaminophen 110-15-6, Succinic acid, biological studies 149-32-6, Erythritol 585-88-6, Maltitol 6915-15-7, Malic acid 9004-53-9, Dextrin 9057-02-7, Pullulan 21187-98-4, Gliclazide 68291-97-4, Zonisamide 132810-10-7, Blonanserin 147254-64-6, Ranirestat 219846-31-8 367514-88-3 , Lurasidone hydrochloride 609768-14-1 636582-62-2, Mosapride citrate dihydrate 914389-14-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caking-free granular prepns. containing sugar alcs. and acids and polysaccharides)

IT 367514-88-3, Lurasidone hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caking-free granular prepns. containing sugar alcs. and acids and polysaccharides)

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

(2 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB Disclosed are combinations and combination therapies for the treatment of insomnia in patients with psychotic disorders or with psychotic features, patients with bipolar depression, and patients with major depression with psychotic features.

ACCESSION NUMBER: 2007:1363699 CAPLUS Full-text
DOCUMENT NUMBER: 148:24465
TITLE: Melatonin agonist and antipsychotic agent combinations for treatment of insomnia
INVENTOR(S): Polymeropoulos, Mihael H.; Wolfgang, Curt D.; Birznieks, Gunther; Phadke, Deepak
PATENT ASSIGNEE(S): Vanda Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 20pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007137224	A2	20071129	WO 2007-US69366	20070521 <--
WO 2007137224	A3	20080124		

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-60747866 P 20060522 <--
IPCI A61K0031-519 [I]; A01N0043-34 [I]; A01N0043-38 [I]; A61K0031-40 [I]; A61K0031-40 [I]
IPCR A01N0043-34 [I]; A01N0043-38 [I]; A61K0031-40 [I]; A61K0031-40 [I]
CC 1-11 (Pharmacology)
IT 50-52-2, Thioridazine 50-52-2D, Thioridazine, metabolites 50-53-3, Chlorpromazine, biological studies 50-53-3D, Chlorpromazine, metabolites 52-86-8, Haloperidol 52-86-8D, Haloperidol, metabolites 58-38-8, Prochlorperazine 58-38-8D, Prochlorperazine, metabolites 58-39-9, Perphenazine 58-39-9D, Perphenazine, metabolites 69-23-8, Fluphenazine 69-23-8D, Fluphenazine, metabolites 73-31-4, Melatonin 92-84-2D, Phenothiazine, derivs. 113-59-7, Chlorprothixene 113-59-7D, Chlorprothixene, metabolites 117-89-5, Trifluoperazine 117-89-5D, Trifluoperazine, metabolites 261-31-4D, Thioxanthene, derivs. 271-95-4D, 1,2-Benzisoxazole, derivs. 312-84-5, D-Serine 312-84-5D, D-Serine, metabolites 495-40-9D, Butyrophenone, derivs. 1393-25-5, Secretin 1393-25-5D, Secretin, metabolites 1977-10-2, Loxapine 1977-10-2D, Loxapine, metabolites 2062-78-4, Pimozide 2062-78-4D, Pimozide, metabolites 3313-26-6, Thiothixene 3313-26-6D, Thiothixene, metabolites 5588-33-0, Mesoridazine 5588-33-0D, Mesoridazine, metabolites 5786-21-0, Clozapine 5786-21-0D, Clozapine, metabolites 7416-34-4, Molindone 7416-34-4D, Molindone, metabolites 15676-16-1, Sulpiride 15676-16-1D, Sulpiride, metabolites 31096-91-0, Phenylindole

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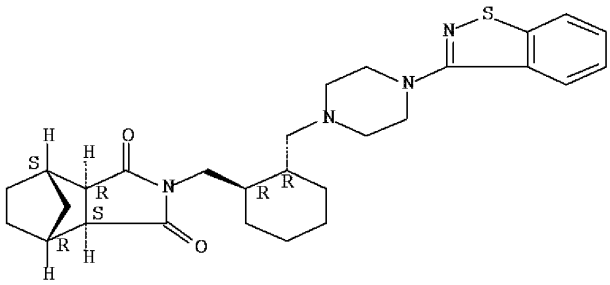
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melatonin agonist and antipsychotic agent combinations for treatment of insomnia)

IT 367514-88-3, SM-13496 367514-88-3D, SM-13496, metabolites
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melatonin agonist and antipsychotic agent combinations for treatment of insomnia)

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

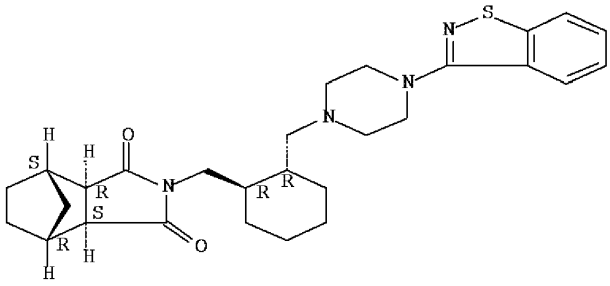
Absolute stereochemistry.



● HCl

RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB The invention relates to the use of the compound escitalopram (INN-name), i.e. (S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile, or a pharmaceutically acceptable salt thereof for the preparation of a medicament for improving cognition in a condition where the cognitive processes are diminished.

ACCESSION NUMBER:	2007:1277443 CAPLUS Full-text
DOCUMENT NUMBER:	147:515074
TITLE:	Escitalopram for improving diminished cognition processes
INVENTOR(S):	Svensson, Hans Torgny
PATENT ASSIGNEE(S):	H. Lundbeck A/S, Den.
SOURCE:	PCT Int. Appl., 24 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

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LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
     PATENT NO.          KIND  DATE        APPLICATION NO.          DATE
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     WO 2007124757        A2   20071108    WO 2007-DK50050          20070430 <--
     WO 2007124757        A3   20080724
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             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
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             BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
     AU 2007245983        A1   20071108    AU 2007-245983           20070430 <--
     CA 2651002           A1   20071108    CA 2007-2651002          20070430 <--
     AR 60732             A1   20080710    AR 2007-101874           20070430 <--
     EP 2026793           A2   20090225    EP 2007-722705           20070430 <--
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR,
             AL, BA, HR, MK, RS
     JP 2009535367        T    20091001    JP 2009-508134           20070430 <--
     ZA 2008008632        A    20100127    ZA 2008-8632             20070430 <--
     BR 2007010230        A2   20110802    BR 2007-10230            20070430 <--
     KR 2009009820        A    20090123    KR 2008-7025797          20081022 <--
     CN 101426494         A    20090506    CN 2007-80014675         20081023 <--
     MX 2008013911        A    20081112    MX 2008-13911            20081030 <--
     IN 2008CN05930       A    20090327    IN 2008-CN5930           20081031 <--
     NO 2008005009        A    20081216    NO 2008-5009             20081202 <--
PRIORITY APPLN. INFO.:                      DK 2006-621          A  20060502 <--
                                            WO 2007-DK50050      W  20070430
IPCI A61K0031-343 [I]; A61P0025-28 [I]; A61P0025-16 [I]; A61P0025-22 [I];
     A61P0025-24 [I]; A61P0025-30 [I]; A61K0031-343 [I]; A61K0031-343 [I];
     A61P0025-00 [I]; A61P0025-16 [I]; A61P0025-22 [I]; A61P0025-24 [I];
     A61P0025-28 [I]; A61P0025-30 [I]
IPCR A61K0031-343 [I]; A61P0025-16 [I]; A61P0025-22 [I]; A61P0025-24 [I];
     A61P0025-28 [I]; A61P0025-30 [I]
CC   1-11 (Pharmacology)
     Section cross-reference(s): 63
IT   50-52-2, Thioridazine   50-53-3, Chlorpromazine, biological studies
     52-86-8, Haloperidol   58-38-8, Prochlorperazine   58-39-9, Perphenazine
     58-40-2, Promazine   60-99-1, Levomepromazine   61-00-7, Acepromazine
     69-23-8, Fluphenazine   84-01-5, Chlorproethazine   84-06-0, Thiopropazate
     84-97-9, Perazine   113-59-7, Chlorprothixene   117-89-5, Trifluoperazine
     146-54-3, Triflupromazine   153-87-7, Oxypertine   303-69-5, Prothipendyl
     316-81-4, Thioproperazine   548-73-2, Droperidol   653-03-2, Butaperazine
     749-13-3, Trifluperidol   982-24-1, Clopenthixol   1050-79-9, Moperone
     1480-19-9, Fluanisone   1841-19-6, Fluspirilene   1893-33-0, Pipamperone
     1977-10-2, Loxapine   2058-52-8, Clotiapine   2062-78-4, Pimozide
     2062-84-2, Benperidol   2470-73-7, Dixyrazine   2622-26-6, Periciazine
     2709-56-0, Flupentixol   2751-68-0, Acetophenazine   3313-26-6, Tiotixene
     3546-03-0, Cyamemazin   3575-80-2, Melperone   5588-33-0, Mesoridazine
     5786-21-0, Clozapine   6104-71-8, ACP 104   7416-34-4, Molindone
     10457-90-6, Bromperidol   15676-16-1, Sulpiride   23672-07-3,
     Levosulpiride   26615-21-4, Zotepine   26864-56-2, Penfluridol
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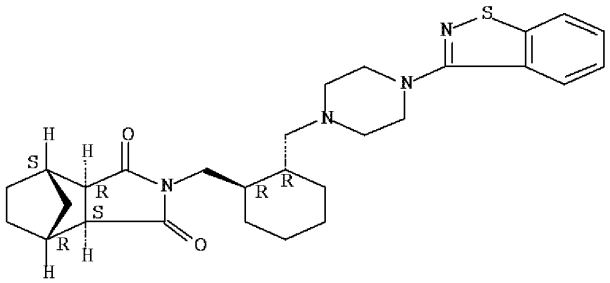
39860-99-6, Pipotiazine 51012-32-9, Tiapride 53583-79-2, Sultopride
53772-83-1, Zuclopenthixol 59729-33-8, Citalopram 65576-45-6,
Asenapine 66644-81-3, Veralipride 71620-89-8, Reboxetine 71675-85-9,
Amisulpride 80125-14-0, Remoxipride 89419-40-9, Mosapramine
106266-06-2, Risperidone 106516-24-9, Sertindole 111974-69-7,
Quetiapine 128196-01-0, Escitalopram 128196-01-0D, Escitalopram, salt
128196-02-1 129029-23-8, Ocaperidone 129722-12-9, Aripiprazole
132539-06-1, Olanzapine 132810-10-7, Blonanserin 133454-47-4,
Iloperidone 144598-75-4, Paliperidone 146939-27-7, Ziprasidone
174636-32-9, Talnetant 221058-54-4, Y-931 264869-71-8, SLV 310
346688-38-8, ACR 16 350992-10-8, Bifeprunox 367514-87-2,
Lurasidone 839712-12-8, RGH 188 932034-23-6, YKP 1358 949119-38-4,
SLV 314 955400-63-2, GW 773812
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(escitalopram for improving diminished cognitive processes)

IT 367514-87-2, Lurasidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(escitalopram for improving diminished cognitive processes)

RN 367514-87-2 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA
INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB The invention discloses the use of the compound escitalopram (INN-name), i.e. (S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile, or a pharmaceutically acceptable salt thereof for the preparation of a medicament for improving cognition in a condition where the cognitive processes are diminished.

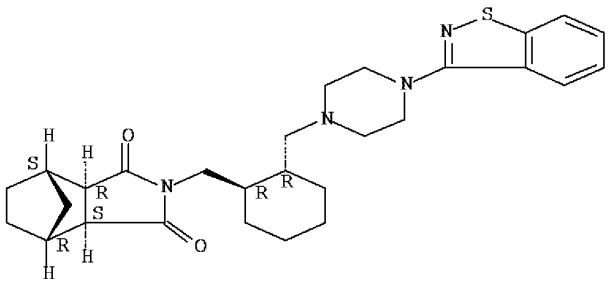
ACCESSION NUMBER: 2007:1270852 CAPLUS Full-text
DOCUMENT NUMBER: 147:496359
TITLE: Use of escitalopram for improvement of cognition in a condition where the cognitive processes are diminished
INVENTOR(S): Svensson, Hans Torgny
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: U.S. Pat. Appl. Publ., 11pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20070259952	A1	20071108	US 2007-741371		20070427	<--
PRIORITY APPLN. INFO.:			US 2006-60746238	P	20060502	<--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
INCL 514469000
IPCI A61K0031-343 [I]
IPCR A61K0031-343 [I]
NCL 514/469.000
CC 1-11 (Pharmacology)
IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies
52-86-8, Haloperidol 58-38-8, Prochlorperazine 58-39-9, Perphenazine
58-40-2, Promazine 60-99-1, Levomepromazine 61-00-7, Acepromazine
69-23-8, Fluphenazine 84-01-5, Chlorproethazine 84-06-0, Thiopropazate
84-97-9, Perazine 113-59-7, Chlorprothixene 117-89-5, Trifluoperazine
146-54-3, Triflupromazine 153-87-7, Oxypertine 303-69-5, Prothipendyl
316-81-4, Thioproperazine 548-73-2, Droperidol 653-03-2, Butaperazine
749-13-3, Trifluperidol 982-24-1, Clopenthixol 1050-79-9, Moperone
1480-19-9, Fluanisone 1841-19-6, Fluspirilene 1893-33-0, Pipamperone
1977-10-2, Loxapine 2058-52-8, Clotiapine 2062-78-4, Pimozide
2062-84-2, Benperidol 2470-73-7, Dixyrazine 2622-26-6, Periciazine
2709-56-0, Flupentixol 2751-68-0, Acetophenazine 3313-26-6, Tiotixene
3546-03-0, Cyamemazine 3575-80-2, Melperone 5588-33-0, Mesoridazine
5786-21-0, Clozapine 6104-71-8 7416-34-4, Molindone 10457-90-6,
Bromperidol 15676-16-1, Sulpiride 23672-07-3, Levosulpiride
26615-21-4, Zotepine 26864-56-2, Penfluridol 39860-99-6, Pipotiazine
51012-32-9, Tiapride 53583-79-2, Sultopride 53772-83-1, Zuclopenthixol
65576-45-6, Asenapine 66644-81-3, Veralipride 71675-85-9, Amisulpride
80125-14-0, Remoxipride 89419-40-9, Mosapramine 106266-06-2,
Risperidone 106516-24-9, Sertindole 111974-69-7, Quetiapine
128196-01-0, Escitalopram 129029-23-8, Ocaperidone 129722-12-9,
Aripiprazole 132539-06-1, Olanzapine 132810-10-7, Blonanserin
133454-47-4, Iloperidone 144598-75-4, Paliperidone 146939-27-7,
Ziprasidone 174636-32-9, Talnetant 221058-54-4, Y-931 264869-71-8,
SLV 310 346688-38-8, ACR 16 350992-10-8, Bifeprunox
367514-87-2, Lurasidone 751477-01-7 839712-12-8, RGH 188
932034-23-6, YKP 1358 949119-38-4, SLV 314 955400-63-2, GW 773812
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(escitalopram for improvement of cognition in condition with diminished
cognitive processes)
IT 367514-87-2, Lurasidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(escitalopram for improvement of cognition in condition with diminished
cognitive processes)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA
INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB A solution-type preparation comprises lurasidone or its acid addition salts, preferably hydrochloride salt, as an active ingredient and at least one substance selected from benzyl alc., N,N-dimethylacetamide, lactic acid and propylene glycol. The solns. comprise high concentration of lurasidone for the treatment of mental disorders.

ACCESSION NUMBER: 2006:1337840 CAPLUS Full-text
DOCUMENT NUMBER: 146:68724
TITLE: Pharmaceutical solutions containing lurasidone
INVENTOR(S): Otoda, Kazuya; Nakamura, Mayumi; Ariyama, Teruko; Nakagawa, Takashi
PATENT ASSIGNEE(S): Dainippon Sumitomo Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006134864	A1	20061221	WO 2006-JP311739	20060612 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1891956	A1	20080227	EP 2006-766601	20060612 <--
EP 1891956	B1	20120829		
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KR 2008024118	A	20080317	KR 2007-7028359	20060612 <--
KR 1328857	B1	20131113		
CN 101198331	A	20080611	CN 2006-80021027	20060612 <--
CN 101198331	B	20120502		
JP 4866349	B2	20120201	JP 2007-521271	20060612 <--
ES 2390353	T3	20121112	ES 2006-766601	20060612 <--
US 20090286805	A1	20091119	US 2007-922015	20071212 <--

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     US 8283352           B2   20121009
     HK 1109088           A1   20130215    HK 2008-103361          20080326 <--
PRIORITY APPLN. INFO.:                     JP 2005-172725       A  20050613 <--
                                           WO 2006-JP311739     W  20060612 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IPCI A61K0031-496 [I]; A61K0009-08 [I]; A61K0047-10 [I]; A61K0047-12 [I];
     A61K0047-16 [I]; A61P0025-18 [I]; A61P0025-28 [I]
IPCR A61K0031-496 [I]; A61K0009-08 [I]; A61K0047-10 [I]; A61K0047-12 [I];
     A61K0047-16 [I]; A61P0025-18 [I]; A61P0025-28 [I]
CC   63-6 (Pharmaceuticals)
IT   50-21-5, Lactic acid, biological studies   57-55-6, Propylene glycol,
     biological studies   64-17-5, Ethanol, biological studies   64-19-7,
     Acetic acid, biological studies   100-51-6, Benzyl alcohol, biological
     studies   127-19-5, N,N-Dimethylacetamide   367514-87-2,
     Lurasidone   367514-88-3, Lurasidone hydrochloride
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical solns. containing lurasidone)
IT   367514-87-2, Lurasidone   367514-88-3, Lurasidone
     hydrochloride
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical solns. containing lurasidone)
RN   367514-87-2  CAPLUS
CN   4,7-Methano-1H-isoindole-1,3(2H)-dione,
     2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)-  (CA
     INDEX NAME)

Absolute stereochemistry.
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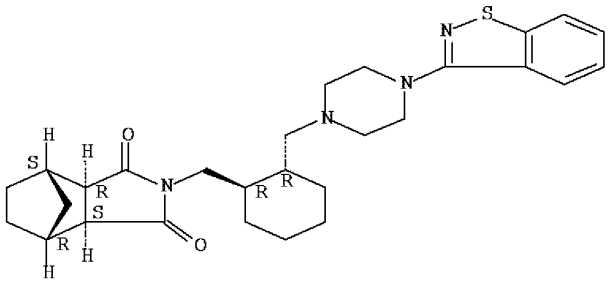

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RN   367514-88-3  CAPLUS
CN   4,7-Methano-1H-isoindole-1,3(2H)-dione,
     2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
     (3aR,4S,7R,7aS)-  (CA INDEX NAME)

Absolute stereochemistry.
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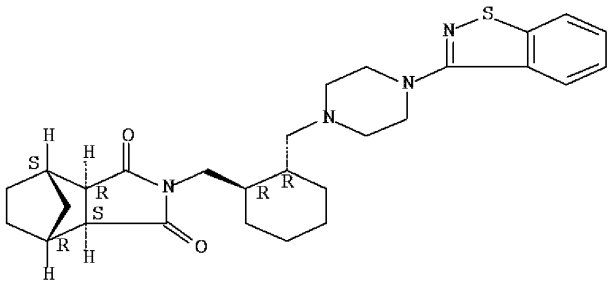

● HCl

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB A preparation for oral administration comprises a pregelatinized starch comprising N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone hydrochloride) as an active ingredient; a water-soluble excipient; and a water-soluble polymeric binder, where the preparation exhibits an invariant level of elution behavior even when the content of its active ingredient is varied. For example, tablets were formulated containing lurasidone 80, mannitol 144, pregelatinized starch 80, croscarmellose sodium 4, hydroxypropyl Me cellulose 8, and Mg stearate 4 mg per tablet and film coated with a composition containing hydroxypropyl Me cellulose, titania, polyethylene glycol, and carnauba wax.

ACCESSION NUMBER: 2006:1252571 CAPLUS Full-text
DOCUMENT NUMBER: 146:13212
TITLE: Oral pharmaceutical compositions of lurasidone
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Dainippon Sumitomo Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126681	A1	20061130	WO 2006-JP310571	20060526 <--

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM

AU 2006250340	A1	20061130	AU 2006-250340	20060526	<--
AU 2006250340	B2	20120209			
CA 2606510	A1	20061130	CA 2006-2606510	20060526	<--
CA 2606510	C	20140722			
EP 1884242	A1	20080206	EP 2006-746900	20060526	<--
EP 1884242	B1	20130417			
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR					
KR 2008012306	A	20080211	KR 2007-7027270	20060526	<--
KR 1380088	B1	20140410			
CN 101184489	A	20080521	CN 2006-80018223	20060526	<--
CN 101184489	B	20110119			
RU 2398586	C2	20100910	RU 2007-148997	20060526	<--
BR 2006011409	A2	20101123	BR 2006-11409	20060526	<--
CN 102048734	A	20110511	CN 2010-10564784	20060526	<--
CN 102048734	B	20131120			
JP 4733120	B2	20110727	JP 2007-517921	20060526	<--
EP 2422783	A1	20120229	EP 2011-181100	20060526	<--
EP 2422783	B1	20150408			
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PT 1884242	E	20130521	PT 2006-746900	20060526	<--
ES 2408687	T3	20130621	ES 2006-746900	20060526	<--
KR 2013122019	A	20131106	KR 2013-7027051	20060526	<--
KR 1552033	B1	20150909			
ES 2535478	T3	20150512	ES 2011-181100	20060526	<--
TW I359020	B	20120301	TW 2006-121223	20060614	<--
US 20090143404	A1	20090604	US 2007-919678	20071031	<--
US 8729085	B2	20140520			
MX 2007014872	A	20080215	MX 2007-14872	20071123	<--
IN 2007CN05369	A	20080125	IN 2007-CN5369	20071126	<--
IN 267160	A1	20150703			
HK 1108379	A1	20130726	HK 2008-102367	20080303	<--
JP 2011126915	A	20110630	JP 2011-61211	20110318	<--
JP 5285105	B2	20130911			
US 20140235651	A1	20140821	US 2014-14183283	20140218	<--
US 8883794	B2	20141111			
US 20150056284	A1	20150226	US 2014-14512189	20141010	<--
US 20150265611	A1	20150924	US 2015-14733204	20150608	<--

PRIORITY APPLN. INFO.:	JP 2005-153508	A	20050526	<--
	CN 2006-80018223	A3	20060526	<--
	EP 2006-746900	A3	20060526	<--
	JP 2007-517921	A3	20060526	<--
	KR 2007-7027270	A3	20060526	<--
	WO 2006-JP310571	W	20060526	<--
	US 2007-919678	A1	20071031	
	US 2014-14183283	A1	20140218	
	US 2014-14512189	A1	20141010	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

IPCI A61K0031-496 [I]; A61K0009-20 [I]; A61K0047-10 [I]; A61K0047-26 [I]; A61K0047-38 [I]; C07D0417-12 [I]

IPCR A61K0031-496 [I]; A61K0009-20 [I]; A61K0047-10 [I]; A61K0047-26 [I]; A61K0047-38 [I]; C07D0417-12 [I]

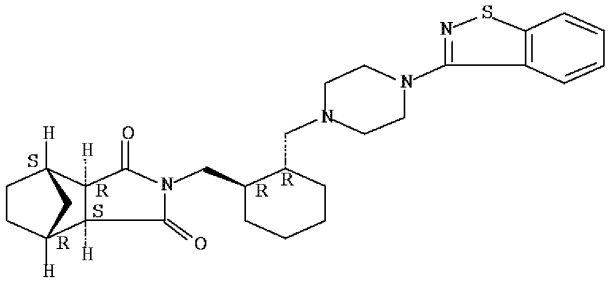
CC 63-6 (Pharmaceuticals)

IT 63-42-3, Lactose 69-65-8, D-Mannitol 9005-25-8D, Starch, pregelatinized 367514-87-2, Lurasidone 367514-88-3, Lurasidone hydrochloride

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. of lurasidone with improved dissoln. profile)

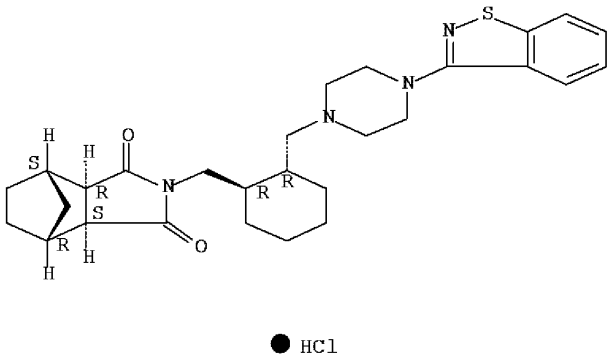
IT 367514-87-2, Lurasidone 367514-88-3, Lurasidone hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. of lurasidone with improved dissoln. profile)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB The invention relates to new pharmaceutical compns. for the treatment and/or prevention of schizophrenia and methods for the preparation thereof. In a preferred embodiment, the instant invention is directed to pharmaceutical combinations comprising flibanserin as one active ingredient in combination with at least one addnl. active ingredient for the treatment and/or prevention of schizophrenia and methods for the preparation thereof.

ACCESSION NUMBER: 2006:950847 CAPLUS Full-text
DOCUMENT NUMBER: 145:342440
TITLE: Pharmaceutical compositions for the treatment and/or prevention of schizophrenia and related diseases
INVENTOR(S): Pyke, Robert; Ceci, Angelo
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co KG
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006096439	A2	20060914	WO 2006-US7379	20060227 <--
WO 2006096439	A3	20070208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2599699	A1	20060914	CA 2006-2599699	20060228 <--
US 20060204486	A1	20060914	US 2006-364306	20060228 <--
EP 1858517	A2	20071128	EP 2006-736660	20060228 <--
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008531715	T	20080814	JP 2007-558203	20060228 <--
PRIORITY APPLN. INFO.:			US 2005-60658566 P	20050304 <--
			WO 2006-US7379 W	20060227 <--

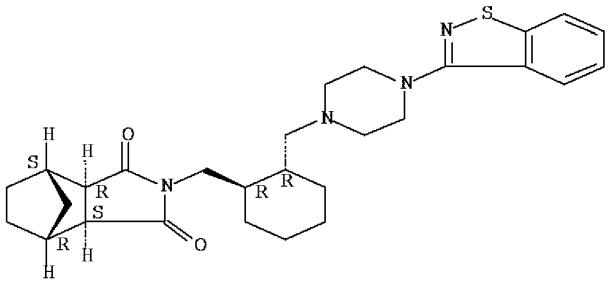
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IPCI A61K0031-496 [I]; A61K0009-30 [I]; A61K0009-48 [I]; A61P0025-00 [I]; A61K0031-496 [I]; A61K0009-36 [I]; A61K0009-48 [I]; A61P0025-18 [I]
IPCR A61K0031-496 [I]; A61K0009-36 [I]; A61K0009-48 [I]; A61P0025-18 [I]
CC 63-6 (Pharmaceuticals)
IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 52-86-8, Haloperidol 58-39-9, Perphenazine 68-41-7, Cycloserine 69-23-8, Fluphenazine 117-89-5, Trifluoperazine 312-84-5, D-Serine 2062-78-4, Pimozide 3313-26-6, Thiothixene 5786-21-0, Clozapine 6104-71-8, N-Desmethylclozapine 23672-07-3, Levosulpiride 65576-45-6, Asenapine 73310-10-8, LAX 101 75272-39-8, Nemonapride 79944-58-4, Idazoxan 84371-65-3, Mifepristone 87760-53-0, Tandospirone 97240-79-4, Topiramate 106266-06-2, Risperidone 106516-24-9, Sertindole 111974-69-7, Quetiapine 123039-93-0, Dihydrexidine 129029-23-8, Ocaperidone 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 132810-10-7, Blonanserin 133454-47-4, Iloperidone 143249-88-1, Dexefaroxan 144598-75-4, Paliperidone 146939-27-7,

Ziprasidone 149409-57-4, Ne100 150915-41-6, Perospirone 154235-83-3, Cx516 160492-56-8, Osanetant 161417-03-4, Abt089 161611-99-0, Du125530 163000-63-3, Neboglamine 167933-07-5, Flibanserin 174636-32-9, Talnetant 183849-43-6, Abaperidone 189681-70-7, Aplindore 211735-76-1, Org 24448 222551-17-9, Slv313 223502-85-0, Ssr181507 250266-51-4, Pnu177864 264618-44-2, Ssr146977 264869-71-8, Slv310 288104-79-0, Sr147778 350992-10-8, Bifeprunox 367514-87-2, Lurasidone 367514-88-3, SM 13496 402713-80-8, Sb399885 452917-21-4, Ave5997 464213-10-3, Slv319 612801-85-1, RG 1068 700834-58-8, Tc1698 706782-28-7, ACP 103 868855-08-7, EMR 62218 909712-38-5, PNU 170413 909712-39-6, POL 255 909712-49-8, LAX 111
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(flibanserin compns. for the treatment and/or prevention of schizophrenia and related diseases)

IT 367514-87-2, Lurasidone 367514-88-3, SM 13496
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(flibanserin compns. for the treatment and/or prevention of schizophrenia and related diseases)

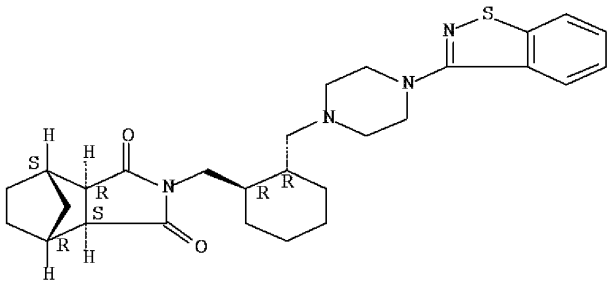
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
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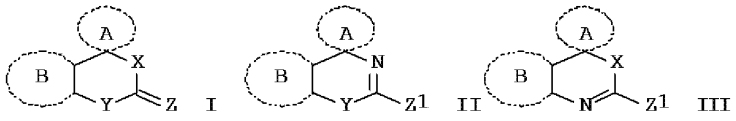
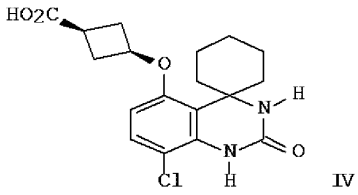


I II III



IV

AB Compds. I-III [Ring B = (un)substituted six-membered aryl or heteroaryl ring; Ring A = (un)substituted spirocycle or spiroheterocycle; X = O or NH, NNH2, etc.; Y = O, S, NH, etc.; Z = CHNO2, O, S, etc.; Z1 = H, Me, NH2, etc.] are disclosed as phosphodiesterase 7 (PDE7) inhibitors for use in the manufacture of a medicament for the treatment of neuropathic pain and to a method of treating neuropathic pain using an inhibitor of PDE7. Methods for preparing title compds. are given. Thus, e.g., IV was prepared by substitution of trans-3-[(benzyloxy)methyl]cyclobutyl p-toluenesulfonate (preparation given) with 8'-chloro-5'-hydroxy-1'H-spiro[cyclohexane-1,4'- quinazolin]-2'(3'H)-one

followed by deprotection and oxidation In PDE7A inhibition assays, IV demonstrated a Ki value of 1.9 (nM).

ACCESSION NUMBER: 2006:918625 CAPLUS Full-text
DOCUMENT NUMBER: 145:315008
TITLE: Preparation of spiro[cyclohexane-1,4'-quinazoline] derivatives for use as PDE7 inhibitors for the treatment of neuropathic pain
INVENTOR(S): Cox, Peter; Kinloch, Ross Anderson; Maw, Graham Nigel
PATENT ASSIGNEE(S): Pfizer Limited, UK
SOURCE: PCT Int. Appl., 108pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2006092691	A1	20060908	WO 2006-IB369		20060216	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW						
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
AU 2006219643	A1	20060908	AU 2006-219643		20060216	<--
CA 2599662	A1	20060908	CA 2006-2599662		20060216	<--
EP 1855686	A1	20071121	EP 2006-710434		20060216	<--
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BR 2006007402	A2	20090901	BR 2006-7402		20060216	<--
AR 53687	A1	20070516	AR 2006-100717		20060227	<--
JP 2006241159	A	20060914	JP 2006-53415		20060228	<--
JP 4512052	B2	20100728				
ZA 2007007147	A	20081126	ZA 2007-7147		20070823	<--
KR 2007107099	A	20071106	KR 2007-7020010		20070831	<--
MX 2007010721	A	20071113	MX 2007-10721		20070831	<--
IN 2007DN07221	A	20071012	IN 2007-DN7221		20070919	<--
CN 101146539	A	20080319	CN 2006-80009067		20070920	<--
US 20090111837	A1	20090430	US 2008-817528		20081106	<--
PRIORITY APPLN. INFO.:			GB 2005-4209	A	20050301	<--
			US 2005-60675761	P	20050427	<--
			WO 2006-IB369	W	20060216	<--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 145:315008; MARPAT 145:315008
IPCI A61K0031-527 [I]; A61K0031-357 [I]; A61K0031-537 [I]; A61K0031-547 [I]; A61P0025-00 [I]; A61P0025-02 [I]
IPCR A61K0031-527 [I]; A61K0031-357 [I]; A61K0031-537 [I]; A61K0031-547 [I]; A61P0025-00 [I]; A61P0025-02 [I]
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 350992-10-8, Bifeprunox 351862-32-3, Sarizotan 364067-22-1
367514-87-2, Lurasidone 404385-91-7 415903-37-6 441351-27-5
556063-02-6, DPC 11870-11 620550-84-7 691010-00-1 691010-31-8
691010-34-1 691010-49-8 847727-81-5

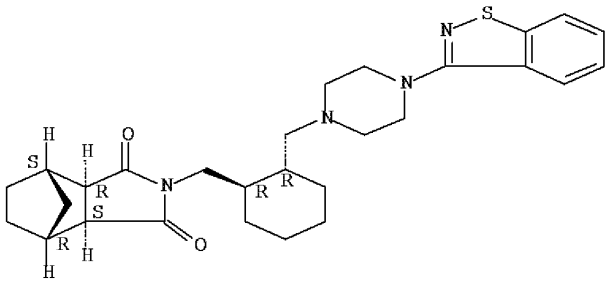
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 7 inhibiting compds. useful in treatment of neuropathic pain)

IT 367514-87-2, Lurasidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 7 inhibiting compds. useful in treatment of neuropathic pain)

RN 367514-87-2 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

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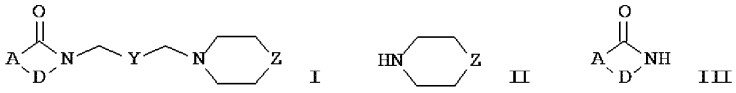


I II III

AB The imides I [A = C2-4 alkylene, C2-4 alkenylene; D = CO, SO2; Y = C1-2 alkylene; Z = (substituted) CH2, (substituted) NH], useful for psychotropic agents for treatment of schizophrenia, senile psychosis, manic-depressive psychosis, neuropathy, etc. (no data), are prepared by treatment of cyclic amines II (Z = same as above) with Y(CH2X)2 (X = anion-generating group; Y = same as above) in the presence of K2CO3 having sp. surface area <1.8 m2/g, and treatment of the resulting spiro quaternary ammonium salts with imides III (A, D = same as above) in the presence of solid inorg. bases. Thus, (1R,2R)-1,2-bis(methanesulfonyloxymethyl)cyclohexane was treated with 4-(1,2-benzisothiazol-3-yl)piperazine in the presence of K2CO3 (sp. surface area 0.6 m2/g) and Bu4N+HSO4-, and treated with

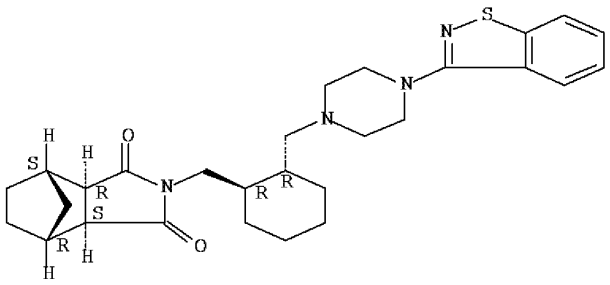
hexahydro(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione in the presence of K2CO3 and H2O to give 2-[[(1R,2R)-2-[[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione with yield of carbonic acid-derived byproduct 1.5%.

ACCESSION NUMBER: 2006:627401 CAPLUS Full-text
DOCUMENT NUMBER: 145:83396
TITLE: Preparation of imides as intermediates for psychotropic agents
INVENTOR(S): Ae, Nobuyuki; Bando, Hisashi
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan; Dainippon Pharmaceutical Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006169155	A	20060629	JP 2004-362562	20041215 <--
JP 4708012	B2	20110622		

PRIORITY APPLN. INFO.: JP 2004-362562 20041215 <--
OTHER SOURCE(S): CASREACT 145:83396; MARPAT 145:83396
IPCI C07D0471-10 [I]; C07D0417-12 [I]; C07B0061-00 [N]; C07D0487-10 [I]; C07D0417-12 [I]; C07B0061-00 [N]
IPCR C07D0471-10 [I]; C07B0061-00 [N]; C07D0417-12 [I]; C07D0487-10 [I]
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 367514-87-2P, 2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of imides as intermediates for psychotropic agents from cyclic amines via spiro quaternary ammonium salts by using K2CO3 with predetd. sp. surface area)
IT 367514-87-2P, 2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of imides as intermediates for psychotropic agents from cyclic amines via spiro quaternary ammonium salts by using K2CO3 with predetd. sp. surface area)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
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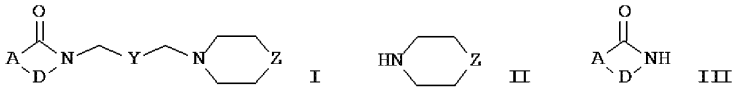

AB The imides I [A = C2-4 alkylene, C2-4 alkenylene; D = CO, SO2; Y = C1-2 alkylene; Z = (substituted) CH2, (substituted) NH], useful for psychotropic agents for treatment of schizophrenia, senile psychosis, manic-depressive psychosis, neuropathy, etc. (no data), are prepared by treatment of cyclic amines II (Z = same as above) with Y(CH2X)2 (X = anion-generating group; Y = same as above) in the presence of K2CO3 having average particle size (50%D) ≤200 μm, and treatment of the resulting spiro quaternary ammonium salts with imides III (A, D = same as above) in the presence of solid inorg. bases. Thus, (1R,2R)-1,2-bis(methanesulfonyloxymethyl)cyclohexane was treated with 4-(1,2-benzisothiazol-3-yl)piperazine in the presence of K2CO3 (50%D 11 μm) and Bu4N+HSO4-, and treated with hexahydro(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione in the presence of K2CO3 and H2O to give 2-[[(1R,2R)-2-[[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione.

ACCESSION NUMBER: 2006:627400 CAPLUS Full-text
DOCUMENT NUMBER: 145:83395
TITLE: Preparation of imides as intermediates for psychotropic agents
INVENTOR(S): Ae, Nobuyuki; Bando, Hisashi
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan; Dainippon Pharmaceutical Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 2006169154 A 20060629 JP 2004-362561 20041215 <--
PRIORITY APPLN. INFO.: JP 2004-362561 20041215 <--
OTHER SOURCE(S): MARPAT 145:83395
IPCI C07D0417-12 [I]; C07D0471-10 [I]; C07B0061-00 [N]
IPCR C07D0417-12 [I]; C07B0061-00 [N]; C07D0471-10 [I]
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 367514-87-2P, 2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of imides as intermediates for psychotropic agents from cyclic amines via spiro quaternary ammonium salts by using K2CO3 with predetd. sp. surface area)
IT 367514-87-2P, 2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
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RN 367514-87-2 CAPLUS
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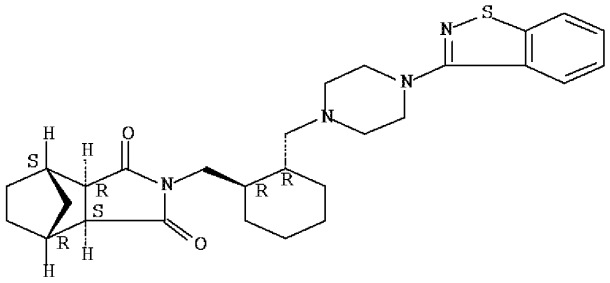
Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB A method of evaluating memory/learning functions with the use of a model with glutamic acid N-methyl-D-aspartate (NMDA) type receptor dysfunction as an animal model of schizophrenia and with the use of reference memory problems, wherein there has been found concrete means for detecting any difference in activity between typical antipsychotic drug and atypical antipsychotic drug. There is provided an in vivo animal model for screening of an ameliorating agent for cognitive dysfunction by schizophrenia.
ACCESSION NUMBER: 2005:962496 CAPLUS Full-text
DOCUMENT NUMBER: 143:242037
TITLE: Method of in vivo screening of therapeutic agent for

memory/learning dysfunction by schizophrenia
INVENTOR(S): Ishiyama, Takeo
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005080976	A1	20050901	WO 2005-JP2838	20050216 <--
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1726952	A1	20061129	EP 2005-710541	20050216 <--
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EP 2357474	A1	20110817	EP 2011-160001	20050216 <--
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US 20090176800	A1	20090709	US 2009-401958	20090311 <--
US 8835438	B2	20140916		
US 20140356292	A1	20141204	US 2014-14460316	20140814 <--

PRIORITY APPLN. INFO.:

JP 2004-44986	A	20040220 <--
EP 2005-710541	A3	20050216 <--
WO 2005-JP2838	W	20050216 <--
US 2006-589804	A3	20060817 <--
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
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CC 1-11 (Pharmacology)
IT 52-86-8, Haloperidol 5786-21-0, Clozapine 77086-22-7 106266-06-2, Risperidone 111974-69-7, Quetiapine 129722-12-9, Aripiprazole 132539-06-1, Olanzapine 367514-87-2, Lurasidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of in vivo screening of therapeutic agent for memory/learning dysfunction by schizophrenia)
IT 367514-87-2, Lurasidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of in vivo screening of therapeutic agent for memory/learning

dysfunction by schizophrenia)
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CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
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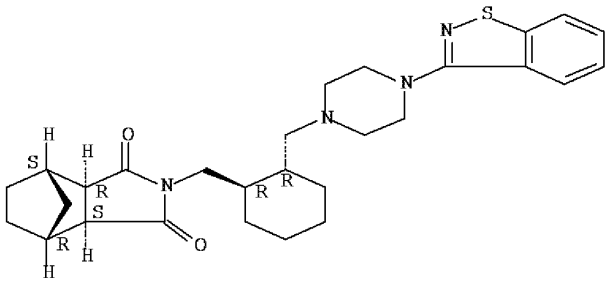
INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB The present invention relates to methods of treating the underlying dysregulation of the emotional functionality of mental disorders (i.e. affect instability-hypersensitivity-hyperaesthesia-dissociative phenomena-...) using compds. and compns. of compds. having D4 and/or 5-HT2A antagonistic, partial agonistic or inverse agonistic activity. The invention also relates to methods comprising administering to a patient diagnosed as having a neuropsychiatric disorder a pharmaceutical composition containing (i) compds. having D4 antagonistic, partial agonistic or inverse agonistic activity and/or (ii) compds. having 5-HT2A antagonistic, partial agonistic or inverse agonistic, and/or (iii) any known medicinal compound and compns. of said compds. The combined D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic effects may reside within the same chemical or biol. compound or in two different chemical and/or biol. compds. The combination can also be used to augment the therapeutic effect of or to provide a faster onset of the therapeutic effect of a selective serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitor, or a musculoskeletal disease-treating COX-2 inhibitor. Pharmaceutical compns. are also claimed.
ACCESSION NUMBER: 2005:474939 CAPLUS Full-text
DOCUMENT NUMBER: 143:1317
TITLE: Method of treating mental disorders using D4 and 5-HT2A antagonists, inverse agonists or partial agonists
INVENTOR(S): Buntinx, Erik
PATENT ASSIGNEE(S): Belg.
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050119253	A1	20050602	US 2003-725965	20031202 <--

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     US 7884096           B2   20110208
     US 20050119248       A1   20050602    US 2004-752423          20040106 <--
     US 7855195           B2   20101221
     US 20050119249       A1   20050602    US 2004-803793          20040318 <--
     US 20050203130       A1   20050915    US 2004-984683          20041109 <--
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     PT 1708790           E    20100709    PT 2004-801138          20041202 <--
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     US 8304431           B2   20121106
     US 20110172251       A1   20110714    US 2011-931313          20110126 <--
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                                            US 2004-752423       A2 20040106 <--
                                            CA 2004-2461248      A  20040318 <--
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                                            US 2004-803793       A2 20040318 <--
                                            EP 2004-25035        A  20041021 <--
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
INCL 514220000; 514259410; 514419000; 514217000; 514469000; 514317000;
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IPCI A01N0043-46 [I]; A01N0043-26 [I]; A01N0033-02 [I]; A01N0033-24 [I];
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NCL  514/220.000; 514/217.000; 514/259.410; 514/317.000; 514/419.000;
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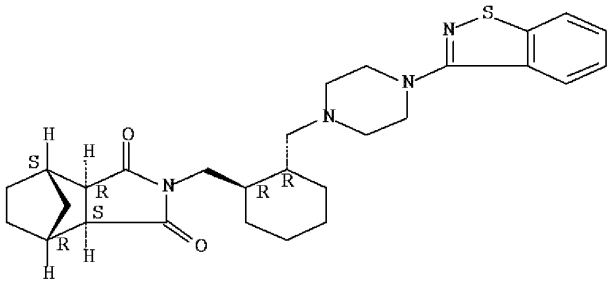
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies
52-86-8, Haloperidol 58-39-9, Perphenazine 69-23-8, Fluphenazine
117-89-5, Trifluoperazine 5588-33-0, Mesoridazine 71675-85-9,
Amisulpride 84225-95-6, Raclopride 111974-69-7, Quetiapine
129722-12-9, Aripiprazole 130579-75-8, Eplivanserin 132810-10-7,
Blonanserin 133454-47-4, Iloperidone 146362-70-1, SR-48692
149409-57-4, NE-100 150915-41-6, Perospirone 160492-56-8, Osanetant
168273-06-1, SR-141716 170858-33-0, Sonepiprazole 202720-27-2, SR
31742 209481-20-9, SB-271046 209745-47-1, Lu 35-138 211735-76-1, CX
691 220120-14-9, E-5842 350992-13-1 351862-32-3, Sarizotan
367514-88-3, SM 13496 441351-21-9, CP 361428 441351-23-1, WAY
135452 441351-24-2, BSF 201640 441351-25-3, BSF 190555 441351-26-4,
LAX 101a 441351-27-5, Balaperidone
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neuroleptic agent, augmenting therapeutic effect of; treating
underlying dysregulation of emotional functionality of mental disorders
using D4 and 5-HT2A antagonists, inverse agonists or partial agonists)
IT 367514-88-3, SM 13496
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neuroleptic agent, augmenting therapeutic effect of; treating
underlying dysregulation of emotional functionality of mental disorders
using D4 and 5-HT2A antagonists, inverse agonists or partial agonists)
RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
(3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB The present invention relates to methods of treating of the underlying dysregulation of the emotional functionality of mental disorders (i.e. affect instability-hypersensitivity-hyperaesthesia-dissociative phenomena-...) using compds. and compns. of compds. having D4 and/or 5-HT2A antagonistic, partial

agonistic or inverse agonistic activity. The invention also relates to methods comprising administering to a patient diagnosed as having a neuropsychiatric disorder a pharmaceutical composition containing (i) compds. having D4 antagonistic, partial agonistic or inverse agonistic activity and/or (ii) compds. having 5-HT2A antagonistic, partial agonistic or inverse agonistic, and/or (iii) any known medicinal compound and compns. of said compds. The combined D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic effects may reside within the same chemical or biol. compound or in two different chemical and/or biol. compds. The combination can also be used to augment the therapeutic effect of or to provide a faster onset of the therapeutic effect of a selective serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitor, an NK1 antagonist, or a musculoskeletal disease-treating COX-2 inhibitor. Pharmaceutical compns. are also claimed.

ACCESSION NUMBER: 2005:474936 CAPLUS Full-text
DOCUMENT NUMBER: 143:1315
TITLE: Method of treating mental disorders using D4 and 5-HT2A antagonists, inverse agonists or partial agonists
INVENTOR(S): Buntinx, Erik
PATENT ASSIGNEE(S): Belg.
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 725,965.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

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US 20050119248	A1	20050602	US 2004-752423	20040106 <--
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
INCL 514217000; 514220000; 514259410; 514469000; 514317000; 514649000
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CC 1-11 (Pharmacology)
Section cross-reference(s): 63
IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies
52-86-8, Haloperidol 58-39-9, Perphenazine 69-23-8, Fluphenazine
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LAX 101a 441351-27-5, Balaperidone
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neuroleptic agent, augmenting therapeutic effect of; treating
underlying dysregulation of emotional functionality of mental disorders
using D4 and 5-HT2A antagonists, inverse agonists or partial agonists)
IT 367514-88-3, SM 13496
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neuroleptic agent, augmenting therapeutic effect of; treating
underlying dysregulation of emotional functionality of mental disorders
using D4 and 5-HT2A antagonists, inverse agonists or partial agonists)
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2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
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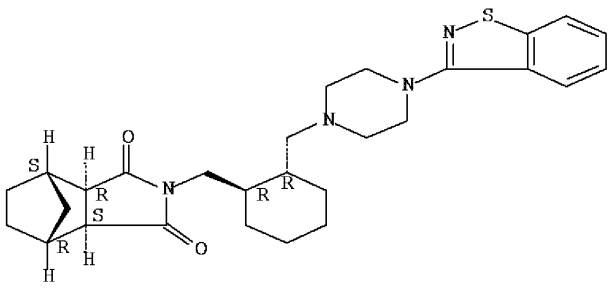
(3aR,4S,7R,7aS)- (CA INDEX NAME)

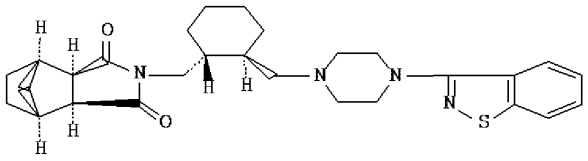
Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
GI



I

AB Claimed is a process for producing the title compound I.HCl or enantiomers thereof by treating I or enantiomers thereof with an aqueous hydrochloric acid solution in a hydrophilic solvent and crystallizing I.HCl or enantiomers thereof. I.HCl is a psychotropic agent (no data). Thus, I in acetone was heated under reflux; an aqueous HCl solution was added over 15 min to the solution of I in acetone at 55℃; the resulting solution was stirred at 60℃ for 1 h; said solution was cooled to 0℃ and stirred at 0℃ for 1 h to give I.HCl.

ACCESSION NUMBER: 2005:99501 CAPLUS Full-text
DOCUMENT NUMBER: 142:198101
TITLE: Process for producing benzisothiazolylpiperazinylmethylcyclohexylmethylbicycloheptanedicarboxyimide hydrochloride
INVENTOR(S): Kakiya, Yuzo; Oda, Mayumi
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004259305        A1   20050203    AU 2004-259305          20040727 <--
     AU 2004259305        B2   20090604
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     EP 1652848           B1   20120201
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     KR 2006052840        A    20060519    KR 2006-7001255         20040727 <--
     KR 1085806           B1   20111122
     CN 1832946           A    20060913    CN 2004-80022168        20040727 <--
     CN 100422178         C    20081001
     BR 2004013081        A    20061003    BR 2004-13081           20040727 <--
     JP 4610485           B2   20110112    JP 2005-512110          20040727 <--
     AT 543817            T    20120215    AT 2004-748182          20040727 <--
     ES 2378990           T3   20120419    ES 2004-748182          20040727 <--
     US 20060194970       A1   20060831    US 2006-565105          20060119 <--
     US 7605260           B2   20091020
     US 45573             E1   20150623    US 2006-14137464        20060119 <--
     MX 2006001128        A    20060907    MX 2006-1128            20060127 <--
     IN 2006CN00349       A    20070706    IN 2006-CN349           20060127 <--
PRIORITY APPLN. INFO.:                      JP 2003-281860       A  20030729 <--
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         CASREACT 142:198101
IPCI C07D0417-12 [ICM,7]; A61K0031-496 [ICS,7]; A61P0025-28 [ICS,7];
     C07M0007-00 [ICS,7]
IPCR A61K0031-496 [I]; A61P0025-28 [I]; C07D0417-12 [I]
CC   28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
IT   367514-88-3P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (crystallization of
benzisothiazolylpiperazinylmethylcyclohexylmethylbicyclohep
        tanedicarboxyimide hydrochloride)
IT   7647-01-0, Hydrochloric acid, reactions   367514-87-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (crystallization of
benzisothiazolylpiperazinylmethylcyclohexylmethylbicyclohep
        tanedicarboxyimide hydrochloride)
IT   367514-88-3P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (crystallization of
benzisothiazolylpiperazinylmethylcyclohexylmethylbicyclohep
        tanedicarboxyimide hydrochloride)
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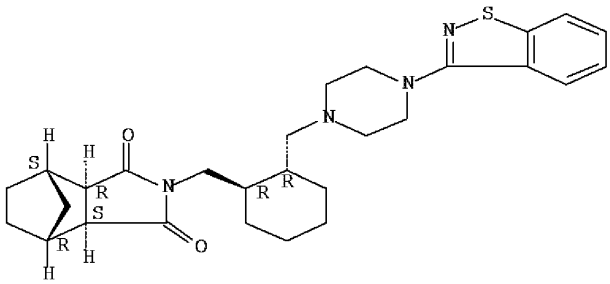
RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
(3aR,4S,7R,7aS)- (CA INDEX NAME)

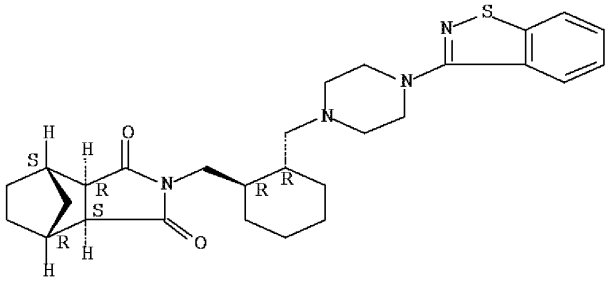
Absolute stereochemistry.



● HCl

IT 367514-87-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystallization of
benzisothiazolylpiperazinylmethylcyclohexylmethylbicyclohep
tanedicarboxyimide hydrochloride)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA
INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD
(10 CITINGS)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB It is intended to provide a novel method of treating integration dysfunction syndrome. Namely, 5 mg to 120 mg/day of an active compound (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptane dicarboxyimide or its pharmaceutically acceptable salt (for example, hydrochloride) is orally administered to a patient with integration dysfunction syndrome once a day. According to this method, broad symptoms of integration dysfunction syndrome, in particular, pos. symptoms and neg. symptoms, can be ameliorated without causing any extrapyramidal reactions.

ACCESSION NUMBER: 2004:182710 CAPLUS Full-text
DOCUMENT NUMBER: 140:210810
TITLE: Remedy for integration dysfunction syndrome
INVENTOR(S): Nakamura, Mitsutaka; Ogasa, Masaaki; Sami, Shunsuke
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2004017973	A1	20040304	WO 2003-JP10490		20030820	<--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
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EP 1535616	A1	20050601	EP 2003-792731		20030820	<--
EP 1535616	B1	20090513				
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EP 1944030	A1	20080716	EP 2008-153777		20030820	<--
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ES 2326078	T3	20090930	ES 2003-792731		20030820	<--
EP 2295061	A1	20110316	EP 2010-13201		20030820	<--
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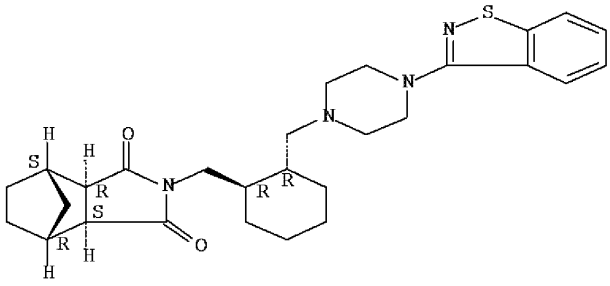
JP 4745661	B2	20110810	JP 2004-530573		20030820	<--
US 20060025422	A1	20060202	US 2005-525021		20050218	<--
US 9174975	B2	20151103				
US 20140371236	A1	20141218	US 2014-14471919		20140828	<--
PRIORITY APPLN. INFO.:			US 2002-60404927	P	20020822	<--
			EP 2003-792731	A3	20030820	<--
			EP 2008-153777	A3	20030820	<--
			WO 2003-JP10490	W	20030820	<--
			US 2005-525021	A1	20050218	<--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IPCI A61K0031-496 [ICM,7]; A61P0025-18 [ICS,7]; C07D0417-12 [ICS,7]
IPCR A61K0031-496 [I]; A61P0025-18 [I]; C07D0417-12 [I]
CC 1-11 (Pharmacology)
Section cross-reference(s): 63

IT 367514-88-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedy for integration dysfunction syndrome)
IT 367514-88-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedy for integration dysfunction syndrome)
RN 367514-88-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB The invention discloses a treatment for schizophrenia. It has been discovered that schizophrenia will respond to the combination of an atypical antipsychotic, e.g. olanzapine, and a valproate compound, e.g. divalproex sodium. This combination is especially useful for alleviating the acute symptoms of schizophrenia. The invention also extends to new formulations containing an antipsychotic in combination with a valproate compound
ACCESSION NUMBER: 2003:633455 CAPLUS Full-text
DOCUMENT NUMBER: 139:159958
TITLE: Valproate compound-atypical antipsychotic agent combination therapy for treatment of schizophrenia
INVENTOR(S): Sommerville, Kenneth W.; Gilbert, Adrienne L.; Tracy, Katherine A.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003066039	A1	20030814	WO 2003-US2540		20030129 <--
W: CA, JP, MX					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR					
CA 2475839	A1	20030814	CA 2003-2475839		20030129 <--
EP 1480629	A1	20041201	EP 2003-737557		20030129 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY, TR, BG, CZ, EE, HU, SK					
JP 2006505489	T	20060216	JP 2003-565463		20030129 <--
MX 2004007752	A	20050617	MX 2004-7752		20040809 <--
PRIORITY APPLN. INFO.:			US 2002-71733	A	20020208 <--
			WO 2003-US2540	W	20030129 <--

IPCI A61K0031-19 [ICM,7]; A61K0031-55 [ICS,7]; A61K0031-519 [ICS,7]; A61K0031-496 [ICS,7]; A61K0031-445 [ICS,7]

IPCR A61K0031-19 [I]; A61K0031-445 [I]; A61K0031-496 [I]; A61K0031-519 [I]; A61K0031-55 [I]; A61K0045-06 [I]

CC 1-11 (Pharmacology)

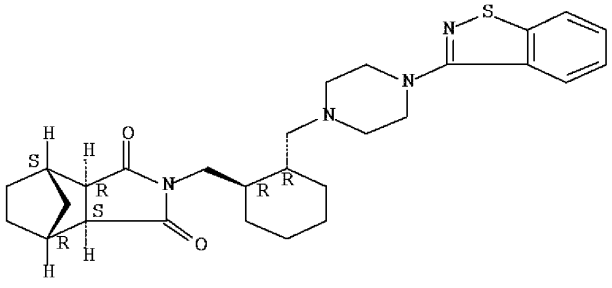
IT 99-66-1D, Valproic acid, derivs. 5786-21-0, Clozapine 26615-21-4, Zotepine 76584-70-8, Divalproex sodium 85650-56-2, Org-5222 106266-06-2, Risperidone 106516-24-9, Sertindole 111974-69-7, Quetiapine 129722-12-9, Aripiprazole 130579-75-8, Eplivanserin 132539-06-1, Olanzapine 132810-10-7, Blonanserin 133454-47-4, Iloperidone 139290-65-6, MDL 100907 146939-27-7, Ziprasidone 150915-41-6, Perospirone 367514-88-3, SM-13496 573990-60-0 573990-61-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(valproate compound-atypical antipsychotic agent combination therapy for treatment of schizophrenia)

IT 367514-88-3, SM-13496
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(valproate compound-atypical antipsychotic agent combination therapy for treatment of schizophrenia)

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
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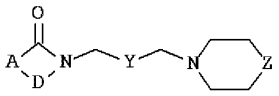
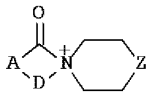


I

II



III

AB Imides I [A = (un)substituted C2-4 alkylene, (un)substituted C2-4 alkenylene; D = CO, SO2; Y = (un)substituted C1-2 alkylene; Z = (un)substituted CH2, (un)substituted NH], useful for psychotropic agents for treatment of schizophrenia, manic-depressive psychosis, neuropathy, etc., are prepared by treatment of imides II (A, D = same as above) with quaternary ammonium salts III (Y, Z = same as above; X- = anion) in the presence of solid inorg. bases and H2O in aromatic hydrocarbon solvents. Thus, MePh solution of 4'-(1,2-benzisothiazol-3-yl)-(3aR,7aR)-octahydro-spiro[2H-isoindole-2,1'-piperazinium] methanesulfonate was refluxed with hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione, K2CO3, and H2O for 2 h to give 83% 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione.

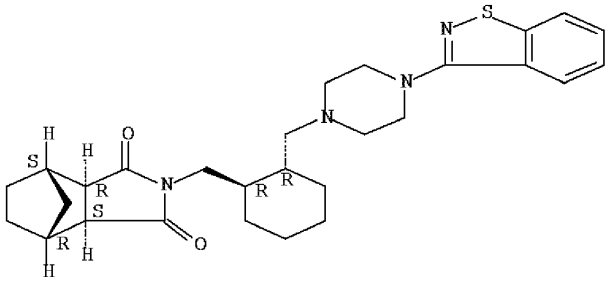
ACCESSION NUMBER: 2003:424505 CAPLUS Full-text
DOCUMENT NUMBER: 139:6890
TITLE: Preparation of imides as intermediates for psychotropic agents
INVENTOR(S): Kiyoshima, Yujiro; Bando, Hisashi
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan; Sumitomo Pharmaceuticals Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003160583	A	20030603	JP 2001-360426	20011127 <--
JP 4175800	B2	20081105		

PRIORITY APPLN. INFO.: JP 2001-360426 20011127 <--

OTHER SOURCE(S): MARPAT 139:6890
IPCI C07D0417-12 [I]
IPCR C07D0417-12 [I]
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 367514-87-2P 535933-87-0P,
N-[[2-[[4-(1,2-Benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-4,7-methano-1H-isoindole-
1,3(2H)-dione
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
(Preparation)
(preparation of imides as intermediates for psychotropic agents in presence
of solid inorg. bases and water)
IT 367514-87-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
(Preparation)
(preparation of imides as intermediates for psychotropic agents in presence
of solid inorg. bases and water)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA
INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN
AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a salt; and (b) 1 or more neuroleptics is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating schizophrenia. A pharmaceutical composition was prepared by combining reboxetine with a neuroleptic in an acceptable carrier. The composition contains 0.01-10 mg rebexetine and 25-300 mg clozapine.
ACCESSION NUMBER: 2002:521465 CAPLUS Full-text
DOCUMENT NUMBER: 137:98994
TITLE: Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics
INVENTOR(S): Wong, Erik Ho Fong; Gallen, Christopher C.; Svensson, Torgny
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA; Pharmacia AB
SOURCE: PCT Int. Appl., 22 pp.

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                        CODEN: PIXXD2
DOCUMENT TYPE:          Patent
LANGUAGE:               English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
     PATENT NO.          KIND  DATE        APPLICATION NO.          DATE
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     WO 2002053140        A2   20020711    WO 2001-US45871          20011227 <--
     WO 2002053140        A3   20021024
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2431041           A1   20020711    CA 2001-2431041          20011227 <--
     AU 2002232470        A1   20020716    AU 2002-232470           20011227 <--
     AU 2002232470        B2   20051103
     EP 1353675           A2   20031022    EP 2001-991997           20011227 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004517112        T    20040610    JP 2002-554091           20011227 <--
     NZ 526801            A    20050729    NZ 2001-526801           20011227 <--
     US 20020156067       A1   20021024    US 2001-35100            20011228 <--
     US 6964962           B2   20051115
     MX 2003006003        A    20050908    MX 2003-6003             20030702 <--
     US 20060003992       A1   20060105    US 2005-219901           20050906 <--
PRIORITY APPLN. INFO.:                      US 2001-60259286     P   20010102 <--
                                            WO 2001-US45871      W   20011227 <--
                                            US 2001-35100        A3  20011228 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IPCI A61K0031-00 [ICM,7]
IPCR A61K0031-135 [I]; A61K0031-138 [I]; A61K0031-165 [I]; A61K0031-185 [I];
     A61K0031-343 [I]; A61K0031-352 [I]; A61K0031-381 [I]; A61K0031-40 [I];
     A61K0031-407 [I]; A61K0031-435 [I]; A61K0031-439 [I]; A61K0031-4418 [I];
     A61K0031-451 [I]; A61K0031-454 [I]; A61K0031-497 [I]; A61K0031-517 [I];
     A61K0031-519 [I]; A61K0031-522 [I]; A61K0031-535 [I]; A61K0031-5375 [I];
     A61K0031-5415 [I]; A61K0031-55 [I]; A61K0031-551 [I]; A61K0031-5513 [I];
     A61K0031-554 [I]; A61K0045-06 [I]; A61P0003-04 [I]; A61P0009-12 [I];
     A61P0013-00 [I]; A61P0015-00 [I]; A61P0025-00 [I]; A61P0025-06 [I];
     A61P0025-18 [I]; A61P0025-20 [I]; A61P0025-24 [I]; A61P0025-30 [I];
     A61P0037-00 [I]
CC   63-6 (Pharmaceuticals)
     Section cross-reference(s): 1
IT   50-52-2, Thioridazine   50-53-3, Chlorpromazine, biological studies
     51-41-2, Norepinephrine   52-86-8, Haloperidol   58-39-9, Perphenazine
     69-23-8, Fluphenazine   117-89-5, Trifluoperazine   5588-33-0,
     Mesoridazine   5786-21-0, Clozapine   7182-51-6, Talopram   21489-20-3,
     Talsupram   21489-22-5, Prindamine   24526-64-5, Nomifensine   26615-21-4,
     Zotepine   37751-39-6, Ciclazindol   42408-79-7, Pirandamine   42408-80-0,
     Tandamine   46817-91-8, Viloxazine   70384-91-7, Lortalamine   71620-89-8,
     Reboxetine   71675-85-9, Amisulpride   83015-26-3, Tomoxetine
     84225-95-6, Raclopride   85650-56-2, ORG-5222   92623-85-3, Milnacipran
     93413-69-5, Venlafaxine   98819-76-2   105182-45-4, Fluparoxan
     106266-06-2, Risperidone   106516-24-9, Sertindole   111974-69-7,
     Quetiapine   116539-59-4, Duloxetine   129722-12-9, Aripiprazole
     130579-75-8, Eplivanserin   132539-06-1, Olanzapine   132810-10-7,
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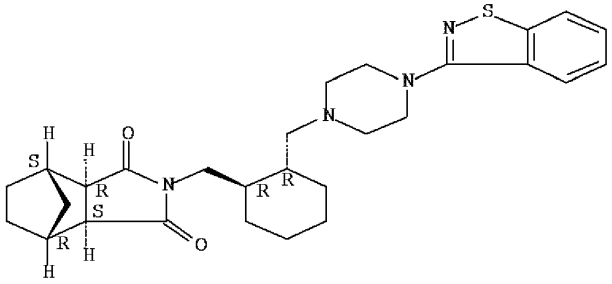
Blonanserin 133454-47-4, Iloperidone 146362-70-1, SR-48692
146939-27-7, Ziprasidone 149409-57-4, NE-100 150915-41-6, Perospirone
160492-56-8, Osanetant 168273-06-1, SR-141716 170858-33-0,
Sonepiprazole 200398-40-9, S-18327 202720-27-2, SR 31742
209481-20-9, SB-271046 209745-47-1, Lu 35-138 211735-76-1, CX-691
220120-14-9, E-5842 350992-13-1, DU-127090 351862-32-3, Sarizotan
367514-88-3 441351-21-9, CP 361428 441351-23-1, WAY 135452
441351-24-2, BSF 201640 441351-25-3, BSF 190555 441351-26-4, LAX 101a
441351-27-5, Balaperidone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(pharmaceuticals containing combination of norepinephrine reuptake
inhibitors and neuroleptics)

IT 367514-88-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(pharmaceuticals containing combination of norepinephrine reuptake
inhibitors and neuroleptics)

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
(3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB Disclosed are oral compns. containing a hardly water-soluble active ingredient and having favorable disintegration characteristics which comprise a molded solid article (for example, granules) obtained by mixing the hardly water-soluble active ingredient, a first disintegrating agent and a water-soluble filler with the use of a water-soluble polymer binder and then mixing this molded solid article with a second disintegrating agent, or a molded solid article obtained by mixing the hardly water-soluble active ingredient, a disintegrating agent and a sugar alc. with the use of a water-soluble polymer binder. When orally administered, these prepns. show excellent elution of the active ingredient in the digestive tract. Moreover, these prepns. can show the same elution behavior at different contents

of the active ingredient and thus enable the selection of the most suitable drug for each patient, which makes these prepns. highly useful in clin. medicine. A film-coated tablet was prepared form granules containing N-[4-[4-(1,2-benzisothiazole-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride 10, lactose 50, sodium croscarmellose 6 mg, and polyvinyl alc. 1.2 mg, calcium hydrogen phosphate anhydride 35, crystalline cellulose 17, and magnesium stearate 0.8 mg, and a coating material containing hydroxypropyl Me cellulose 1.95, titanium oxide 0.6, concentrate glycerin 0.45 mg, and carnauba wax q.s.

ACCESSION NUMBER: 2002:240535 CAPLUS Full-text
DOCUMENT NUMBER: 136:268164
TITLE: Oral compositions with favorable disintegration characteristics
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024166	A1	20020328	WO 2001-JP7983	20010914 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2824077	A1	20020328	CA 2001-2824077	20010914 <--
CA 2824077	C	20160126		
AU 2001086237	A	20020402	AU 2001-86237	20010914 <--
CA 2424001	A1	20030320	CA 2001-2424001	20010914 <--
CA 2424001	C	20131022		
EP 1327440	A1	20030716	EP 2001-965637	20010914 <--
EP 1327440	B1	20090513		
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EP 1974724	A2	20081001	EP 2008-156778	20010914 <--
EP 1974724	A3	20081112		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR				
AT 431136	T	20090515	AT 2001-965637	20010914 <--
ES 2325764	T3	20090916	ES 2001-965637	20010914 <--
JP 4868695	B2	20120201	JP 2002-528202	20010914 <--
TW I289062	B	20071101	TW 2001-123036	20010919 <--
TW I289063	B	20071101	TW 2005-103731	20010919 <--
US 20040028741	A1	20040212	US 2003-381036	20030321 <--
US 7727553	B2	20100601		

PRIORITY APPLN. INFO.:	JP 2000-288234	A	20000922 <--
	CA 2001-2424001	A3	20010914 <--
	EP 2001-965637	A3	20010914 <--
	WO 2001-JP7983	W	20010914 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IPCI A61K0009-16 [ICM,7]; A61K0009-20 [ICS,7]; A61K0009-30 [ICS,7];

A61K0031-496 [ICS,7]; A61K0045-00 [ICS,7]; A61K0047-10 [ICS,7];
A61K0047-26 [ICS,7]; A61K0047-30 [ICS,7]

IPCR A61K0009-00 [I]; A61K0009-16 [I]; A61K0009-20 [I]; A61K0009-30 [I];
A61K0031-496 [I]

CC 63-6 (Pharmaceuticals)

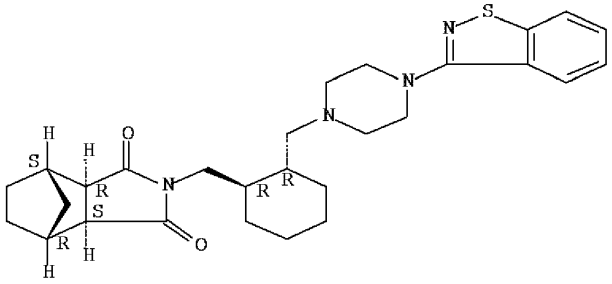
IT 63-42-3, Lactose 69-65-8, D-Mannitol 557-04-0, Magnesium stearate
7757-93-9, Calcium hydrogen phosphate 9002-89-5, Polyvinyl alcohol
9003-39-8, Polyvinyl pyrrolidone 9004-34-6, Crystalline cellulose,
biological studies 9004-65-3, Hydroxypropyl methyl cellulose
9005-25-8, Corn starch, biological studies 74811-65-7, Sodium
croscarmellose 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing
hardly water-soluble active ingredients)

IT 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing
hardly water-soluble active ingredients)

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione,
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
(3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2016 ACS on STN

AB Disclosed are pH-independent sustained release prepns. capable of releasing a drug independently from the pH value in the gastric tract. These sustained release prepns. are characterized in that a drug-containing core is coated with (1) a first layer made of a water-insol. polymer, and (2) a second layer made of an enteric polymer and a water-soluble polymer. Core granules were prepared containing perospirone·HCl, crystalline cellulose, PVP, starch and silica. The granules were coated with a first composition containing Et cellulose, talc, tri-Et citrate, ethanol, and water, and then a second composition containing methacrylate copolymer, PVP, sucrose ester, Macrogol 6000, and water.

ACCESSION NUMBER: 2001:762782 CAPLUS Full-text

DOCUMENT NUMBER: 135:322722
TITLE: Coating agents for sustained-release oral preparations containing basic drugs
INVENTOR(S): Nishii, Hiroyuki; Kobayashi, Hirohisa; Otoda, Kazuya
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076557	A1	20011018	WO 2001-JP3024	20010409 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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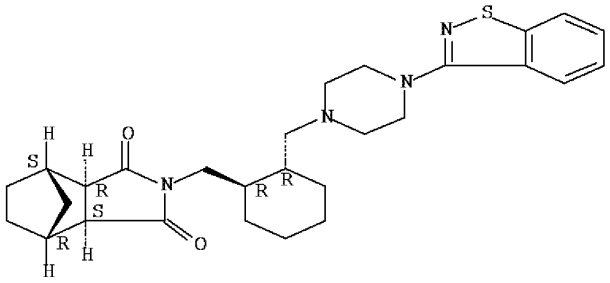
PRIORITY APPLN. INFO.: JP 2000-107671 A 20000410 <--
IPCI A61K0009-14 [ICM,7]; A61K0009-16 [ICS,7]; A61K0009-36 [ICS,7]; A61K0047-32 [ICS,7]; A61K0047-38 [ICS,7]; A61K0031-4178 [ICS,7]; A61K0031-496 [ICS,7]; A61K0031-506 [ICS,7]; A61K0031-5377 [ICS,7]
IPCR A61K0009-28 [I]; A61K0009-36 [I]; A61K0009-50 [I]
CC 63-6 (Pharmaceuticals)
IT 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinylpyrrolidone 9004-35-7, Cellulose acetate 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 21829-25-4, Nifedipine 25086-15-1, Methacrylic acid-methyl methacrylate copolymer 25212-88-8, Ethyl acrylate-methacrylic acid copolymer 37205-99-5, Carboxymethyl ethyl cellulose 68377-91-3, Arotinolol hydrochloride 68377-92-4, Arotinolol 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 87760-53-0, Tandospirone 100986-85-4, Levofloxacin 112457-95-1, Tandospirone citrate 129273-38-7 150915-41-6, Perospirone 367514-87-2 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polymeric coating agents for sustained-release oral prepns. containing basic drugs)
IT 367514-87-2 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polymeric coating agents for sustained-release oral prepns. containing basic drugs)
RN 367514-87-2 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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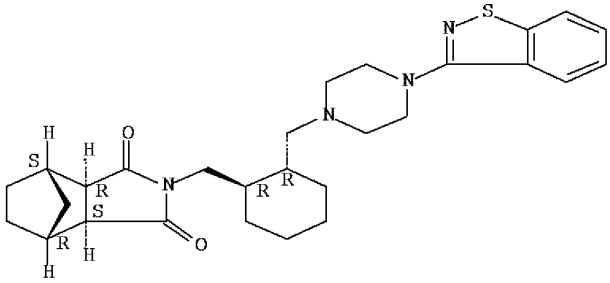
2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1),
(3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



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L2 13 S 367514-87-2/CRN

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L4           21 S L3 AND (PY<=2006 OR PRY<=2006 OR AY<=2006)

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                D L1
L2           13 SEA SPE=ON  ABB=ON  PLU=ON  367514-87-2/CRN

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L4           21 SEA SPE=ON  ABB=ON  PLU=ON  L3 AND (PY<=2006 OR PRY<=2006 OR
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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 180.53     191.05

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:27:56 ON 04 FEB 2016
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PATENT
Attorney Docket No. 05273.0147-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Kazuyuki FUJIHARA	Group Art Unit: 1627
Application No.: 14/512,189	Examiner: Sarah, PIHONAK
Filed: October 10, 2014	Confirmation No.: 5575
For: PHARMACEUTICAL COMPOSITION	**VIA EFS-WEB**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the attention of the Examiner the document on the attached form. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

A copy of the listed non patent literature document is attached. A copy of each of the listed U.S. patent publications is not enclosed pursuant to 37 C.F.R. § 1.98(a)(2)(ii).

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making an appropriate notation on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that the listed document is material or constitutes "prior art." If the Examiner applies the document as prior art against any claim in the application and Applicants determine that the cited document does not constitute "prior art" under United

States law, Applicants reserve the right to present to the U.S. Patent and Trademark Office the relevant facts and law regarding the appropriate status of such document.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed document, should the document be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: July 15, 2015

By: Jennifer Gupta
Jennifer R. Gupta
Reg. No. 54,257

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	14/512,189
				Filing Date	October 10, 2014
				First Named Inventor	Kazuyuki FUJIHARA
				Art Unit	1627
				Examiner Name	Sarah PIHONAK
Sheet	1	of	1	Attorney Docket Number	05273.0147-02000

U.S. PATENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

U.S. PUBLISHED PATENT APPLICATIONS

Examiner Initials*	Cite No.[3]	Document Number Number-Kind Code[4] (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-2003/0203020 A1	10-30-2003	Ortyl et al.	
		US-2005/0147669 A1	07-07-2005	Lawrence et al.	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[5] Number[6] Kind Code[7] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation[8]

NONPATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation[8]
		GOHIL, Usha C. et al., "Investigations into the use of pregelatinised starch to deveop powder-filled hard capsules," International Journal of Pharmaceutics 285 (2004) pp. 51-63.	

Examiner Signature	/SARAH PIHONAK/	Date Considered	02/04/2016

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.P/

PTO Notes regarding this form:

[1] Applicant's unique citation designation number (optional).
[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.

[3] Applicant's unique citation designation number (optional).
[4] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.
[5] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).
[6] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.
[7] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.
[8] Applicant is to place a check mark here if English language Translation is attached.
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**.

TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

NOTE: This form is to be submitted with the Power of Attorney by Applicant form to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5. If the Power of Attorney by Applicant form is not accompanied by this transmittal form or an equivalent, the Power of Attorney will not be recognized in the application.

Application Number	14/512,189
Patent Number	
Filing Date	October 10, 2014
Issue Date	
First Named Inventor	Kazuyuki FUJIHARA
Title	PHARMACEUTICAL COMPOSITION
Art Unit	1627
Examiner Name	PIHONAK, SARAH
Attorney Docket Number	472299US40CONT

SIGNATURE of Applicant or Patent Practitioner

Signature	/Yuki Onoe/	Date	07/18/16
Name	Yuki Onoe	Telephone	703-413-3000
Registration Number	68,563		

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications.

■ *Total of 1 forms are submitted.

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

Attorney Docket Number:	472299US40CONT

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

■ Practitioners associated with the Customer Number: 22850

as attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO), in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

■ The address associated with Customer Number: 22850

Assignee Name and Address:
Sumitomo Dainippon Pharma Co., Ltd.
6-8, Dosho-machi 2-chome, Chuo-ku,
Osaka-shi, Osaka 541-8524 Japan

A copy of this form, together with a statement under 37 CFR 3.73(c) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of the practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature	Hitoshi Fujita	Date	July 12, 2016
Name	Hitoshi FUJITA	Telephone	
Title	Director Intellectual Property		

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: SUMITOMO DAINIPPON PHARMA CO., LTD.

Application No./Patent No.: 14/512,189 Filed/Issue Date: October 10, 2014

Entitled: PHARMACEUTICAL COMPOSITION

SUMITOMO DAINIPPON PHARMA CO., LTD. (Name of Assignee) corporation (Type of Assignee, e.g., corporation, partnership, government agency, etc.)

States that it is:

1. ■ the assignee of the entire right, title, and interest; or
2. ☐ an assignee of less than the entire right, title and interest.

The extent (by, percentage) of its ownership interest is _____%

in the patent application/patent identified above by virtue of:

■ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Kazuyuki Fujihara To: Dainippon Sumitomo Pharma Co., Ltd.
   The document was recorded in the United States Patent and Trademark Office at
   Reel 020124, Frame 0821, or for which a copy therefore is attached.
2. From: Dainippon Sumitomo Pharma Co., Ltd. To: SUMITOMO DAINIPPON PHARMA CO., LTD.
   The document was recorded in the United States Patent and Trademark Office at
   Reel 033905, Frame 0778, or for which a copy therefore is attached.

■ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Yuki Onoe/ — Signature

07/18/16 — Date

Yuki Onoe — Printed or Typed Name - Attorney of Record

703-413-3000 — Telephone Number

68,563 — Registration Number

Electronic Acknowledgement Receipt	
EFS ID:	26372720
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22852
Filer:	Bradley Davis Lytle/Ellen Murabito
Filer Authorized By:	Bradley Davis Lytle
Attorney Docket Number:	05273.0147-02000
Receipt Date:	18-JUL-2016
Filing Date:	10-OCT-2014
Time Stamp:	11:32:08
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		472299US-F.pdf	1034718 3af1038d54c6fdb86174d9e860ddf11127f03241	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Power of Attorney	1	2
	Assignee showing of ownership per 37 CFR 3.73	3	3
Warnings:			
Information:			
	Total Files Size (in bytes):	1034718	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/512,189	10/10/2014	Kazuyuki FUJIHARA	472299US40CONT

CONFIRMATION NO. 5575

22850
OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

POA ACCEPTANCE LETTER

OC000000084664001

Date Mailed: 07/28/2016

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/18/2016.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/ytdemisse/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/512,189	10/10/2014	Kazuyuki FUJIHARA	05273.0147-02000

CONFIRMATION NO. 5575

POWER OF ATTORNEY NOTICE

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

OC000000084663979

Date Mailed: 07/28/2016

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/18/2016.

- The Power of Attorney to you in this application has been revoked by the applicant. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/ytdemisse/

DOCKET NO: 472299US40CONT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
KAZUYUKI FUJIHARA	: EXAMINER: PIHONAK, SARAH
SERIAL NO: 14/512,189	:
FILED: OCTOBER 10, 2014	: GROUP ART UNIT: 1627
FOR: PHARMACEUTICAL COMPOSITION	:

AMENDMENT

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Commissioner:

In response to the Office Action dated February 9, 2016, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

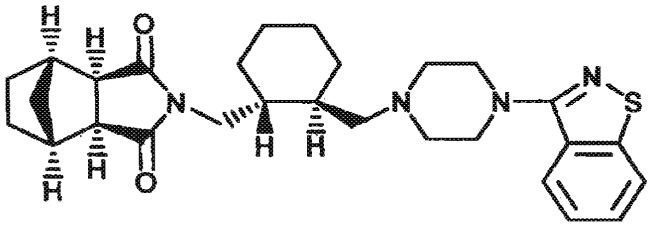
Remarks/Arguments begin on page 10 of this paper.

IN THE CLAIMS

Please amend the claims as follows:

Claim 1-24 (Canceled).

Claim 25 (Currently Amended): An oral preparation, comprising: ~~which comprises~~ N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of [[the]] formula (1):



(1),

a pregelatinized starch[[,]];

a water-soluble excipient; and

a water-soluble polymer binder[[;]],

wherein ~~the content of~~ lurasidone is included in the preparation [[is]] in an amount of from 20 to 45% (wt/wt), and ~~the content of~~ the pregelatinized starch is included in the preparation [[is]] in an amount of from 10 to 50% (wt/wt).

Claim 26 (Currently Amended): The oral preparation of claim 25, wherein the oral preparation is prepared by [[the]] a process which comprises granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by ~~using~~ applying a solution of a water-soluble polymer binder.

Par Pharm., Inc.
Exhibit 1013
Page 277

Claim 27 (Currently Amended): The oral preparation of claim 25, wherein the oral preparation is prepared by [[the]] a process which comprises granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by a solution or dispersion of lurasidone and a water-soluble polymer binder.

Claim 28 (Previously Presented): The oral preparation of claim 25, wherein the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation.

Claim 29 (Previously Presented): The oral preparation of claim 25, wherein the pregelatinized starch is incorporated in an amount of 10 to 30% (wt/wt) based on the weight of the preparation.

Claim 30 (Previously Presented): The oral preparation of claim 25, wherein a content of lurasidone in the preparation is 20 to 40% (wt/wt).

Claim 31 (Currently Amended): The oral preparation of claim 25, wherein the water-soluble excipient is at least one ~~or more~~ selected from the group consisting of mannitol, lactose, saccharose, sorbitol, D-sorbitol, erythritol and xylitol.

Claim 32 (Previously Presented): The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose.

Claim 33 (Previously Presented): The oral preparation of claim 25, wherein a content of the water-soluble excipient per tablet is 30 to 60% (wt/wt).

Par Pharm., Inc.
Exhibit 1013
Page 278

Claim 34 (Previously Presented): The oral preparation of claim 25, wherein the water-soluble polymer binder is hydroxypropyl methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone or hydroxypropylcellulose.

Claim 35 (Previously Presented): The oral preparation of claim 25, wherein a content of the water-soluble polymer binder per tablet is 0.5 to 10% (wt/wt).

Claim 36 (Previously Presented): The oral preparation of claim 25, wherein a content of lurasidone per tablet is 10 to 160 mg.

Claim 37 (Previously Presented): The oral preparation of claim 25, wherein a content of lurasidone per tablet is 20 to 120 mg.

Claim 38 (Previously Presented): The oral preparation of claim 25, wherein a content of lurasidone per tablet is 20 to 160 mg.

Claim 39 (Previously Presented): The oral preparation of claim 25, wherein a content of lurasidone per tablet is 40 to 120 mg.

Claim 40 (Previously Presented): The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40% (wt/wt) and the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation.

Par Pharm., Inc.
Exhibit 1013
Page 279

Claim 41 (Previously Presented): The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40%, the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 20 to 120 mg.

Claim 42 (Previously Presented): The oral preparation of claim 25, wherein the water-soluble excipient is mannitol or lactose, a content of lurasidone in the preparation is 20 to 40%, the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation and a content of lurasidone per tablet is 40 to 120 mg.

Claim 43 (Previously Presented): The oral preparation of claim 25, wherein a pregelatinizing ratio of the pregelatinized starch is 50 to 95%.

Claim 44 (Previously Presented): The oral preparation of claim 25, wherein a 50% by volume particle size of lurasidone is 0.1 to 8 μm.

Claim 45 (Previously Presented): The oral preparation of claim 25, wherein the pregelatinized starch contains water soluble matter of 30% or less.

Claim 46 (Currently Amended): The oral preparation of claim 25, further comprising:
a disintegrant,
wherein a content of the disintegrant per tablet is 0.5 to 5% (wt/wt).

Claim 47 (Currently Amended): The oral preparation of claim 25, further comprising:
a disintegrant,

Par Pharm., Inc.
Exhibit 1013
Page 280

wherein a content of the disintegrant per tablet is 0.5 to 5% (wt/wt);

a content of lurasidone in the preparation is 20 to 40%;

the pregelatinized starch is incorporated in an amount of 10 to 40% (wt/wt) based on the weight of the preparation;

a content of lurasidone per tablet is 40 to 120 mg;

a pregelatinizing ratio of the pregelatinized starch is 50 to 95%;

50% by volume particle size of lurasidone is 0.1 to 8 μm;

the pregelatinized starch contains water soluble matter of 30% or less;

the water-soluble excipient is mannitol or lactose, and a content of the water-soluble excipient per tablet is 30 to 60% (wt/wt);

the water-soluble polymer binder is hydroxypropyl methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone or hydroxypropylcellulose;

and a content of the water-soluble polymer binder per tablet is 0.5 to 10% (wt/wt).

Claim 48 (Currently Amended): The oral preparation of ~~either one of~~ claim 46 or 47, wherein the disintegrant is at least one ~~or more~~ selected from the group consisting of corn starch, crystalline cellulose, low substituted hydroxypropylcellulose, carmellose, carmellose calcium, carmellose sodium, croscarmellose sodium, carboxymethyl starch sodium and crospovidone.

Claim 49 (Previously Presented): The oral preparation of claim 25, wherein a similarity factor f2 of each preparation is in the range of $50 \leq f2 \leq 100$ when a content of lurasidone per tablet changes over a range of 20 to 120 mg.

Claim 50 (Currently Amended): The oral preparation of claim 25, further comprising:

Par Pharm., Inc.
Exhibit 1013
Page 281

a lubricant,

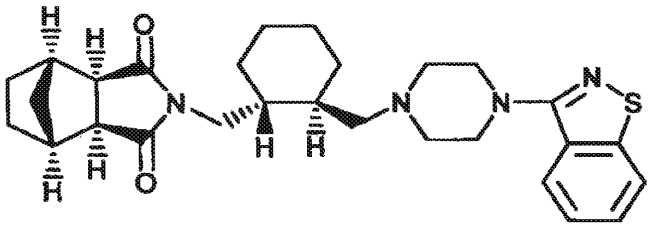
wherein a content of the lubricant per tablet is 1.0% (wt/wt) to 1.43% (wt/wt).

Claim 51 (Currently Amended): The oral preparation of claim 50, wherein the lubricant is at least one selected from the group consisting of magnesium stearate, talc, polyethylene glycol, silica and hydrogenated vegetable oil.

Claim 52 (Previously Presented): The oral preparation of claim 25, wherein the oral preparation is a tablet.

Claim 53 (Currently Amended): An oral preparation, comprising: ~~which comprises~~

N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone) of [[the]] formula (1):



(1),

a pregelatinized starch[[,]];

a water-soluble excipient; and

a water-soluble polymer binder,

wherein the oral preparation contains 20 to 45% (wt/wt) of lurasidone, the oral preparation contains 20 mg to 120 mg of lurasidone, the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the oral preparation, and the oral

preparation exhibits an equivalent dissolution profile across the range of lurasidone per oral preparation.

Claim 54 (Currently Amended): An oral preparation, comprising: ~~which comprises~~

N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone)[[,]];

a pregelatinized starch[[,]];

a water-soluble excipient; and

a water-soluble polymer binder,

wherein ~~a content of~~ lurasidone is included in the preparation [[is]] in an amount of from 20 to 40% (wt/wt),

the ~~content of~~ pregelatinized starch is included in the preparation [[is]] in an amount of from 10 to 40% (wt/wt),

the water-soluble excipient is mannitol or lactose, and

the water-soluble polymer binder is at least one ~~or more agents~~ selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose, polyvinylpyrrolidone and polyvinyl alcohol.

Claim 55 (Currently Amended): An oral preparation, comprising: ~~which comprises~~

N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone)[[,]];

a pregelatinized starch[[,]];

a water-soluble excipient; [[and]]

a water-soluble polymer binder[[,]]; ~~and further comprises~~

a disintegrant; and

Par Pharm., Inc.
Exhibit 1013
Page 283

a lubricant,

wherein the content of lurasidone in the preparation is 20 to 40% (wt/wt),

the content of pregelatinized starch in the preparation is 10 to 30% (wt/wt),

the water-soluble excipient is mannitol,

the water-soluble polymer binder is hydroxypropylmethylcellulose, and

the oral preparation is a tablet.

Claim 56 (Currently Amended): A method for preparing [[of]] the oral preparation of claim 25, ~~wherein the method comprises granulation of a powder mixture which comprises~~ comprising:

granulating a powder mixture comprising lurasidone, a pregelatinized starch and a water-soluble excipient by ~~using~~ applying a solution of a water-soluble polymer binder.

Claim 57 (Currently Amended): A method for preparing [[of]] the oral preparation of claim 25, ~~wherein the method comprises granulation of a powder mixture which comprises~~ comprising:

granulating a powder mixture comprising a pregelatinized starch and a water-soluble excipient by ~~using~~ applying a solution or dispersion of lurasidone and a water-soluble polymer binder.

Claim 58 (Withdrawn): A method of treating psychosis, comprising administering the oral preparation of claim 25, to a patient suffering from psychosis.

Claim 59 (Withdrawn): A method of treating schizophrenia, comprising administering the oral preparation of claim 25, to a patient suffering from schizophrenia.

Par Pharm., Inc.
Exhibit 1013
Page 284

REMARKS/ARGUMENTS

Favorable reconsideration of this application, as presently amended and in light of the following discussion, is respectfully requested.

Claims 25-59 are presently pending, Claims 58 and 59 having been withdrawn, and Claims 25-27, 31, 46-48, 50, 51 and 53-57 having been amended. Support for the amendments is in the original specification and claims. No new matter is added.

Applicant respectfully traverses the obviousness rejection of Claims 25-57 over Fujihara (EP 1327440) in view of Allenspach (US 2004/0186105) and Nakamura (WO 2004/017973).

It is respectfully submitted that none of the cited references is concerned with addressing the problem recognized and solved by Applicant – increasing both the amount and content ratio of lurasidone in a single tablet while maintaining the dissolution profile of lower dose tablets. As the amount or content ratio of lurasidone in the tablet increased, the dissolution profile became lower which in turn affected the lurasidone blood plasma level achieved for the amount dosed. As a result, when a larger dose of lurasidone was desired, the patient had to take multiple tablets at one time or, instead, an unacceptably bigger tablet with a lower content ratio.

In contrast, Applicant has demonstrated on Table 39 (reproduced below) that a single tablet with 80 mg lurasidone had the same dissolution profile as multiple doses of 20 mg and 40 mg tablets. The same was true for the 120 mg tablet as compared with 3 (three) 40 mg tablets or 6 (six) 20 mg tablets. Thus a doctor prescribing a dose of 120 mg lurasidone can prescribe the 120 mg tablet described in the present application with the confidence that the pharmacokinetic properties will be substantially the same as giving multiple doses of the lower strength tablets. Nothing in the cited references suggests that such results could be obtained by using pregelatinized starch and lurasidone at specific ratios.

Par Pharm., Inc.
Exhibit 1013
Page 285

Table 39

Tablet		40 mg tablet	20 mg tablet	80 mg tablet	40 mg tablet	20 mg tablet	120 mg tablet	40 mg tablet	20 mg tablet
Number of tablets		1 tablet	2 tablets	1 tablet	2 tablets	4 tablets	1 tablet	3 tablets	6 tablets
		Dissolution ratio (%)		Dissolution ratio (%)			Dissolution ratio (%)		
Time (min)	10	77	79	77	78	75	77	90	83
	15	90	90	88	86	84	92	94	90
	30	98	98	93	91	90	96	97	94
	45	100	100	94	93	92	97	98	95
f2 value		-	100	-	85	74	-	88	83

Fujihara rather indicates the difficulty, prior to the present application, in increasing both the amount and content ratio of lurasidone in a single tablet while maintaining the dissolution profile of lower dose tablets. Applicant's Test 10 (see Table 35 reproduced below) described in the present application shows that the lurasidone 120 mg tablet (content ratio: 25%) prepared without a pregelatinized starch as in Fujihara had undesirably low dissolution rates, 66% at 15 min and 84% at 45 min.

In contrast, Applicant found that the addition of a pregelatinized starch unexpectedly increased the dissolution rates, 91% dissolution in 15 min and 96% dissolution in 45 min.

Table 35

Components of tablets

Formulations	034-15-120-1000 (Disclosure of the present application)	RP-03323-120-1000 (Disclosure of Patent Document 2)
Lurasidone	120	120
Mannitol	213	222
Partly pregelatinized starch	120	-
Croscarmellose sodium	6	24
Tablettose 70	-	93
Hydroxypropyl methylcellulose	15	15
Magnesium stearate	6	6
Total	480	480
Dissolution profile		
Time (min)	Dissolution rate (%)	
10	83	54
15	91	66
30	95	80
45	96	84
f2 value	-	37

Fujihara is clearly different from the composition of Claim 25, as acknowledged in the Office Action (see page 7, 2nd paragraph). The reference simply describes tablets without a

pregelatinized starch and lacks discussion on controlling the weight ratio (*i.e.*, content ratio) of lurasidone with respect to the total weight of the preparation to fall within the specific range recited in Claim 25. Various preparations are described in Examples, but their components and the ratios are different from those of Claim 25, and the content ratio of lurasidone is 16%[1] or less (wt/wt). Therefore, Claim 25 is distinguishable from Fujihara[2].

Even if the proposed combination of Fujihara with Allenspach and Nakamura were considered, these secondary references cannot cure the deficiencies of Fujihara. Allenspach describes a COX-2 inhibitory drug formulation containing valdecoxib as active ingredient. The reference does not address the problem of increasing both the amount and content ratio of active ingredient in a single tablet while maintaining the dissolution profile of lower dose tablets. In Allenspach, the examples with the pregelatanized starch have the same amount and same content ratio of valdecoxib as in the conventional formulation, BEXTRA® (10 mg/tablet). Allenspach does not suggest that the use of pregelatinized starch could result in single tablets with larger amounts and/or higher content ratios but having the same dissolution profiles as those with the lower dose.

Allenspach indicates that the formulation may include specific pregelatinized starch having low viscosity and/or exhibiting a multimodal particle size distribution (see claim 1 of Allenspach), but the description is related to a completely different composition with a different active ingredient.

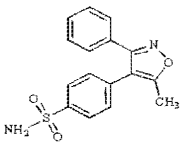
As stated in the attached Declaration under 37 C.F.R. § 1.132, valdecoxib is completely different from lurasidone at least in its physicochemical properties. The physicochemical properties of active ingredients have significant impacts on physical and

[1] For example, Example 23 (see Tables 28 and 29) uses the granule (248 mg) containing 40 mg of Compound 1.
[2] Applicant's original specification provides direct comparison with a composition prepared in accordance with Fujihara (without a pregelatinized starch) (see Test 10, paragraphs 0098-0102, Table 35). Fujihara (EP 1327440) is within the same patent family as WO 2002/024166, which is referenced in Applicant's original specification as Patent Document 2 (see paragraphs 0005-0007 describing that the Fujihara compositions could not have lurasidone at a higher content).

Par Pharm., Inc.
Exhibit 1013
Page 287

chemical interactions (e.g., interactions via intermolecular attractive force including ion bond, hydrogen bond, dipolar interaction, Van der Waals force, hydrophobic interaction, and hydrophilic interaction) with other additives of the composition including a pregelatinized starch. As such, one would not expect that what works with one active ingredient would work with a different active ingredient. For reference purposes, the following are an excerpt from drug label BEXTRA® (valdecoxib tablet indicated for relief of the signs and symptoms of osteoarthritis and adult rheumatoid arthritis and for the treatment of primary dysmenorrhea), and an excerpt from prescribing information of LATUDA® (lurasidone HCL tablet indicated for the treatment of patients with schizophrenia).

Valdecoxib is chemically designated as 4-(5-methyl-3-phenyl-4-isoxazolyl) benzenesulfonamide and is a diaryl substituted isoxazole. It has the following chemical structure:



Valdecoxib

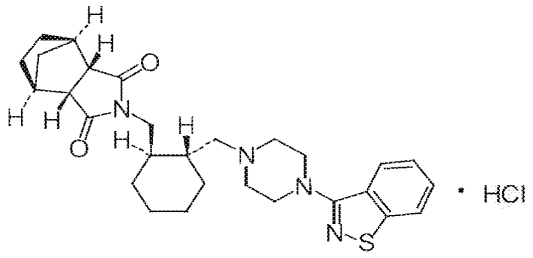
The empirical formula for valdecoxib is $C_{16}H_{14}N_2O_3S$, and the molecular weight is 314.36. Valdecoxib is a white crystalline powder that is relatively insoluble in water (10 µg/mL) at 25°C and pH 7.0, soluble in methanol and ethanol, and freely soluble in organic solvents and alkaline (pH=12) aqueous solutions.

(Excerpt from Drug Label for BEXTRA® - valdecoxib tablet, film coated)

LATUDA is an atypical antipsychotic belonging to the chemical class of benzisothiazol derivatives.

Its chemical name is (3a*R*,4*S*,7*R*,7a*S*)-2-{(1*R*,2*R*)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl] cyclohexylmethyl}hexahydro-4,7-methano-2*H*-isoindole-1,3-dione hydrochloride. Its molecular formula is $C_{28}H_{36}N_4O_2S \cdot HCl$ and its molecular weight is 529.14.

The chemical structure is:



Lurasidone hydrochloride is a white to off-white powder. It is very slightly soluble in water, practically insoluble or insoluble in 0.1 N HCl, slightly soluble in ethanol, sparingly soluble in methanol, practically insoluble or insoluble in toluene and very slightly soluble in acetone.

(Excerpt from Prescribing Information of LATUDA® - lurasidone HCl tablet)

As shown above, valdecoxib has the molecular weight of 314.36, while lurasidone hydrochloride has the molecular weight of 529.14. This difference in the molecular weights causes a significant difference in Van der Waals force. In addition, valdecoxib is freely soluble in alkaline (pH = 12) aqueous solutions and is a mild acidic compound, while a free form of lurasidone is a basic compound. This difference leads to significant differences in ion bond force, hydrogen bond force, and dipolar interaction. Moreover, valdecoxib has lipophilicity: Log P (Log Kow) of 2.67 (estimated)[3], while lurasidone hydrochloride has Log P (Log Kow) of 4.89 (estimated)[4]. This difference in the lipophilicities is $10^{(4.89-2.67)}$, which means that the lipophilicity of lurasidone hydrochloride is around 166 times higher than that of valdecoxib. This causes a significant difference in hydrophobic interaction.

These differences in physicochemical properties of valdecoxib and lurasidone are significant, and the description or experimental results related to the Allenspach valdecoxib formulations would not have directed one to consider using pregelatinized starch in lurasidone preparations described in Fujihara.

[3] https://pubchem.ncbi.nlm.nih.gov/compound/119607#section=Solubility
[4] https://pubchem.ncbi.nlm.nih.gov/compound/213046#section=Solubility

The use of pregelatinized starch could rather adversely affect the drug release rate in some cases. The attached article (Journal of Pharmaceutical Sciences, vol. 93, no. 11, p. 2746-2754 (2004)) published before the present application reported that addition of pregelatinized starch significantly *decreased* the release rate of the drugs, chlorpheniramine maleate and theophylline (see Abstract). The authors specifically attributed the decrease in the release rate to the use of partially pregelatinized starch (see Abstract). As such, at the time of filing the present application, one did not have any expectation that the addition of pregelatinized starch in lurasidone formulations would provide solution to the problem – increasing both the amount and content ratio of lurasidone in a single tablet while maintaining the dissolution profile of lower dose tablets.

As discussed above, neither Fujihara nor Allenspach addresses this problem. In particular, Allenspach simply evaluates the dissolution rate of valdecoxib 10 mg tablet, which is the same or lower dose as compared to conventional BEXTRA tablets (see label information below).

> BEXTRA Tablets for oral administration contain either 10 mg or 20 mg of valdecoxib. Inactive ingredients include lactose monohydrate, microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, magnesium stearate, hypromellose, polyethylene glycol, polysorbate 80, and titanium dioxide.

(Excerpt from Drug Label for BEXTRA - valdecoxib tablet, film coated)

Each example in Allenspach uses the composition of Example 1 (total tablet weight: 200 mg) including valdecoxib of 10 mg (*i.e.*, 5% (wt/wt) as the calculated content ratio). Allenspach performs dissolution tests only for this composition having valdecoxib at a lower content (10 mg) and a lower content ratio (5% (wt/wt)). Also, the reference provides no information as to how pregelatinized starch would impact the dissolution rate in lurasidone formulations.

Thus, even assuming, *arguendo*, that the proposed combination of Fujihara and Allenspach were proper, the references would have been still insufficient to provide solution to the problem addressed in the present application.

Nakamura would not have cured the deficiencies of Fujihara and Allenspach. Nakamura mentions that lurasidone can be administered at 5-120 mg per day. But such information on possible daily dose would not have provided one with insight on any specific drug formulation technique/method and would not have allowed one to find solution to the aforementioned problem. The reference does not teach how to achieve 20% or greater content ratio of the active ingredient and obtain the advantageous effects of rapid dissolution property and consistent dissolution profile over a wide range of the active ingredient content, in particular, higher contents. In this regard, the Office Action states that "it would have been routine and obvious ... to have adjusted the dose of lurasidone to have increased the amount of this drug in the composition" (OA, p. 9). However, Applicant respectfully submits that routine work could not have allowed one to produce a desired formulation of lurasidone.

As stated in the attached Declaration under 37 C.F.R. § 1.132, before the present application, an oral preparation having higher than 40 mg of the active ingredient with an acceptable size (which essentially needs a higher content ratio) could not be achieved. In order to administer more than 40 mg at one time, the administration of multiple tablets (or, instead, administration of an unacceptably bigger tablet) was required. If a tablet with more than 40 mg of the active ingredient was made with an acceptable size, its dissolution profile did not match that of the lower dose tablets. As mentioned above, Test 10 shows that the comparative formulation containing lurasidone at 25% prepared according to Fujihara without pregelatinized starch did not have desired dissolution rate. Also, the formulation of Comparative Example in Fujihara containing lurasidone at about 29% also had poor dissolution rate (see Tables 44 and 46 of Fujihara reproduced below).

Par Pharm., Inc.
Exhibit 1013
Page 291

Table 44

Component	Content (mg)
Compound 1	40
Mannitol	77.0
Croscarmellose sodium	12
Polyvinyl alcohol	4.8
Magnesium stearate	0.9

Table 46

Dissolution test of one FC tablet (40 mg-tablet) (dissolution percentage: %)						
Com. Ex.	0 min	5 min	10 min	15 min	30 min	45 min
3	0	26	53	74	84	88

Applicant overcame such difficulties in preparing a formulation with a higher lurasidone content and a desired dissolution rate, and has managed to obtain an oral preparation including lurasidone at a higher content (mg) and a higher content ratio (% (wt/wt)) by adding an adequate amount of pregelatinized starch. The cited references do not even address the aforementioned problem and fails to teach or suggest any solution to the problem. Despite the previous difficulties, the preparations in the present application can have *not only* higher contents (mg) of lurasidone (such as 80, 120, and 160 mg) *but also* higher content ratios (% (wt/wt)) of lurasidone (*e.g.*, 20 to 45% (wt/wt) in claim 25). Applicant has shown in Test 11 that the formulation achieved an improved dissolution profile at the higher content ratio of 25 to 40% (wt/wt) (see Test 11, paragraphs 0103-0106). Applicant has also found that the preparation has highly desired properties over a wide range of lurasidone content as discussed above. In particular, the preparation containing the active ingredient at a higher content shows a dissolution profile similar to multiple tablets where each tablet includes a lower content of the active ingredient, and the preparation can release the active ingredient at a desired concentration (see, for example, paragraph 0008).

For the foregoing reasons, Claim 25 and its dependent claims are unobvious over Fujihara over Allenspach and Nakamura.

Par Pharm., Inc.
Exhibit 1013
Page 292

Turning to independent Claims 53-55, these claims recite the same or narrower ranges for the contents of lurasidone and the pregelatinized starch. Therefore, for the reasons substantially similar to those set forth above for Claim 25, Claims 53-55 are unobvious over Fujihara over Allenspach and Nakamura.

Applicant notes that the advantageous property of the preparation is recited in Claim 53 which states: "the oral preparation contains 20 to 45% (wt/wt) of lurasidone, the oral preparation contains 20 mg to 120 mg of lurasidone, the pregelatinized starch is incorporated in an amount of 10 to 50% (wt/wt) based on the weight of the oral preparation, and *the oral preparation exhibits an equivalent dissolution profile across the range of lurasidone per oral preparation*" (emphasis added). Such advantageous property is demonstrated in the experiments described in Applicant's specification. For example, Test 13 (paragraphs 0111-0118) shows rapid dissolution of the compositions containing a wide range of contents (*i.e.*, 20 to 120 mg) of lurasidone as well as similarity of the dissolution profiles of the compositions. Test 10 clearly shows the advantage of the presence of a pregelatinized starch (paragraphs 0098-0102). Furthermore, Table 35 shows unpredictable dissolution results of the composition (*i.e.*, 91% dissolution in 15 min and 96% dissolution in 45 min vs. 66% and 84%, respectively, in the comparison). Moreover, most of the compositions in the present application achieved 80% or more of dissolution in 15 min already and all of the compositions achieved 90% or more of dissolution in 45 min (despite their higher content ratios of lurasidone) in contrast to Allenspach's target dissolution that was set at not less than 80% in 45 min in Example 2, which is highly advantageous dissolution profiles unpredictable from the prior art.

For the foregoing reasons, Claim 25 and its dependent claims as well as Claims 53-55 are unobvious over Fujihara over Allenspach and Nakamura.

Par Pharm., Inc.
Exhibit 1013
Page 293

In response to the outstanding rejections under the non-statutory obviousness-type double patenting based on U.S. Patent No. 8,729,085 and U.S. Patent No. 8,883,794, submitted herewith is a terminal disclaimer to overcome these rejections. Applicant respectfully requests that the rejections be withdrawn.

Applicant respectfully traverses the rejection under the non-statutory obviousness-type double patenting based on U.S. Patent No. 7,727,553 ("USP '553") in view of Nakamura and Allenspach.

USP '553 corresponds to Fujihara cited in the obviousness rejection. Claim 1 of USP '553 recites a rapidly disintegrating oral preparation comprising i) granules comprising a water-soluble excipient, a first disintegrant, a water-soluble polymer binder, and an active ingredient, and ii) a second disintegrant. However, USP '553 or its claims do not recite a formulation containing a pregelatinized starch. Nakamura and Allenspach fail to teach or suggest a preparation containing the active ingredient and a pregelatinized starch at the weight ratios specified in Claim 25 of the present application. Allenspach relates to totally different valdecoxib tablets, and Nakamura only generally describes possible daily dose of lurasidone. There is nothing that would have directed one to specifically prepare a composition that combines lurasidone with a pregelatinized starch at the specific ratios.

Therefore, the pending claims are believed to be patentably distinguishable from the claims of USP '553 in view of Nakamura and Allenspach.

Finally, Applicant respectfully traverses the provisional rejection under the non-statutory obviousness-type double patenting over claims 25-50 of U.S. Application No. 14/733,204 ("the '204 application"), Fujihara and Allenspach. Independent Claim 25, 37 and 49 of the '204 application are directed to a tablet for oral administration, and independent Claims 29 and 41 are directed to a method for manufacturing a tablet for oral administration.

Par Pharm., Inc.
Exhibit 1013
Page 294

Claim 25 of the '204 application recites a tablet including 20-120 mg of lurasidone, a pregelatinized starch, a water-soluble excipient, a water-soluble polymer binder, a disintegrant, and a lubricant. Claim 25 does not recite the content of the pregelatinized starch. Claims 37 and 49 do not specify the content of the pregelatinized starch, either.

As discussed above in response to the obviousness rejection, Fujihara and Allenspach are deficient and would not have directed one to specifically prepare a composition that contains the pregelatinized starch at the specific ratio in combination of lurasidone contained at the specific ratio as recited in Claim 25 of the present application.

As to the method claims, Claims 29 and 41 and their dependent claims do not recite formulating a tablet containing a specific ratio of pregelatinized starch. Therefore, the arguments similar to those stated above for composition claims are applicable.

For the foregoing reasons, the pending claims are believed to be patentably distinguishable from the claims of the '204 publication in view of Nakamura and Allenspach.

In view of the amendments and discussions presented above, Applicant respectfully submits that the present application is in condition for allowance, and an early action favorable to that effect is earnestly solicited.

Respectfully Submitted,

OBLON, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

/Yuki Onoe/

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(OMMN 07/09)

Docket No.: 472299US40CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: GROUP: 1627
Kazuyuki FUJIHARA

SERIAL NO: 14/512,189 EXAMINER: PIHONAK, SARAH

FILED: October 10, 2014

FOR: PHARMACEUTICAL COMPOSITION

DECLARATION UNDER 37 C.F.R. § 1.132

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Commissioner:

Now comes Shunsuke Mawatari who deposes and states that:

1. I am a graduate of Kyoto Pharmaceutical University and received my Master of Pharmaceutical Science degree in the year 2000.

2. I have been employed by Sumitomo Dainippon Pharma Co., Ltd. for 8 years as a formulation researcher in the field of Formulation Development.

3. I understand that the U.S. Patent Office has rejected claims in the above-identified application based on Fujihara (EP 1327440), Allenspach (US 2004/0186105) and Nakamura (WO 2004/017973).

4. None of these references is concerned with addressing the problem recognized and solved by Applicant – increasing both the amount and content ratio of lurasidone in a single tablet while maintaining the dissolution profile of lower dose tablets. As the amount or content ratio of lurasidone in the tablet increased, the dissolution profile became lower which in turn affected the lurasidone blood plasma level achieved for the amount dosed. As a result, when a larger dose of lurasidone was desired, the patient had to take multiple tablets at one time or, instead, an unacceptably bigger tablet with a lower content ratio.

5. In contrast, Table 39 in the application shows (reproduced below) that a single tablet with 80 mg lurasidone had the same dissolution profile as multiple doses of 20 mg and 40 mg

tablets. The same was true for the 120 mg tablet as compared with 3 (three) 40 mg tablets or 6 (six) 20 mg tablets. Thus a doctor prescribing a dose of 120 mg lurasidone can prescribe the 120 mg tablet described in the present application with the confidence that the pharmacokinetic properties will be substantially the same as giving multiple doses of the lower strength tablets. Nothing in the references suggests that such results could be obtained by using pregelatinized starch and lurasidone at specific ratios.

Table 39

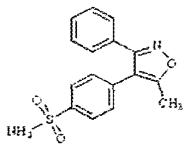
Tablet		40 mg tablet	20 mg tablet	80 mg tablet	40 mg tablet	20 mg tablet	120 mg tablet	40 mg tablet	20 mg tablet
Number of tablets		1 tablet	2 tablets	1 tablet	2 tablets	4 tablets	1 tablet	3 tablets	6 tablets
		Dissolution ratio (%)		Dissolution ratio (%)			Dissolution ratio (%)		
Time (min)	10	77	79	77	78	75	77	90	83
	15	90	90	88	86	84	92	94	90
	30	98	98	93	91	90	96	97	94
	45	100	100	94	93	92	97	98	95
f2 value		-	100	-	85	74	-	88	83

6. Fujihara is related to lurasidone tablets. Allenspach describes dissolution test results of valdecoxib tablets, not lurasidone preparations. In my opinion, valdecoxib is completely different from lurasidone at least in its physicochemical properties.

7. The physicochemical properties of active ingredients have significant impacts on physical and chemical interactions (e.g., interactions via intermolecular attractive force including ion bond, hydrogen bond, dipolar interaction, Van der Waals force, hydrophobic interaction, and hydrophilic interaction) with other additives of the composition including a pregelatinized starch. As such, one would not expect that what works with one active ingredient would work with a different active ingredient.

8. The physicochemical properties of valdecoxib and lurasidone are completely different. The following are an excerpt from drug label BEXTRA® (valdecoxib tablet indicated for relief of the signs and symptoms of osteoarthritis and adult rheumatoid arthritis and for the treatment of primary dysmenorrhea), and an excerpt from prescribing information of LATUDA® (lurasidone HCL tablet indicated for the treatment of patients with schizophrenia).

Valdecoxib is chemically designated as 4-(5-methyl-3-phenyl-4-isoxazolyl) benzenesulfonamide and is a diaryl substituted isoxazole. It has the following chemical structure:



Valdecoxib

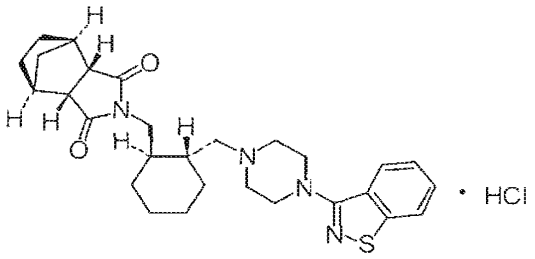
The empirical formula for valdecoxib is $C_{16}H_{14}N_2O_3S$, and the molecular weight is 314.36. Valdecoxib is a white crystalline powder that is relatively insoluble in water (10 µg/mL) at 25°C and pH 7.0, soluble in methanol and ethanol, and freely soluble in organic solvents and alkaline (pH=12) aqueous solutions.

(Excerpt from Drug Label for BEXTRA® - valdecoxib tablet, film coated)

LATUDA is an atypical antipsychotic belonging to the chemical class of benzisothiazol derivatives.

Its chemical name is (3a*R*,4*S*,7*R*,7a*S*)-2-{(1*R*,2*R*)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl] cyclohexylmethyl}hexahydro-4,7-methano-2*H*-isoindole-1,3-dione hydrochloride. Its molecular formula is $C_{28}H_{36}N_4O_2S \cdot HCl$ and its molecular weight is 529.14.

The chemical structure is:



Lurasidone hydrochloride is a white to off-white powder. It is very slightly soluble in water, practically insoluble or insoluble in 0.1 N HCl, slightly soluble in ethanol, sparingly soluble in methanol, practically insoluble or insoluble in toluene and very slightly soluble in acetone.

(Excerpt from Prescribing Information of LATUDA® - lurasidone HCl tablet)

9. As shown above, valdecoxib has the molecular weight of 314.36, while lurasidone hydrochloride has the molecular weight of 529.14. This difference in the molecular weights causes a significant difference in Van der Waals force. In addition, valdecoxib is freely soluble in alkaline (pH = 12) aqueous solutions and is a mild acidic compound, while a free form of lurasidone is a basic compound. This difference leads to significant differences in ion bond force, hydrogen bond force, and dipolar interaction. Moreover, valdecoxib has

lipophilicity: Log P (Log Kow) of 2.67 (estimated)[1], while lurasidone hydrochloride has Log P (Log Kow) of 4.89 (estimated)[2]. This difference in the lipophilicities is $10^{(4.89-2.67)}$, which means that the lipophilicity of lurasidone hydrochloride is around 166 times higher than that of valdecoxib. This causes a significant difference in hydrophobic interaction.

10. These differences in physicochemical properties of valdecoxib and lurasidone are significant, and the description or experimental results related to the Allenspach valdecoxib formulations would not have directed one to consider using pregelatinized starch in lurasidone preparations described in Fujihara.

11. The use of pregelatinized starch could rather adversely affect the drug release rate. The attached article (Journal of Pharmaceutical Sciences, vol. 93, no. 11, p. 2746-2754 (2004)) published before the present application reported that addition of pregelatinized starch significantly *decreased* the release rate of the drugs, chlorpheniramine maleate and theophylline (see Abstract). The authors specifically attributed the decrease in the release rate to the use of partially pregelatinized starch (see Abstract). As such, at the time of filing the present application, one did not have any expectation that the addition of pregelatinized starch in lurasidone formulations would provide solution to the problem – increasing both the amount and content ratio of lurasidone in a single tablet while maintaining the dissolution profile of lower dose tablets.

12. In the present application, Applicant found in Test 10 (Table 35 reproduced below) that the lurasidone 120 mg tablet (content ratio: 25%) including pregelatinized starch had unexpectedly high dissolution rates (*i.e.*, 91% dissolution in 15 min and 96% dissolution in 45 min as compared to 66% and 84%, respectively, in the comparative formulation without pregelatinized starch as in Fujihara).

[1] https://pubchem.ncbi.nlm.nih.gov/compound/119607#section=Solubility
[2] https://pubchem.ncbi.nlm.nih.gov/compound/213046#section=Solubility

Table 35

Components of tablets

Formulations	034-15-120-1000 (Disclosure of the present application)	RP-03323-120-1000 (Disclosure of Patent Document 2)
Lurasidone	120	120
Mannitol	213	222
Partly pregelatinized starch	120	-
Croscarmellose sodium	6	24
Tablettose 70	-	93
Hydroxypropyl methylcellulose	15	15
Magnesium stearate	6	6
Total	480	480

Dissolution profile

Time (min)	Dissolution rate (%)	
10	83	54
15	91	66
30	95	80
45	96	84
f2 value	-	37

13. With regard to the formulations in the attached article, I note that the model formulation (which appears to be a tablet) containing chlorpheniramine maleate or theophylline contained hydroxypropyl methylcellulose (HPMC) (see Abstract). HPMC is also used in lurasidone formulations described in the present application. Despite such a common ingredient, the formulations with pregelatinized starch (PPS) described in the article had slower dissolution rates (see Figs. 5 and 6 showing the increased amount of PPS caused even slower rates). The authors explicitly stated that "PPS actively contributes to the dissolution kinetics." (p. 2751, left column, above Fig. 5). In this case, PPS adversely contributed to the dissolution rate.

14. Before the present application, an oral preparation having higher than 40 mg of the active ingredient with an acceptable size (which essentially needs a higher content ratio) could not be achieved. In order to administer more than 40 mg at one time, the administration of multiple tablets (or, instead, administration of an unacceptably bigger tablet) was required. If a tablet with more than 40 mg of the active ingredient was made with an acceptable size, its dissolution profile did not match that of the lower dose tablets. As mentioned above, Test 10 shows that the comparative formulation containing lurasidone at 25% prepared according to

Fujihara without pregelatinized starch did not have desired dissolution rate. Also, the formulation of Comparative Example in Fujihara containing lurasidone at about 29% also had poor dissolution rate (see Tables 44 and 46 of Fujihara reproduced below).

Table 44

Component	Content (mg)
Compound 1	40
Mannitol	77.0
Croscarmellose sodium	12
Polyvinyl alcohol	4.8
Magnesium stearate	0.9

Table 46

Dissolution test of one FC tablet (40 mg-tablet) (dissolution percentage: %)						
Com. Ex.	0 min	5 min	10 min	15 min	30 min	45 min
3	0	26	53	74	84	88

15. Applicant overcame such difficulties in preparing a formulation with a higher lurasidone content and a desired dissolution rate, and has managed to obtain an oral preparation including lurasidone at a higher content (mg) and a higher content ratio (% (wt/wt)) by adding an adequate amount of pregelatinized starch. Fujihara, Allenspach and Nakamura do not even address the aforementioned problem and fails to teach or suggest any solution to the problem.

16. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

17. Further deponent saith not.

Signature Shunsuke Nawatari

Date Aug. 3, 2016

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The Influence of Excipients on Drug Release from Hydroxypropyl Methylcellulose Matrices

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Received 29 October 2003; revised 26 March 2004; accepted 7 June 2004

Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/jps.20181

ABSTRACT: The influence of commonly used excipients, spray-dried lactose (SDL), microcrystalline cellulose (MCC), and partially pregelatinized maize starch (Starch 1500®) on drug release from hydroxypropyl methylcellulose (HPMC, hypromellose) matrix system has been investigated. A model formulation contained 30%w/w drug, 20%w/w HPMC, 0.5%w/w fumed silica, 0.25%w/w magnesium stearate, and 49.25%w/w filler. Chlorpheniramine maleate and theophylline were used as freely (1 in 4) and slightly (1 in 120) water-soluble drugs, respectively. It was found that for both drugs, addition of 20 to 49.25%w/w Starch 1500 resulted in a significant reduction in drug release rates compared to when MCC or SDL was used. The study showed that using lactose or microcrystalline cellulose in the formulations resulted in faster drug release profiles. Partially pregelatinized maize starch contributed to retardation of both soluble and slightly soluble drugs. This effect may be imparted through synergistic interactions between Starch 1500 and HPMC and the filler actively forming an integral part within the HPMC gel structure. © 2004 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 93:2746–2754, 2004

Keywords: hypromellose; HPMC; Starch 1500; sustained release; pregelatinized starch; matrix system

INTRODUCTION

Nonionic cellulose ethers, and most frequently hydroxypropyl methylcellulose (HPMC, hypromellose) have been widely studied for their applications in oral sustained release (SR) systems.[1] When in contact with water, HPMC hydrates rapidly and forms a gelatinous barrier layer around the tablet. The rate of drug release from HPMC matrix is dependent on various factors such as type of polymer, drug, polymer/drug ratio, particle size of drug and polymer, and the type and amount of fillers used in the formulation.

Starch is one of the most widely used excipients in the manufacture of solid dosage forms. Most native starches consist of two polymers of glucose, that is, branched amylopectin and essentially linear amylose. Physically or chemically modified starches have been used in sustained release tablets because of their cold water-swelling capacity and gel barrier formation. Rak et al.[2] and Van Aerde and Remon[3] studied the possibility of using thermally modified starches for controled drug release. Herman and Remon[4] found that only fully pregelatinized starches containing a low amount of amylose (25% and lower) could produce a strong enough gel layer to ensure a sustained drug release. These findings are in agreement with Michailova et al.,[5] who claimed that the amylose molecules decrease the gel cohesion and accelerate the erosion of the gel layer. Mulhbacher et al.[6] studied crosslinked high amylose starch derivatives as matrices for controlled release of high drug loadings. They found that these polymeric excipients are able to control the release over 20 h from tablets loaded with 20 to 60% drug. Lenaerts et al.[7] used crosslinked high amylose starch for the

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Journal of Pharmaceutical Sciences, Vol. 93, 2746–2754 (2004)
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Par Pharm., Inc.
Exhibit 1013
Page 303

preparation of sustained release matrix tablets. They claimed the possibility for high active ingredient core loading and achieving either zero-order or Fickian release for most drugs. Other advantages of crosslinked high amylose starches may be the absence of erosion, limited swelling and the fact that increasing degree of crosslinking results in increased water uptake rate, drug release rate, and equilibrium swelling.[7]

Partially pregelatinized maize starches are normally used as binder-disintegrants in immediate release tablet formulations.[8] Leach et al.[9] claimed that these materials have a very limited obstructive gel formation capability at the surface of the tablet, which makes them not particularly suitable for SR applications. However, the use of partially pregelatinized starches in combination with other polymers, such as hypromellose, in SR tablets have not been fully examined. Therefore, the influence of Starch 1500, in comparison to MCC and SDL, on drug release from HPMC 2208 has been investigated in this study.

EXPERIMENTAL

Materials

Chlorpheniramine maleate (CPM) was obtained from Avocado Research Chemicals Ltd. (Lancas., UK), theophylline (TP) was obtained from Knoll AG (Ludwigshafen, Germany), and were used at 30%w/w in the formulation. Aqueous solubility for CPM is 1 in 4 (w/w), and for theophylline is 1 in 120 (w/w).

To study the effect of fillers on drug release, in all formulations only 20%w/w hydroxypropyl methylcellulose (HPMC, hypromellose) (Methocel® K4M, Dow Chemical Co., USA) was used. Higher HPMC levels may mask the differences impacted by the fillers on drug release.

Three commonly used fillers were studied: partially pregelatinized maize starch (PPS) (Starch 1500®, Colorcon, Dartford, UK), spray dried lactose (Fast Flo® #316, Foremost Farms, Wisconsin) and microcrystalline cellulose (MCC) (Avicel® PH102, FMC, Brussels, Belgium). Average particle size for Starch 1500 is 70, for MCC—90, and for spray dried lactose—100 microns. This relatively large particle size for all three materials can guarantee good powder flow in direct compression applications.

Fumed silica (Aerosil® A-200, Degussa AG, Dusseldorf, Germany) was used at 0.5%w/w level as a flow aid and magnesium stearate (Peter Greven, Venlo, The Netherlands) was used at 0.25%w/w level as a lubricant.

Model formulations (Table 1) were blended in a Turbular mixer (Type T2A, Pleuger, Basel, Switzerland). All ingredients with the exception of magnesium stearate were blended for 10 min, then magnesium stearate was added and mixed for an additional 5 min.

Bulk Properties of the Mixtures

The flow and packing properties of the powder mixtures were determined using an automatic tap volumeter (STAV 2003, J. Engelsmann AG, Ludwigshafen am Rhein, Germany). A 250-mL graduated glass cylinder was used. The tapping frequency was 250 ± 15 taps/min and the lift height 3.0 ± 0.2 mm. One hundred grams of powder were carefully filled into the measuring cylinder ensuring a flat top surface of the powder. The maximum bulk volume, V_o, was recorded. Then tapped volume, V_f, and compressibility index, $100 \times (V_o - V_f)/V_o$, were determined according to the USP.[10]

Tableting

Tablets (333 mg, 100 mg drug load) were compressed on the instrumented rotary Piccola tablet press (Riva, Argentina) at 30 rpm using 9-mm concave tooling, at compression forces from 4 to 14 kN. Upper compression and ejection forces were recorded.

The tablet weight and tablet weight variation were obtained for 20 tablets taken during each tableting run for each formulation. The accuracy of the weight determination was ±1 mg.

Dissolution Testing

The drug release from the matrices was measured using a Caleva ST7 dissolution tester (G.B. Caleva Ltd., Dorset, UK), USP apparatus II

Table 1. Model HPMC Formulations Used in This Study

Ingredients	Concentration (%w/w)
Drug	30.00
HPMC	20.00
Filler	49.25
Fumed silica	0.50
Magnesium stearate	0.25

Par Pharm., Inc.
Exhibit 1013
Page 304

(paddle) at 37 ± 1°C and 100 rpm. The drug concentration was measured using a UV spectrophotometer Model CE3021 (Cecil Instruments Ltd., Cambridge, UK), at 271 nm for theophylline and at 261 nm for chlorpheniramine maleate. The media used were purified water and phosphate buffer (pH 7.4). The buffer was prepared according to British Pharmacopoeia[11] by adding 250 mL of 0.2 M potassium dihydrogen orthophosphate to 393.4 mL of 0.1 M sodium hydroxide. For each formulation and condition, dissolution rates of at least three individual tablets were determined and means and standard deviation values were calculated.

Contact Angle Analysis

The process of water penetration into the hydrophilic matrix tablets was examined using FTÅ200 dynamic contact angle analyser (Camtel Ltd., UK) with a flexible video system allowing fast image acquisition (up to 60 images per second). Twenty-microliter droplets of purified water were deposited on the face surface of dry tablet samples by positioning the dispenser tip just above the surface and growing the pendant drop until its bottom touched the sample and the droplet detached. The contact angle was measured over the first 15 seconds as the water spread/absorbed and recorded as a function of time. Nonlinear capture timing was used with fast timing at the beginning of the test (15 measurements/s) and the slow capture (2 measurements/s) during the final absorption stage.

RESULTS AND DISCUSSION

Tableting Properties of Matrices

All formulations, regardless of type of excipient, had good flow (Table 2) with compressibility index of no more than 20. Tablet weight variations for all batches prepared in this study were found to be less than 1%, also an indication of good flow.

Table 2 also shows that both CPM and TP formulations with lactose produced the highest ejection forces, whereas Starch 1500 due to its inherent lubricity produced the lowest ejection forces.

All tablets had high mechanical strength. The rank order for tablet breaking force was: formulations containing MCC > spray dried lactose > PPS.

Influence of Different Fillers and Compression Force on Drug Release

Several authors[12–17] have stated that compression force had very little (not statistically significant) effect on drug release from HPMC matrices. However, in this study it was found that the applied compression force influenced drug release rate (Table 3), the extent of which was dependent on the type of filler used. The time taken for 50% drug release from formulations manufactured at different compression forces indicates that drug release become slower with increasing applied force. This effect is particularly profound when comparing tablets manufactured at a very low compression force of 4 kN with the tablets manufactured at higher compression forces of 10 and 14 kN. Depending on the compressibility behavior of the fillers, the porosity of the matrices may be reduced with increasing compression force, leading to slower water uptake and water front movement into the matrix, which in turn, may lead to slower drug release.

Figures 1 and 2 show drug release profiles from matrices compressed at 4 and 14 kN, for chlorpheniramine maleate and theophylline, respectively. Drug release from tablets made with lactose as a tiller was the fastest. Matrices containing partially pregelatinized starch produced the slowest drug release at all compression forces for both drugs.

Table 2. Powder and Tablet Characterization of HPMC Matrix Formulations Studied Here

Drug	Filler	Bulk Volume (g/cm^3) $n = 3$	Tapped Volume (g/cm^3) $n = 3$	Compress. Index	Tablet Ejection Force (N)	Tablet Weight Variation (%) $n = 20$
CPM	PPS	141 ± 1	115 ± 1	18	374 ± 22	0.2–0.4
	MCC	200 ± 1	166 ± 0	17	530 ± 27	0.4–0.7
	lactose	194 ± 2	165 ± 0	15	1079 ± 48	0.1–0.6
TP	PPS	84 ± 1	71 ± 1	15	82 ± 3	0.2–0.4
	MCC	230 ± 2	185 ± 1	20	96 ± 4	0.1–0.8
	lactose	197 ± 0	172 ± 0	13	238 ± 9	0.1–0.9

Par Pharm., Inc.
Exhibit 1013
Page 305

Table 3. The Influence of Compression Force on Drug Release ($T_{50\%}$) from HPMC Matrices Containing Different Fillers

		$T_{50\%}$ (min) for Tablets Manufactured at Various Compression Forces		
Drug	Filler	4 kN	10 kN	14 kN
CPM	PPS	215 ± 2	380 ± 2	420 ± 2
	MCC	185 ± 2	280 ± 2	300 ± 2
	lactose	95 ± 2	160 ± 2	175 ± 2
TP	PPS	290 ± 1	470 ± 1	470 ± 1
	MCC	230 ± 1	340 ± 1	360 ± 1
	lactose	190 ± 2	200 ± 2	230 ± 2

The drug release differences between tablets containing excipients such as lactose and MCC can be attributed mainly to the excipients solubility. However, the effect of Starch 1500 on drug release cannot be explained only by its solubility in water. It is more soluble compared to MCC, and produces slower drug release. Use of partially pregelatinized starch in HPMC matrices may bring about different effects resulting from interactions between HPMC and Starch 1500 that can affect the properties of the gel layer around the tablet.

To investigate the mechanism of drug release and to compare the performance of various matrix formulations, the percent drug released versus time profiles were used. Data corresponding to 5–60% release show a good fit to the Power Law Model[18] expressed in eq. 1:

$$M_t/M_{\text{inf}} = kt^n \qquad (1)$$

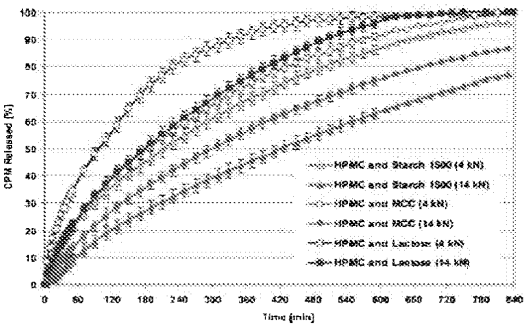

Figure 1. The influence of compression force (4 and 14 kN) on chlorpheniramine maleate release in water from HPMC matrices containing different fillers. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

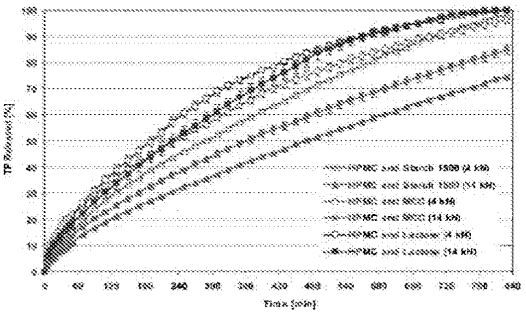

Figure 2. The influence of compression force (4 and 14 kN) on theophylline release in water from HPMC matrices containing different fillers. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

where M_t is the amount of drug released at time t, M_{inf} is the amount of drug released after infinite time, k is a kinetic constant incorporating structural and geometric characteristics of the tablet, and n is the diffusional exponent indicative of the drug release mechanism. The values of the kinetic constant (k), the release exponent (n), and correlation coefficient (R^2) determined from the drug release data are presented in Table 4. The correlation coefficients for the data were >0.99. For matrix tablets, an n value of near 0.5 indicates diffusion control, and an n value of near 1.0 indicates erosion or relaxation control.[19,20] Intermediate values suggest that diffusion and erosion contribute to the overall release mechanism. The values of n and k are inversely related. A very high k value may suggest a burst drug release from the matrix.[21]

Values of n for all matrices studied here were between 0.54 and 0.81, indicating an anomalous behavior corresponding to diffusion, erosion, and swelling mechanisms. In all these matrices availability of the water within the gel structure is also limited, and therefore a dissolution-controlled release is also involved. Comparing tablets manufactured at the same compression force, separately for chlorpheniramine maleate and theophylline, a linear trend of decreasing n values can be observed from PPS to MCC and to lactose. Matrices containing lactose exhibited a drug release closer to a diffusion-controlled process compared to MCC and Starch 1500.

Slower drug release from matrices with pregelatinized starch may be due to a slower penetration

Par Pharm., Inc.
Exhibit 1013
Page 306

Table 4. Values of the Kinetic Constant (k), Diffusional Exponent (n) Derived from Equation 1 and Correlation Coefficients (R^2), for HPMC Matrices Containing Different Fillers

Filler	Compression Force	CPM			TP		
		k	n	R^2	k	n	R^2
PPS	4 kN	1.1332	0.6878	0.9999	1.2495	0.6517	0.9982
	10 kN	0.5638	0.8048	0.9948	0.8673	0.6591	0.9997
	14 kN	0.3861	0.8081	0.9976	0.7816	0.6755	0.9997
MCC	4 kN	1.4910	0.6759	0.9976	2.4406	0.5540	0.9994
	10 kN	0.7197	0.7426	0.9971	1.1485	0.6371	0.9996
	14 kN	0.6304	0.7708	0.9967	1.1077	0.6451	0.9998
Lactose	4 kN	3.5188	0.5822	0.9993	2.6826	0.5497	0.9952
	10 kN	1.2356	0.7268	0.9961	2.6563	0.5508	0.9915
	14 kN	1.2152	0.7367	0.9966	2.6339	0.5614	0.9956

of the water front towards the central core of the matrix. Matrices with swelling restrictions, like those with Starch 1500, exhibit a shift towards drug release by erosion mechanism.[22] Tablets with partially pregelatinized starch would result in a more concentrated gel and increased gel tortuosity. Thus, the diffusional path would become more convoluted and the diffusion rate would therefore decrease. The effect of increased tortuosity and a delayed water penetration is expressed as low kinetic constant k values for tablets made with Starch 1500.

Although HPMC hydration and gel formation is not affected by changes in pH[23] (at pH ranges of gastrointestinal tract), the pH of the dissolution fluid is known to affect release rates of drugs from HPMC matrices.[24] Attempts have been made to quantify the influences of the solutions containing phosphate and chloride ions at different ionic strengths on dissolution rates from HPMC SR tablets.[25] In this study the effect of phosphate buffer (pH 7.4) on the matrix integrity and drug release from HPMC compacts containing different fillers was investigated. No significant changes in drug dissolution in buffer compared to water medium were observed for chlorpheniramine maleate (Fig. 3). Theophylline release in phosphate buffer compared to water was slightly different for lactose and MCC containing matrices (Fig. 4). Theophylline dissolution profiles for tablets made with pregelatinized starch were similar in water and in buffer. Drug release from matrices containing Starch 1500 in both water and phosphate buffer was slower than when lactose or MCC was used.

Influence of Starch 1500 Concentration on Drug Release from HPMC Matrices

Figures 5 and 6 show drug release profiles from HPMC matrices containing partially pregelatinized starch and lactose at different ratios, for CPM and TP, respectively. For both drugs, as the level of PPS increased the dissolution of drugs became significantly slower. Data in the range of 5–60% drug release were fitted into eq. 1, and the results are shown in Table 5. The correlation coefficients for most of the data were >0.99. For chlorpheniramine maleate matrices studied here, the values of n ranged from 0.7367 to 0.8081, and the k values ranged from 0.3861 to 1.2152. For theophylline tablets, the values of n ranged

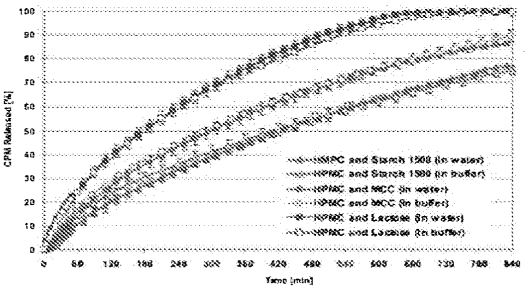

Figure 3. Chlorpheniramine maleate release from HPMC matrices containing different fillers manufactured at 14 kN in water and in phosphate buffer (pH 7.4). [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

Par Pharm., Inc.
Exhibit 1013
Page 307

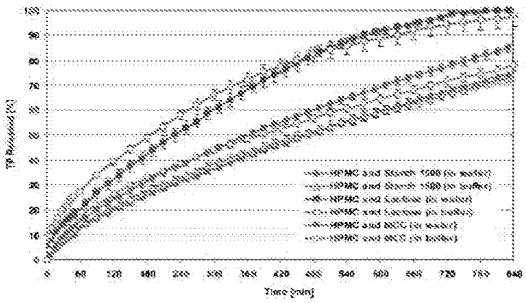

Figure 4. Theophylline release from HPMC matrices containing different fillers manufactured at 14 kN in water and phosphate buffer (pH 7.4). [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

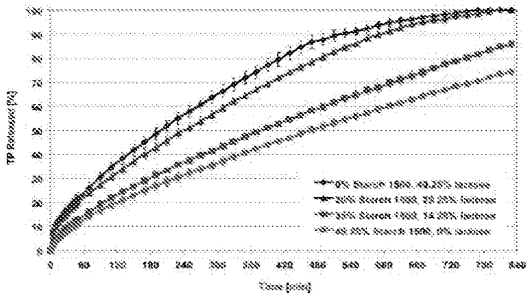

Figure 6. Effect of Starch 1500 levels on theophylline release from HPMC matrices manufactured at 14 kN. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

from 0.5614 to 0.6755, and the k values ranged from 0.7816 to 2.6339. Values of n for all matrices studied here were between 0.56 and 0.81, indicating an anomalous behavior corresponding to diffusion, erosion, and swelling mechanisms. Comparing tablets with the same drug, separately for chlorpheniramine maleate and theophylline, a linear trend of increasing n values can be observed with an increase in PPS concentration. Matrices containing more lactose exhibited a drug release closer to a diffusion-controlled process compared to tablets containing higher levels of Starch 1500. Thus, the effect seen with Starch 1500 is not just a spatial effect due to the presence of any filler, but PPS actively contributes to the dissolution kinetics. This contribution is imparted through possible contribution of Starch 1500 in gel formation of HPMC, that is, the filler actively forming an integral structure within the HPMC gel layer at lower concentrations of HPMC in the formulation.

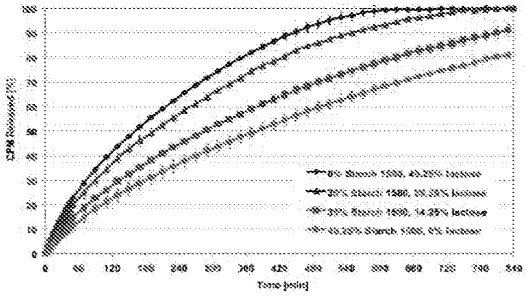

Figure 5. Effect of Starch 1500 levels on chlorpheniramine mleate release from HPMC matrices manufactured at 14 kN. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

Michailova et al.[26] characterized HPMC/pregelatinized starch hydrogels as "filled" composite systems where starch filler functions as a supporting frame, while the linear hypromellose forms the continuous disperse medium. In comparison with the cellulose derivative, the pregelatinized starch hydrates to a considerably lower degree due to the formation of intramolecular hydrogen bonds in the highly branched amylopectin.[27] These bonds suppress the polymer segments' mobility and diminish the degree of HPMC/pregelatinized starch hydration[28] resulting in a reduced gel layer diffusivity and decreased drug velocity from matrices containing higher pregelatinized starch quantity. For this reason, at 20% of HPMC and low concentration of the pregelatinized starch gel structure is quite porous with increased diffusion capability. With the increase in PPS concentration (35–49%), the swelled starch particles form strong supporting structure with comparatively strong rigidity. This HPMC/PPS gel structure may explain the slower drug release with increasing pregelatinized starch concentration in the formulation.

Testing of Water Absorption Rate

Drug release from HPMC matrix tablets is based on the glassy transition of the polymer into a rubbery gel that occurs as a result of water absorption/hydration of the polymer in the

Par Pharm., Inc.
Exhibit 1013
Page 308

Table 5. Values of the Kinetic Constant (k), Diffusional Exponent (n) Derived from Equation 1 and Correlation Coefficients (R^2), for HPMC Matrices Containing Various Levels of Starch 1500 and Manufactured at 14 kN

PPS Concentration (%w/w)	Lactose Concentration (%w/w)	CPM			TP		
		k	n	R^2	k	n	R^2
0.00	49.25	1.2152	0.7367	0.9966	2.6339	0.5614	0.9956
20.00	29.25	0.9771	0.7462	0.9957	2.4985	0.6116	0.9893
35.00	14.25	0.8780	0.7516	0.9992	0.9678	0.6639	0.9999
49.25	0.00	0.3861	0.8081	0.9976	0.7816	0.6755	0.9997

matrix. The drug release mechanism is determined by the structural characteristics of the gel layer (swelling, uniformity of polymer hydration, diffusion capability, and gel strength), and by gel layer erosion. Therefore, rapid gel formation (rubbery phase) to prevent rapid ingress of water into the matrix as well as high gel strength are critical factors in drug release from HPMC matrices. It was found that water penetration into tablets containing Starch 1500 was much slower compared to matrices containing MCC or lactose (Fig. 7). This observation was confirmed by contact angle measurements (Fig. 8). Table 6 shows that the initial contact angle for all the samples was similar (57–72°) and less than 90°, indicating good surface wettability behavior of these matrices, when the water drop flattens out and spreads on the tablet surface. However, for MCC and lactose containing matrices, the water droplet was rapidly absorbed into the matrix (within 2–7 s), which was much faster (6–13 times) than for the matrices containing Starch 1500 (>30 s). It was also found that the rate of contact angle change was significantly faster for chlorpheniramine maleate as a freely water soluble drug compared to theophylline.

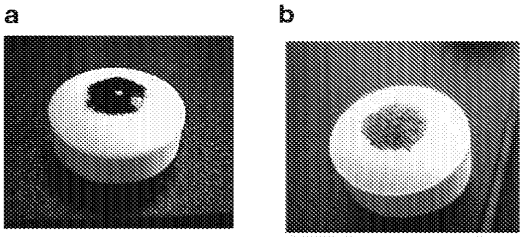

Figure 7. Water droplet and its absorption into (a) PPS and (b) microcrystalline cellulose or lactose containing HPMC matrices. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

The presence of free water within the gel layer plays an important part in drug movement across this barrier. Decreased availability of free water may lead to decreased drug diffusion across the gel layer. Partially pregelatinized starch and hypromellose combinations may be producing a gelled interlocked frame consisting of HPMC fibers and amylose reinforced by the swollen starch granules.[29,30] This network restrains water penetration into SR matrices and prevents fast drug release.[31]

CONCLUSIONS

All HPMC SR formulations had good powder flow, tablet weight uniformity, and mechanical strength. Formulations with lactose produced the highest ejection forces. On the other hand, partially pregelatinized starch due to its inherent lubricity produced the lowest ejection forces.

All formulations regardless of type of filler resulted in a slow drug release for both candidate drugs. Drug release was found to be affected by

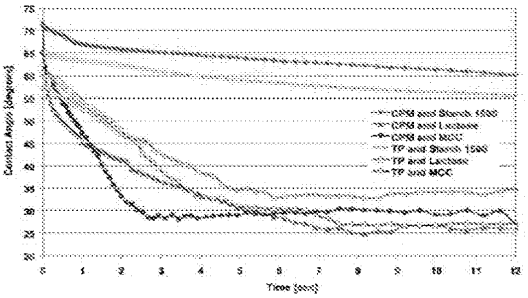

Figure 8. Contact angle measurements for water droplets on the surface of HPMC matrices containing different fillers. [Color figure can be seen in the online version of this article, available on the website, www.interscience.wiley.com.]

Par Pharm., Inc.
Exhibit 1013
Page 309

Table 6. Contact Angle Analysis of Purified Water on the Surface of HPMC Matrices Containing Different Fillers

Drug	Filler	Initial Contact Angle (Degrees)	Absorption Time (Seconds)	Rate of Contact Angle Change (Degree/s)
CPM	PPS	71	>30.0	1.1
	MCC	65	2.4	14.5
	lactose	72	7.0	6.6
TP	PPS	62	>30.0	0.5
	MCC	60	6.7	4.6
	lactose	57	5.4	4.2

applied compression force. At all compression forces and with both drugs, when Starch 1500 was used, drug release was slower compared to formulations containing MCC or lactose. Similar results were produced in phosphate buffer. These results may suggest that partially pregelatinized starch is not an inert filler in HPMC matrices (with low HPMC contents), but it actively contributes to the mechanism of drug release.

It was shown that for both drugs, increasing concentrations of Starch 1500 (20, 35 and 49.25%w/w) in the formulations caused a decrease in drug release rates. Therefore, use of blends of Starch 1500 with other fillers (e.g. lactose) can be used for tailoring the desired release profile of HPMC matrix systems.

It was found that water absorption into tablet containing partially pregelatinized starch was much slower compared to matrices containing MCC or lactose. This observation was confirmed by contact angle analysis. These results may explain the slower drug release from HPMC matrices containing Starch 1500 compared to those containing MCC or lactose.

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Page 310

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Par Pharm., Inc.
Exhibit 1013
Page 311

RELATED CASE STATUS UPDATE

Application No: 14/512,189

Reexam Control No:

Aug-09-2016

Application No	Reexam Control No	PTO Action Description	PTO Mail Date	Applicant Action Description	Date Filed
14/733,204		1st Office Action	Mar-29-2016		

Par Pharm., Inc.
Exhibit 1013
Page 312

Docket No. 472299US40CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Kazuyuki FUJIHARA

SERIAL NO: 14/512,189 GAU: 1627

FILED: October 10, 2014 EXAMINER: PIHONAK, SARAH

FOR: PHARMACEUTICAL COMPOSITION

TERMINAL DISCLAIMER

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Commissioner:

Now comes the undersigned, Attorney of Record in the present application, who avers as follows:

SUMITOMO DAINIPPON PHARMA CO., LTD. is the owner of the entire right, title and interest in and to the invention claimed and disclosed in the above-captioned patent application by virtue of assignment, said Assignment having been recorded in the U.S. Patent and Trademark Office at reel no. 020124, frame(s) 0821 (Change of Name reel no. 033905, frame(s) 0778).

SUMITOMO DAINIPPON PHARMA CO., LTD. hereby disclaims the terminal part of any patent granted on the above-captioned application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. 154 and 173 as shortened by any terminal disclaimer of U.S. Patent Nos. 8,729,085 and 8,883,794, and hereby agrees that any patent so granted on said above-captioned application shall be enforceable only for and during such period that it and Patent Nos. 8,729,085 and 8,883,794 are commonly owned. This agreement runs with any patent granted on the above-captioned application and is binding upon the grantee, its successors or assigns.

SUMITOMO DAINIPPON PHARMA CO., LTD. does not disclaim any terminal part of any patent granted on the above-captioned application that would extend to the full statutory term as defined in 35 U.S.C. 154 and 173 as shortened by any terminal disclaimer of U.S. Patent Nos. 8,729,085 and 8,883,794 in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid, is statutorily disclaimed in whole or terminally disclaimed under 37 C.F.R. 1.321(a), has all claims canceled by a reexamination certificate, is reissued, or is otherwise terminated prior to the expiration of its statutory term as shortened by any terminal disclaimer, except for the separation of common ownership stated above.

Respectfully Submitted,

OBLON, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

/Yuki Onoe/

August 9, 2016

Date Signed

Richard D. Kelly
Registration No. 27,757

Yuki Onoe
Registration No. 68,563

Customer Number
22850
Tel. (703) 413-3000
Fax. (703) 413-2220
(OMMN 11/09)

Electronic Patent Application Fee Transmittal

Application Number:	14512189
Filing Date:	10-Oct-2014
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Filer:	Bradley Davis Lytle/Naomi Lewis
Attorney Docket Number:	472299US40CONT

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 3 months with $0 paid	1253	1	1400	1400
Miscellaneous:				
Statutory or Terminal Disclaimer	1814	1	160	160
		Total in USD ($)		**1560**

Electronic Acknowledgement Receipt	
EFS ID:	26593094
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22850
Filer:	Bradley Davis Lytle/Naomi Lewis
Filer Authorized By:	Bradley Davis Lytle
Attorney Docket Number:	472299US40CONT
Receipt Date:	09-AUG-2016
Filing Date:	10-OCT-2014
Time Stamp:	16:44:38
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1560
RAM confirmation Number	3508
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		472299USAmendment.pdf	557849 37a24c847e05923338adc77f5ba40d5be54d7868	yes	40

Multipart Description/PDF files in .zip description

Document Description	Start	End
Miscellaneous Incoming Letter	1	1
Extension of Time	2	2
Amendment/Req. Reconsideration-After Non-Final Reject	3	3
Claims	4	11
Applicant Arguments/Remarks Made in an Amendment	12	22
Affidavit-traversing rejectns or objectns rule 132	23	29
Applicant Arguments/Remarks Made in an Amendment	30	38
Miscellaneous Incoming Letter	39	39
Terminal Disclaimer Filed	40	40

Warnings:

Information:

2	Fee Worksheet (SB06)	fee-info.pdf	32597 b788d8c32924e86f45134f43c01fbb8e52d4c6c2	no	2

Warnings:

Information:

Total Files Size (in bytes):	590446

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No. 472299US40CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S) Kazuyuki FUJIHARA

SERIAL NO: 14/512,189 ART UNIT: 1627

FILING DATE: October 10, 2014 EXAMINER: PIHONAK, SARAH

FOR: PHARMACEUTICAL COMPOSITION

FEE TRANSMITTAL

☐ No additional fee is required

☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 is claimed.

☐ Track 1 Prioritized Examination

The Fee has been calculated as shown below:

FOR	NUMBER FILED	NUMBER EXTRA	RATE	CALCULATIONS
TOTAL CLAIMS	35 - 36 =	0	x $80 =	$ 0.00
INDEPENDENT CLAIMS	4 - 4 =	0	x $420 =	$ 0.00
☐ MULTIPLE DEPENDENT CLAIMS (If applicable)			+ $780 =	$0.00
☐ LATE FILING OF DECLARATION			+ $140 =	$0.00
☐ NON-ELECTRONIC FILING FEE			+ $400 =	$0.00
			BASIC FEES	$0.00
			TOTAL OF ABOVE CALCULATIONS	$ 0.00
☐ REDUCTION BY 50% FOR FILING BY SMALL ENTITY				$0.00
☐ FILING IN NON-ENGLISH LANGUAGE			+ $140 =	$0.00
			TOTAL	$ 0.00

☐ Please charge Deposit Account No. **15-0030** in the amount of **$0.00**

■ Credit card payment is being made online (if electronically filed), or is attached hereto (if paper filed), in the amount of **$1,560.00**.

■ The Director is hereby authorized to charge any additional fees which may be required for the papers being filed herewith and for which no payment is enclosed herewith, or credit any overpayment to Deposit Account No. **15-0030**, with the **EXCEPTION** of deficiencies in fees for multiple dependent claims in new applications.

■ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. §1.136, and any additional fees required under 37 C.F.R. §1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030.

Submitted by: /Yuki Onoe/

Richard D. Kelly
Registration No. 27,757

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(OMMN 02/12)

Yuki Onoe
Registration No. 68,563

Docket No. 472299US40CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	Kazuyuki FUJIHARA		
SERIAL NO:	14/512,189	GAU:	1627
FILED:	October 10, 2014	EXAMINER:	PIHONAK, SARAH
FOR:	PHARMACEUTICAL COMPOSITION		

REQUEST FOR EXTENSION OF TIME UNDER 37 C.F.R. 1.136

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Commissioner:

It is hereby requested that a **three** month extension of time be granted to August 9, 2016 for

■ filing a response to the Official Action dated: February 9, 2016

☐ responding to the requirements in the Notice of Allowability dated:

☐ responding to the Notice to File Missing Parts of Application dated:

☐ filing a Notice of Appeal. A timely response to the final rejection, due has been filed.

☐ filing an Appeal Brief. A Notice of Appeal was filed on:

☐ Applicant claims small entity status. See 37 CFR 1.27.

The required fee of $1,400.00 is being made by credit card payment online (if electronically filed), or is attached hereto (if paper filed), and any further charges may be made against the Attorney of Record's Deposit Account No. **15-0030**.

Respectfully Submitted,

OBLON, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

/Yuki Onoe/

Richard D. Kelly
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(OMMN 07/09)

Yuki Onoe
Registration No. 68,563

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/512,189	Filing Date 10/10/2014	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	08/09/2016	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 36	Minus	** 36	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 4	Minus	***4	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	**0**

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
MARGARET BYARS

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	14/512,189	FUJIHARA, KAZUYUKI	

Document Code - DISQ	Internal Document – DO NOT MAIL

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed : 8/9/16	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
jean proctor

U.S. Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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NOTICE OF ALLOWANCE AND FEE(S) DUE

22850 7590 11/07/2016

OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 11/07/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	472299US40CONT	5575

TITLE OF INVENTION: PHARMACEUTICAL COMPOSITION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	02/07/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 02/11)

Par Pharm., Inc.
Exhibit 1013
Page 323

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22850 7590 11/07/2016
OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	472299US40CONT	5575

TITLE OF INVENTION: PHARMACEUTICAL COMPOSITION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	02/07/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
PIHONAK, SARAH	1627	514-254040

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): (**Please first reapply any previously paid issue fee shown above**)
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29
  NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27
  NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status.
  NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Par Pharm., Inc.
Exhibit 1013
Page 324

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	472299US40CONT	5575

22850 7590 11/07/2016

OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 11/07/2016

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 14/512,189	Applicant(s) FUJIHARA, KAZUYUKI	
	Examiner SARAH PIHONAK	Art Unit 1627	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *8/9/16*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *25-57 and 59*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☒ All b) ☐ Some *c) ☐ None of the:
   1. ☒ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☒ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

1. The present application is being examined under the pre-AIA first to invent provisions.

Terminal Disclaimer

2. The terminal disclaimer filed on 8/9/16 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of USP 8,729,085 and USP 8,883,794 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Declaration Submitted under 37 C.F.R. § 1.132

3. The declaration of Shunsake Mawatari submitted under 37 CFR 1.132 filed 8/9/16 is sufficient to overcome the rejection of claims 25-57 based upon 35 USC 103(a) as being unpatentable over Fujihara, in view of Allenspach, and Nakamura. The declaration shows that a lurasidone tablet containing 120 mg. of lurasidone (25% by weight of the tablet), and 25% by weight pregelatinized starch exhibited improved dissolution compared to a tablet preparation taught by Fujihara, comprising 120 mg. lurasidone and lacking pregelatinized starch:

Table 35

Components of tablets

Formulations	034-15-120-1000 (Disclosure of the present application)	RP-03323-120-1000 (Disclosure of Patent Document 2)
Lurasidone	120	120
Mannitol	213	222
Partly pregelatinized starch	120	-
Croscarmellose sodium	6	24
Tablettose 70	-	93
Hydroxypropyl methylcellulose	15	15
Magnesium stearate	6	6
Total	480	480

Dissolution profile

Time (min)	Dissolution rate (%)	
10	83	54
15	91	66
30	95	80
45	96	84
f2 value	-	37

The declaration also refers to Levina et. al., Journal of Pharmaceutical Sciences, 93(11), 2746-2754, (2004), which showed that two different formulations of active agents (chlorpheniramine maleate and theophylline, 30% by weight in each composition) comprising from 20-49.5% by weight pregelatinized starch exhibited reduced dissolution profiles compared to formulations lacking pregelatinized starch (see Abstract; p. 2749, Figs. 1-2; p. 2750, Fig. 3; p. 2753, left col., last 2 para). Levina et. al. also shows that the dissolution profile of a theophylline tablet containing 35% and 40.25% pregelatinized starch was significantly reduced compared to a theophylline tablet containing 20% pregelatinized starch (see p. 2751, Fig. 6). The declaration provides evidence that pregelatinized starch can have unpredictable effects on the dissolution profile of active agents, and that the claimed oral preparations comprising pregelatinized starch within the amount range cited improves the dissolution profile

compared to the oral lurasidone preparation taught by Fujihara which lacks pregelatinized starch. This evidence is not taught or suggested by the prior art.

Status of Claims

4. Claims 25-59 are pending as of the response filed on 8/9/16. Claims 58-59 are withdrawn from consideration, as these claims are directed to a non-elected invention.

5. The rejections for nonstatutory double patenting over the claims of USP 8,729,085 and USP 8,883,794 are withdrawn in acceptance of the terminal disclaimer filed on 8/9/16. The provisional rejection for nonstatutory double patenting over the claims of appl. 14/733204 is withdrawn as a terminal disclaimer was filed during prosecution of 14/733204 and is of record for 14/733204. The rejection for nonstatutory double patenting over the claims of USP 7,727,553 in view of Nakamura and Allenspach is withdrawn in consideration of the unexpected results provided in the declaration and the instant specification.

6. The rejection of claims 25-57 under 103(a) over Fujihara et. al., EP 1327440, in view of Allenspach et. al., US 2004/0186105, and Nakamura, WO 2004/017973 is withdrawn in consideration of the declaration submitted under 1.132 and in consideration of Applicant's response.

7. Claims 25-57 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claim 59, directed to the process of making or using the allowable product, previously withdrawn from consideration as a result of a restriction

requirement, is hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between inventive groups I-II as set forth in the Office action mailed on 11/3/15 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

8. Claims 25-57 and 59 are allowed.

Examiner's Amendment

9. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in an interview with Akihiro Yamazaki on 11/2/16.

Please amend the claims accordingly:

10. Delete claim 58.

Reasons for Allowance

11. The following is an examiner's statement of reasons for allowance: there is no prior art which teaches or suggests an oral preparation comprising lurasidone in an amount from 20-45% by weight; pregelatinized starch from 10-50% by weight; a water-soluble excipient; and a water soluble polymer binder. The closest prior art is Fujihara et. al., EP 1327440; and Allenspach et. al., US 2004/0186105 (both references are of previous record). Fujihara teaches an oral formulation comprising lurasidone but does not teach or suggest pregelatinized starch. Allenspach teaches an oral formulation comprising a drug of low water solubility and pregelatinized starch in an amount from about 1-50% by weight of the composition, for increasing the dissolution rate. Allenspach does not teach lurasidone. Applicants have provided the reference of Levina et. al., Journal of Pharmaceutical Sciences, 93(11), 2746-2754, (2004), which showed that two different formations of active agents (chlorpheniramine maleate and theophylline, 30% by weight in each composition) comprising from 20-49.5% by weight pregelatinized starch exhibited reduced dissolution profiles compared to formulations lacking pregelatinized starch (see Abstract; p. 2749, Figs. 1-2; p. 2750, Fig. 3; p. 2753,

left col., last 2 para). Levina et. al. also shows that the dissolution profile of a theophylline tablet containing 35% and 40.25% pregelatinized starch was significantly reduced compared to a theophylline tablet containing 20% pregelatinized starch (see p. 2751, Fig. 6). Levina, published the same year as Allenspach, therefore provides evidence that pregelatinized starch, in an amount from 20-49.5% by weight, can decrease the dissolution profile of active agents.

In contrast, Applicant has provided evidence to show that preparations containing lurasidone in amounts of 25%, 28.6%, 33.3%, and 40%; and pregelatinized starch in amounts of 25%, 28.6%, 33.3%, and 40% exhibit similar dissolution profiles, as shown by the f2 values, which fall within the range of 50≤f2≤100 (see p. 37 of the instant specification, Table 36):

Table 36

Formulations	034-15-80-1000	RP-03320	RP-03321	RP-03322
Lurasidone	80	80	80	80
Mannitol	142	104	67	30
Partly pregelatinized starch	80	80	80	80
Croscarmellose sodium	4	4	4	4
Hydroxypropyl methylcellulose	10	8	6	4
Magnesium stearate	4	4	3	2
Total	320	280	240	200

Dissolution profile

Time (min)	Dissolution ratio (%)			
10	85	73	71	68
15	89	80	80	81
30	93	88	88	89
45	94	90	91	91
f2 value	-	60	60	63

Additionally, it has been shown that compositions comprising 25% lurasidone and about 12.5%, 31.25%, and 25% pregelatinized starch exhibit similar dissolution profiles (see instant specification, p. 22, Tables 10-13):

Component	Example No.			
	1	4	5	6
Lurasidone	80	80	80	80
Mannitol	144	176	116	136
Partly pregelatinized starch	80	40	100	80
Croscarmellose sodium	4	8	8	8
Hydroxypropyl methylcellulose	8	12	12	12

Component	Example No.			
	1	4	5	6
Granules in the above (a)	316	316	316	316
Magnesium stearate	4	4	4	4

Similarity factor	Example No.			
	1	4	5	6
f2	-	67	60	62

The results are not taught or suggested by the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled “Comments on Statement of Reasons for Allowance.”

Conclusion

12. Claims 25-57 and 59 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	14/512,189	FUJIHARA, KAZUYUKI	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

All participants (applicant, applicant's representative, PTO personnel):

(1) *SARAH PIHONAK*. (3)_____.

(2) *Akihiro Yamazaki*. (4)_____.

Date of Interview: *02 November 2016*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *25-59*.

Identification of prior art discussed: _____.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

A voicemail message was left for Yuki Onoe discussing the proposed amendment to delete withdrawn claim 58 and rejoin withdrawn claim 59. Akihiro Yamazaki contacted the examiner on behalf of Yuki Onoe and approved the proposed amendment. Claims 25-57 and 59 are allowed.

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/SARAH PIHONAK/ Primary Examiner, Art Unit 1627	

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	**Art Unit**
	SARAH PIHONAK	1627

CPC						
Symbol					**Type**	**Version**
A61K		31	/	496	F	2013-01-01
A61K		9	/	2018	I	2013-01-01
A61K		9	/	2059	I	2013-01-01
C07D		417	/	12	I	2013-01-01
A61K		9	/	0053	I	2013-01-01
A61K		9	/	2009	I	2013-01-01
A61K		9	/	2027	I	2013-01-01
A61K		9	/	2031	I	2013-01-01
A61K		9	/	2054	I	2013-01-01
A61K		9	/	2095	I	2013-01-01
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			/			

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	34	
/SARAH PIHONAK/ Primary Examiner.Art Unit 1627	11/02/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	**Art Unit**
	SARAH PIHONAK	1627

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION														
CLASS	SUBCLASS	CLAIMED									NON-CLAIMED					
		A	6	1	K	31 / 496 (2006.01.01)										
CROSS REFERENCE(S)		A	6	1	K	9 / 00 (2006.01.01)										
		A	6	1	K	9 / 20 (2006.01.01)										
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)	C	0	7	D	417 / 12 (2006.01.01)										

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	34	
/SARAH PIHONAK/ Primary Examiner.Art Unit 1627	11/02/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	**Art Unit**
	SARAH PIHONAK	1627

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		17	9	33	25	49								
	2		18	10	34	26	50								
	3		19	11	35	27	51								
	4		20	12	36	28	52								
	5		21	13	37	29	53								
	6		22	14	38	30	54								
	7		23	15	39	31	55								
	8		24	16	40	32	56								
	9	1	25	17	41	33	57								
	10	2	26	18	42		58								
	11	3	27	19	43	34	59								
	12	4	28	20	44										
	13	5	29	21	45										
	14	6	30	22	46										
	15	7	31	23	47										
	16	8	32	24	48										

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	34	
/SARAH PIHONAK/ Primary Examiner.Art Unit 1627	11/02/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Par Pharm., Inc.
Exhibit 1013
Page 339

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 NEWS 16  APR 26  Data Quality Improved in CNFULL and FRFULL
 NEWS 17  JUN 16  Latest New STN Release Now Available
 NEWS 18  JUN 24  May 2016 Update to Emtree in STN Provides Expanded
                  Terminology for Biomedical and Pharmacological Searchers
 NEWS 19  JUL 21  Non-conventional Patent Families for Chinese Dual Filings
                  in INPADOC on STN

 NEWS EXPRESS 17 OCT 2016 CURRENT WINDOWS VERSION IS V8.6,
              AND CURRENT DISCOVER FILE IS DATED 17 OCT 2016.

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     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.27       0.27

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FILE COVERS 1907 - 27 Oct 2016 VOL 165 ISS 19
FILE LAST UPDATED: 26 Oct 2016 (20161026/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Dec 2015

CAplus includes complete International Patent Classification (IPC)
reclassification data for the fourth quarter of 2016.
```

CAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s us 20150056284/pn
L1            1 US 20150056284/PN
                (US20150056284/PN)

=> d l1 abs ibib it

L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2016 ACS on STN
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AB A preparation for oral administration comprises a pregelatinized starch comprising N-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride (lurasidone hydrochloride) as an active ingredient; a water-soluble excipient; and a water-soluble polymeric binder, where the preparation exhibits an invariant level of elution behavior even when the content of its active ingredient is varied. For example, tablets were formulated containing lurasidone 80, mannitol 144, pregelatinized starch 80, croscarmellose sodium 4, hydroxypropyl Me cellulose 8, and Mg stearate 4 mg per tablet and film coated with a composition containing hydroxypropyl Me cellulose, titania, polyethylene glycol, and carnauba wax.

ACCESSION NUMBER: 2006:1252571 CAPLUS Full-text
DOCUMENT NUMBER: 146:13212
TITLE: Oral pharmaceutical compositions of lurasidone
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Dainippon Sumitomo Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126681	A1	20061130	WO 2006-JP310571	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006250340	A1	20061130	AU 2006-250340	20060526
AU 2006250340	B2	20120209		
CA 2606510	A1	20061130	CA 2006-2606510	20060526
CA 2606510	C	20140722		
EP 1884242	A1	20080206	EP 2006-746900	20060526

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     EP 1884242           B1   20130417
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
     KR 2008012306        A    20080211    KR 2007-7027270         20060526
     KR 1380088           B1   20140410
     CN 101184489         A    20080521    CN 2006-80018223        20060526
     CN 101184489         B    20110119
     RU 2398586           C2   20100910    RU 2007-148997          20060526
     BR 2006011409        A2   20101123    BR 2006-11409           20060526
     CN 102048734         A    20110511    CN 2010-10564784        20060526
     CN 102048734         B    20131120
     JP 4733120           B2   20110727    JP 2007-517921          20060526
     EP 2422783           A1   20120229    EP 2011-181100          20060526
     EP 2422783           B1   20150408
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
     PT 1884242           E    20130521    PT 2006-746900          20060526
     ES 2408687           T3   20130621    ES 2006-746900          20060526
     KR 2013122019        A    20131106    KR 2013-7027051         20060526
     KR 1552033           B1   20150909
     ES 2535478           T3   20150512    ES 2011-181100          20060526
     TW I359020           B    20120301    TW 2006-121223          20060614
     US 20090143404       A1   20090604    US 2007-919678          20071031
     US 8729085           B2   20140520
     MX 2007014872        A    20080215    MX 2007-14872           20071123
     IN 2007CN05369       A    20080125    IN 2007-CN5369          20071126
     IN 267160            A1   20150703
     HK 1108379           A1   20130726    HK 2008-102367          20080303
     JP 2011126915        A    20110630    JP 2011-61211           20110318
     JP 5285105           B2   20130911
     US 20140235651       A1   20140821    US 2014-14183283        20140218
     US 8883794           B2   20141111
     US 20150056284       A1   20150226    US 2014-14512189        20141010 <--
     US 20150265611       A1   20150924    US 2015-14733204        20150608
PRIORITY APPLN. INFO.:                      JP 2005-153508       A  20050526
                                            CN 2006-80018223     A3 20060526
                                            EP 2006-746900       A3 20060526
                                            JP 2007-517921       A3 20060526
                                            KR 2007-7027270      A3 20060526
                                            WO 2006-JP310571     W  20060526
                                            US 2007-919678       A1 20071031
                                            US 2014-14183283     A1 20140218
                                            US 2014-14512189     A1 20141010
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IT   Dissolution
     Particle size
     Pharmaceutical coated tablets
     Pharmaceutical granules
     Pharmaceutical tablets
        (oral compns. of lurasidone with improved dissoln. profile)
IT   63-42-3, Lactose   69-65-8, D-Mannitol   9005-25-8D, Starch,
     pregelatinized   367514-87-2, Lurasidone   367514-88-3, Lurasidone
     hydrochloride
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (oral compns. of lurasidone with improved dissoln. profile)
OS.CITING REF COUNT:     3     THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
                               (4 CITINGS)
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> e dissolution/ct
E#   FREQUENCY    AT     TERM
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E1           0     1     DISSOLN./CT
E2           0     1     DISSOLUTA/CT
E3      104446    28 --> DISSOLUTION/CT
E4           0     2     DISSOLUTION (L) SALTING-IN/CT
E5           0     2     DISSOLUTION ENTHALPY/CT
E6        6234     2     DISSOLUTION RATE/CT
E7           0     1     DISSOLUTUM/CT
E8           0     1     DISSOLVAN/CT
E9           0     2     DISSOLVAN 4411/CT
E10          0     1     DISSOLVANT/CT
E11          0     2     DISSOLVANT APV/CT
E12          0     1     DISSOLVED/CT

=> set expand continuous
SET COMMAND COMPLETED

=> s e3,e6
        104446 DISSOLUTION/CT
          6234 "DISSOLUTION RATE"/CT
L2      110455 (DISSOLUTION/CT OR "DISSOLUTION RATE"/CT)

=> file registry
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  14.85      15.12

FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   26 OCT 2016  HIGHEST RN 2020110-79-4
DICTIONARY FILE UPDATES:  26 OCT 2016  HIGHEST RN 2020110-79-4

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http://www.cas.org/legal/infopolicy

TSCA INFORMATION NOW CURRENT THROUGH APRIL 29, 2016

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/training/stn/database-specific

=> e lurasidone/cn
E13          1     LURAPRET TX-PMC 28/CN
E14          1     LURASAN/CN
E15          1 --> LURASIDONE/CN
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E16           1     LURASIDONE HYDROCHLORIDE/CN
E17           1     LURATEX A 25/CN
E18           1     LURAZEPAM/CN
E19           1     LURAZOL BLACK BA/CN
E20           1     LURAZOL BLACK DFN/CN
E21           1     LURAZOL BLACK E/CN
E22           1     LURAZOL BLACK RS/CN
E23           1     LURAZOL BLACK SD/CN
E24           1     LURAZOL BLACK SN/CN

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L3            1 LURASIDONE/CN

=> d l3 str rsd

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2016 ACS on STN

Absolute stereochemistry.
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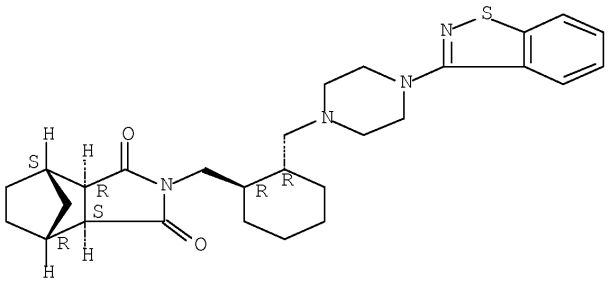

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


Ring System Data

Elemental|Elemental| Size of |Ring System|   Ring    |   RID
Analysis |Sequence |the Rings|  Formula  |Identifier|Occurrence
   EA    |   ES    |   SZ    |    RF     |   RID    |  Count
=========+=========+=========+===========+==========+==========
C6       |C6       |6        |C6         |46.150.1  |1
C4N2     |NC2NC2   |6        |C4N2       |46.383.1  |1
C3NS-C6  |NSC3-C6  |5-6      |C7NS       |333.255.8 |1
C4N-C5-C5|NC4-C5-C5|5-5-5    |C9N        |553.5.1   |1

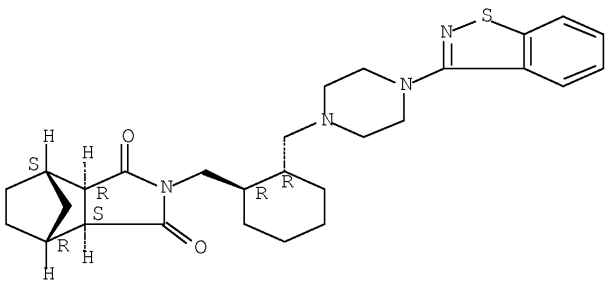


=> d l3

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2016 ACS on STN
RN   367514-87-2  REGISTRY
ED   Entered STN:  07 Nov 2001
CN   4,7-Methano-1H-isoindole-1,3(2H)-dione,
     2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-
     piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, (3aR,4S,7R,7aS)-  (CA
```

INDEX NAME)
OTHER CA INDEX NAMES:
CN (3aR,4S,7R,7aS)-2-[[(1R,2R)-2-[[4-(1,2-Benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-4,7-methano-1H-isoindole-1,3(2H)-dione
OTHER NAMES:
CN 2-[[(1R,2R)-2-[[4-(1,2-Benzoisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-(3aS,4R,7S,7aR)-4,7-methano-1H-isoindole-1,3(2H)-dione
CN Lurasidone
FS STEREOSEARCH
MF C28 H36 N4 O2 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, EMBASE, IMSRESEARCH, IPA, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

258 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
273 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e starch 1500/cn
E25 1 STARCH 10-PHENOXARSINYL ETHER/CN
E26 1 STARCH 11-(4'-CYANOBIPHENYL-4-YLOXY)UNDECANOATE/CN
E27 1 --> STARCH 1500/CN
E28 1 STARCH 1500 X/CN
E29 1 STARCH 2,4-D ESTER/CN
E30 1 STARCH 2-(DIETHYLAMINO)ETHYL 3-SULFOPROPYL ETHER ACETATE HYDROCHLORIDE/CN
E31 1 STARCH 2-(DIETHYLAMINO)ETHYL HYDROXYETHYL 3-SULFOPROPYL ETHER, HYDROCHLORIDE/CN
E32 1 STARCH 2-(DIETHYLAMINO)ETHYL HYDROXYETHYL HYDROXYPROPYL 3-SULFOPROPYL ETHER, HYDROCHLORIDE/CN
E33 1 STARCH 2-(DIETHYLAMINO)ETHYL HYDROXYPROPYL 3-SULFOPROPYL ETHER, HYDROCHLORIDE/CN
E34 1 STARCH 2-CHLOROETHYLAMINODIPROPIONATE/CN
E35 1 STARCH 2-HYDROXY-2-PHENYLETHYL ETHER/CN

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E36          1     STARCH 2-HYDROXY-3-(METHACRYLOYLOXY)PROPYL ETHER/CN

=> s e27
L4           1 "STARCH 1500"/CN

=> d l4

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2016 ACS on STN
RN   9005-25-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Starch  (CA INDEX NAME)
OTHER NAMES:
CN   α-Starch
CN   1000Y (starch)
CN   75A
CN   75A (polysaccharide)
CN   A 1FB004215
CN   Absorbo HP
CN   AccuGel
CN   Ace P 320
CN   ADM Clineo 716
CN   Advance Snow P
CN   Aeromyl 115
CN   Agglofroid 009
CN   Agglofroid 313E
CN   Allbond 200
CN   Alphajel KS 37
CN   Alstar B
CN   Alstar E
CN   Alstar H
CN   Amaizo 100
CN   Amaizo 213
CN   Amaizo 310
CN   Amaizo 5
CN   Amaizo 71
CN   Amaizo 710
CN   Amaizo W 13
CN   Amalean I-A 2131
CN   Amalean I-A 7081
CN   Amerikor 818
CN   Amicoa
CN   Amidex 3001
CN   Amidex 3005
CN   Amidex 4001
CN   Amido-STA 1500
CN   Amidomax 4800
CN   Amigel
CN   Amigel 12014
CN   Amigel 30076
CN   Amijel VA 160
CN   Amilofaks
CN   Amilofax 00
CN   Amilys 100
CN   Amisol 3408
CN   Amycol HF
CN   Amycol K
CN   Amycol W
CN   Amylex 20/20
CN   Amylofiber SH
CN   Amylogel
```

```
CN   Amylogel 03001
CN   Amylogel 03003
CN   Starch 1500
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
     DISPLAY
DEF  A high-polymeric carbohydrate material primarily composed of amylopectin
     and amylose.  It is usually derived from cereal grains such as corn, wheat
     and sorghum, and from roots and tubers such as potatoes and tapioca. It
     includes starch which has been pregelatinized by heating in the presence
     of water.
DR   9057-05-0, 42616-76-2, 53112-52-0, 53262-79-6, 60496-95-9, 67674-80-0,
     75138-75-9, 75398-82-2, 85746-25-4, 118550-61-1, 131800-97-0, 152987-55-8,
     154636-77-8, 730985-55-4, 730985-56-5, 730985-57-6, 955949-61-8,
     1309960-29-9, 1374255-25-0
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration, Polyother, Polyother only
SR   CA
LC   STN Files:   ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS,
       CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFIALL,
       IPA, MEDLINE, MSDS-OHS, NAPRALERT, PIRA, RTECS*, TOXCENTER, USPAT2,
       USPATFULL, USPATOLD
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

          192224 REFERENCES IN FILE CA (1907 TO DATE)
           16782 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          196773 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1            1 S US 20150056284/PN
                E DISSOLUTION/CT
                SET EXPAND CONTINUOUS
L2       110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                E LURASIDONE/CN
L3            1 S E15
                E STARCH 1500/CN
L4            1 S E27

=> s 367514-87-2/crn
L5           13 367514-87-2/CRN

=> file caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  22.46      37.58

FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
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FILE COVERS 1907 - 27 Oct 2016 VOL 165 ISS 19
FILE LAST UPDATED: 26 Oct 2016 (20161026/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2016.

CAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1             1 S US 20150056284/PN
               E DISSOLUTION/CT
               SET EXPAND CONTINUOUS
L2        110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
               E LURASIDONE/CN
L3             1 S E15
               E STARCH 1500/CN
L4             1 S E27
L5            13 S 367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016

=> s l3 or l5
            273 L3
            128 L5
L6          336 L3 OR L5

=> s l4
L7       196773 L4
```

```
=> s l6 and l7
L8          18 L6 AND L7

=> s (gelatin? or pregelatin?) (l) (starch)
        181451 GELATIN?
          3509 PREGELATIN?
        318460 STARCH
         14065 STARCHES
        319856 STARCH
                  (STARCH OR STARCHES)
L9       22051 (GELATIN? OR PREGELATIN?) (L) (STARCH)

=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1            1 S US 20150056284/PN
                E DISSOLUTION/CT
                SET EXPAND CONTINUOUS
L2       110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                E LURASIDONE/CN
L3            1 S E15
                E STARCH 1500/CN
L4            1 S E27
L5           13 S 367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6          336 S L3 OR L5
L7       196773 S L4
L8           18 S L6 AND L7
L9        22051 S (GELATIN? OR PREGELATIN?) (L) (STARCH)

=> s l6 and l9
L10          4 L6 AND L9

=> s l10 and (py<=2006 or ay<=2006 or pry<=2006)
       27666877 PY<=2006
        6032082 AY<=2006
        5526001 PRY<=2006
L11          1 L10 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)

=> s l11 not l1
L12          0 L11 NOT L1

=> s l8 and (py<=2006 or ay<=2006 or pry<=2006)
       27666877 PY<=2006
        6032082 AY<=2006
        5526001 PRY<=2006
L13          2 L8 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)

=> s l13 not l1
L14          1 L13 NOT L1

=> d l14 abs ibib hitind hitstr

L14  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2016 ACS on STN
```

AB Disclosed are oral compns. containing a hardly water-soluble active ingredient and having favorable disintegration characteristics which comprise a molded solid article (for example, granules) obtained by mixing the hardly water-soluble active ingredient, a first disintegrating agent and a water-soluble filler with the use of a water-soluble polymer binder and then mixing this molded solid article with a second disintegrating agent, or a molded solid article obtained by mixing the hardly water-soluble active ingredient, a disintegrating agent and a sugar alc. with the use of a water-soluble polymer binder. When orally administered, these prepns. show excellent elution of the active ingredient in the digestive tract. Moreover, these prepns. can show the same elution behavior at different contents of the active ingredient and thus enable the selection of the most suitable drug for each patient, which makes these prepns. highly useful in clin. medicine. A film-coated tablet was prepared form granules containing N-[4-[4-(1,2-benzisothiazole-3-yl)-1-piperazinyl]-(2R,3R)-2,3-tetramethylene-butyl]-(1'R,2'S,3'R,4'S)-2,3-bicyclo[2,2,1]heptanedicarboxyimide hydrochloride 10, lactose 50, sodium croscarmellose 6 mg, and polyvinyl alc. 1.2 mg, calcium hydrogen phosphate anhydride 35, crystalline cellulose 17, and magnesium stearate 0.8 mg, and a coating material containing hydroxypropyl Me cellulose 1.95, titanium oxide 0.6, concentrate glycerin 0.45 mg, and carnauba wax q.s.

ACCESSION NUMBER: 2002:240535 CAPLUS Full-text
DOCUMENT NUMBER: 136:268164
TITLE: Oral compositions with favorable disintegration characteristics
INVENTOR(S): Fujihara, Kazuyuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024166	A1	20020328	WO 2001-JP7983	20010914 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2824077	C	20160126		
AU 2001086237	A	20020402	AU 2001-86237	20010914 <--
CA 2424001	A1	20030320	CA 2001-2424001	20010914 <--
CA 2424001	C	20131022		
EP 1327440	A1	20030716	EP 2001-965637	20010914 <--
EP 1327440	B1	20090513		
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EP 1974724	A2	20081001	EP 2008-156778	20010914 <--
EP 1974724	A3	20081112		
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ES 2325764	T3	20090916	ES 2001-965637	20010914 <--
JP 4868695	B2	20120201	JP 2002-528202	20010914 <--

TW I289062	B	20071101	TW 2001-123036		20010919 <--
TW I289063	B	20071101	TW 2005-103731		20010919 <--
US 20040028741	A1	20040212	US 2003-381036		20030321 <--
US 7727553	B2	20100601			
PRIORITY APPLN. INFO.:			JP 2000-288234	A	20000922 <--
			CA 2001-2424001	A3	20010914 <--
			EP 2001-965637	A3	20010914 <--
			WO 2001-JP7983	W	20010914 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

IPCI A61K0009-16 [ICM,7]; A61K0009-20 [ICS,7]; A61K0009-30 [ICS,7]; A61K0031-496 [ICS,7]; A61K0045-00 [ICS,7]; A61K0047-10 [ICS,7]; A61K0047-26 [ICS,7]; A61K0047-30 [ICS,7]

IPCR A61K0009-00 [I]; A61K0009-16 [I]; A61K0009-20 [I]; A61K0009-30 [I]; A61K0031-496 [I]

CC 63-6 (Pharmaceuticals)

IT 63-42-3, Lactose 69-65-8, D-Mannitol 557-04-0, Magnesium stearate 7757-93-9, Calcium hydrogen phosphate 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinyl pyrrolidone 9004-34-6, Crystalline cellulose, biological studies 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Corn starch, biological studies 74811-65-7, Sodium croscarmellose 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing hardly water-soluble active ingredients)

IT 9005-25-8, Corn starch, biological studies 367514-88-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. with favorable disintegration characteristics containing hardly water-soluble active ingredients)

RN 9005-25-8 CAPLUS

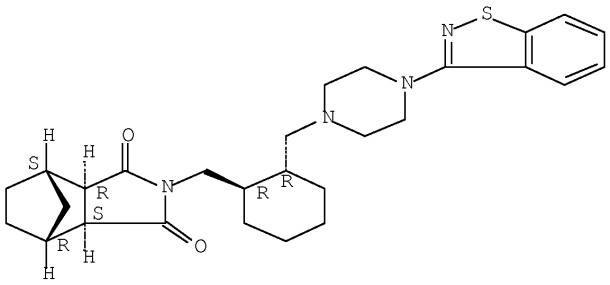
CN Starch (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 367514-88-3 CAPLUS

CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[[(1R,2R)-2-[[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]methyl]cyclohexyl]methyl]hexahydro-, hydrochloride (1:1), (3aR,4S,7R,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

```
REFERENCE COUNT:         6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1             1 S US 20150056284/PN
                 E DISSOLUTION/CT
                 SET EXPAND CONTINUOUS
L2        110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                 E LURASIDONE/CN
L3             1 S E15
                 E STARCH 1500/CN
L4             1 S E27
L5            13 S 367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6           336 S L3 OR L5
L7        196773 S L4
L8            18 S L6 AND L7
L9         22051 S (GELATIN? OR PREGELATIN?) (L) (STARCH)
L10            4 S L6 AND L9
L11            1 S L10 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L12            0 S L11 NOT L1
L13            2 S L8 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L14            1 S L13 NOT L1

=> s l2 and l9
L15          948 L2 AND L9

=> s l15 and (py<=2006 or ay<=2006 or pry<=2006)
       27666877 PY<=2006
        6032082 AY<=2006
        5526001 PRY<=2006
L16          191 L15 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)

=> s (lurasidone) and l16
             369 LURASIDONE
L17            1 (LURASIDONE) AND L16

=> s l17 not l1
L18            0 L17 NOT L1

=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1             1 S US 20150056284/PN
                 E DISSOLUTION/CT
                 SET EXPAND CONTINUOUS
L2        110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                 E LURASIDONE/CN
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```
L3            1 S E15
                E STARCH 1500/CN
L4            1 S E27
L5           13 S 367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6          336 S L3 OR L5
L7       196773 S L4
L8           18 S L6 AND L7
L9        22051 S (GELATIN? OR PREGELATIN?) (L) (STARCH)
L10           4 S L6 AND L9
L11           1 S L10 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L12           0 S L11 NOT L1
L13           2 S L8 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L14           1 S L13 NOT L1
L15         948 S L2 AND L9
L16         191 S L15 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L17           1 S (LURASIDONE) AND L16
L18           0 S L17 NOT L1

=> log hold

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1            1 SEA SPE=ON  ABB=ON  PLU=ON  US 20150056284/PN
                D L1 ABS IBIB IT
                E DISSOLUTION/CT
                SET EXPAND CONTINUOUS
L2       110455 SEA SPE=ON  ABB=ON  PLU=ON  (DISSOLUTION/CT OR "DISSOLUTION
                RATE"/CT)

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                E LURASIDONE/CN
L3            1 SEA SPE=ON  ABB=ON  PLU=ON  LURASIDONE/CN
                D L3 STR RSD
                D L3
                E STARCH 1500/CN
L4            1 SEA SPE=ON  ABB=ON  PLU=ON  "STARCH 1500"/CN
                D L4
L5           13 SEA SPE=ON  ABB=ON  PLU=ON  367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6          336 SEA SPE=ON  ABB=ON  PLU=ON  L3 OR L5
L7       196773 SEA SPE=ON  ABB=ON  PLU=ON  L4
L8           18 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L7
L9        22051 SEA SPE=ON  ABB=ON  PLU=ON  (GELATIN? OR PREGELATIN?) (L)
                (STARCH)
L10           4 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L9
L11           1 SEA SPE=ON  ABB=ON  PLU=ON  L10 AND (PY<=2006 OR AY<=2006 OR
                PRY<=2006)
L12           0 SEA SPE=ON  ABB=ON  PLU=ON  L11 NOT L1
L13           2 SEA SPE=ON  ABB=ON  PLU=ON  L8 AND (PY<=2006 OR AY<=2006 OR
                PRY<=2006)
L14           1 SEA SPE=ON  ABB=ON  PLU=ON  L13 NOT L1
                D L14 ABS IBIB HITIND HITSTR
L15         948 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND L9
L16         191 SEA SPE=ON  ABB=ON  PLU=ON  L15 AND (PY<=2006 OR AY<=2006 OR
                PRY<=2006)
L17           1 SEA SPE=ON  ABB=ON  PLU=ON  (LURASIDONE) AND L16
```

```
L18           0 SEA SPE=ON  ABB=ON  PLU=ON  L17 NOT L1
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                54.15      91.73

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:04:29 ON 27 OCT 2016

Connecting via Winsock to STN at pto-stn on port 23



Welcome to STN International!  Enter x:X

LOGINID:ssptasmp1617

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 16:04:51 ON 27 OCT 2016
FILE 'CAPLUS' ENTERED AT 16:04:51 ON 27 OCT 2016
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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                54.15      91.73

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                54.15      91.73

FILE 'CAPLUS' ENTERED AT 16:05:01 ON 27 OCT 2016
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FILE COVERS 1907 - 27 Oct 2016 VOL 165 ISS 19
FILE LAST UPDATED: 26 Oct 2016 (20161026/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Dec 2015

CAplus includes complete International Patent Classification (IPC)
reclassification data for the fourth quarter of 2016.

CAplus now includes the comprehensive Cooperative Patent Classification
(CPC).  See HELP CPC for details.

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http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> e starch, gelatinize/ct
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E37          0     2     STARCH, CARBOXYMETHYL ETHER, SODIUM SALT/CT
E38          0     2     STARCH, DEXTRINIZED/CT
E39          0       --> STARCH, GELATINIZE/CT
E40          0    70     STARCH, PHOSPHATE/CT
E41          0     2     STARCH, POLYMER WITH 2-PROPENOIC ACID, GRAFT/CT
E42          0     2     STARCH, SOLUBLE/CT
E43          0     2     STARCH, THIN-BOILING/CT
E44          0     2     STARCH, WAXY/CT
E45          0     2     STARCH-2,3-DIALDEHYDE/CT
E46          0     1     STARCH-ACRYLIC/CT
E47          0     2     STARCH-ACRYLIC ACID COPOLYMER/CT
E48          0     2     STARCH-ACRYLIC ACID GRAFT COPOLYMER/CT

=> e starch/ct
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E49          0     2     STARBURST GENERATION 2/CT
E50          0     2     STARBURST POLYMERS/CT
E51          0    42 --> STARCH/CT
E52          0     2     STARCH (BACTERIAL GLYCOGEN) SYNTHASE/CT
E53          0   102     STARCH ACETATE/CT
E54          0     2     STARCH ACETATE FIBERS/CT
E55          0     2     STARCH ACETATE PHOSPHATE FIBERS/CT
E56          1    30     STARCH BINDING DOMAIN-CONTAINING PROTEIN 1/CT
E57          0     2     STARCH BINDING DOMAIN-CONTG. PROTEIN 1/CT
E58          0     2     STARCH COMPDS. SYNTHETIC FIBERS/CT
E59          0     2     STARCH COMPOUND SYNTHETIC FIBERS/CT
E60          0     2     STARCH DEBRANCHING ENZYME/CT

=> e e51+all/ct
E61      15629     BT4  Chemical compounds/CT
E62      14231       BT3  Biochemical compounds/CT
E63      15629     BT4  Chemical compounds/CT
E64      14851       BT3  Macromolecular compounds/CT
E65       1436         BT2  Biomacromolecular compounds/CT
E66      26638     BT4  Materials/CT
E67      14856       BT3  Biological materials/CT
E68      15629   BT5  Chemical compounds/CT
E69      14231     BT4  Biochemical compounds/CT
E70      15629   BT5  Chemical compounds/CT
E71      14851     BT4  Macromolecular compounds/CT
E72       1436       BT3  Biomacromolecular compounds/CT
E73      15629     BT4  Chemical compounds/CT
E74      63509       BT3  Organic compounds/CT
E75      15629   BT5  Chemical compounds/CT
E76      14851     BT4  Macromolecular compounds/CT
E77     321323       BT3  Polymers/CT
E78      18212         BT2  Biopolymers/CT
E79      15629     BT4  Chemical compounds/CT
E80      63509       BT3  Organic compounds/CT
E81     173353         BT2  Carbohydrates/CT
```

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E82     115651           BT1  Polysaccharides/CT
E83          0             -->  Starch/CT
E84                           UF   Corn starch/CT
E85                           UF   Potato starch/CT
E86          0                NT1  Carboxymethyl starch/CT
E87          0                NT1  Hydroxypropyl starch/CT
E88          0                NT1  Sodium carboxymethyl starch/CT
E89          0                NT1  Starch acetate/CT
E90          0                NT1  Starch, phosphate/CT
E91      13958                RT   Bakery products/CT
E92      14183                RT   Dough/CT
E93                           RT   Enzymes (L) starch-degrading/CT
E94                           RT   Enzymes (L) starch-hydrolyzing/CT
E95      23848                RT   Flours and Meals/CT
E96      10302                RT   Food gelling/CT
E97      15630                RT   Food viscosity/CT
E98      10434                RT   Gums and Mucilages/CT
E99       3100                RT   Hydrocolloids/CT
E100      4687                RT   Hydrolyzed starch syrups/CT
E101      8519                RT   Manihot esculenta/CT
E102        17                RT   Starch substitutes/CT
********** END **********

=> d his

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1             1 S US 20150056284/PN
               E DISSOLUTION/CT
               SET EXPAND CONTINUOUS
L2        110455 S E3,E6

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
               E LURASIDONE/CN
L3             1 S E15
               E STARCH 1500/CN
L4             1 S E27
L5            13 S 367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6           336 S L3 OR L5
L7        196773 S L4
L8            18 S L6 AND L7
L9         22051 S (GELATIN? OR PREGELATIN?) (L) (STARCH)
L10            4 S L6 AND L9
L11            1 S L10 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L12            0 S L11 NOT L1
L13            2 S L8 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L14            1 S L13 NOT L1
L15          948 S L2 AND L9
L16          191 S L15 AND (PY<=2006 OR AY<=2006 OR PRY<=2006)
L17            1 S (LURASIDONE) AND L16
L18            0 S L17 NOT L1

     FILE 'CAPLUS' ENTERED AT 16:05:01 ON 27 OCT 2016
               E STARCH, GELATINIZE/CT
               E STARCH/CT
               E E51+ALL/CT
```

```
=> log holf
'HOLF' IS NOT VALID HERE
For an explanation, enter "HELP LOGOFF".

=> log hold

     (FILE 'HOME' ENTERED AT 15:56:02 ON 27 OCT 2016)

     FILE 'CAPLUS' ENTERED AT 15:56:10 ON 27 OCT 2016
L1             1 SEA SPE=ON  ABB=ON  PLU=ON  US 20150056284/PN
                 D L1 ABS IBIB IT
                 E DISSOLUTION/CT
                 SET EXPAND CONTINUOUS
L2        110455 SEA SPE=ON  ABB=ON  PLU=ON  (DISSOLUTION/CT OR "DISSOLUTION
                 RATE"/CT)

     FILE 'REGISTRY' ENTERED AT 15:57:11 ON 27 OCT 2016
                 E LURASIDONE/CN
L3             1 SEA SPE=ON  ABB=ON  PLU=ON  LURASIDONE/CN
                 D L3 STR RSD
                 D L3
                 E STARCH 1500/CN
L4             1 SEA SPE=ON  ABB=ON  PLU=ON  "STARCH 1500"/CN
                 D L4
L5            13 SEA SPE=ON  ABB=ON  PLU=ON  367514-87-2/CRN

     FILE 'CAPLUS' ENTERED AT 15:58:26 ON 27 OCT 2016
L6           336 SEA SPE=ON  ABB=ON  PLU=ON  L3 OR L5
L7        196773 SEA SPE=ON  ABB=ON  PLU=ON  L4
L8            18 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L7
L9         22051 SEA SPE=ON  ABB=ON  PLU=ON  (GELATIN? OR PREGELATIN?) (L)
                 (STARCH)
L10            4 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L9
L11            1 SEA SPE=ON  ABB=ON  PLU=ON  L10 AND (PY<=2006 OR AY<=2006 OR
                 PRY<=2006)
L12            0 SEA SPE=ON  ABB=ON  PLU=ON  L11 NOT L1
L13            2 SEA SPE=ON  ABB=ON  PLU=ON  L8 AND (PY<=2006 OR AY<=2006 OR
                 PRY<=2006)
L14            1 SEA SPE=ON  ABB=ON  PLU=ON  L13 NOT L1
                 D L14 ABS IBIB HITIND HITSTR
L15          948 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND L9
L16          191 SEA SPE=ON  ABB=ON  PLU=ON  L15 AND (PY<=2006 OR AY<=2006 OR
                 PRY<=2006)
L17            1 SEA SPE=ON  ABB=ON  PLU=ON  (LURASIDONE) AND L16
L18            0 SEA SPE=ON  ABB=ON  PLU=ON  L17 NOT L1

     FILE 'CAPLUS' ENTERED AT 16:05:01 ON 27 OCT 2016
                 E STARCH, GELATINIZE/CT
                 E STARCH/CT
                 E E51+ALL/CT
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   1.24      92.97

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:06:25 ON 27 OCT 2016
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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	1	"8883794".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 11:53
L4	7	"1327440".pn.	EPO; JPO; DERWENT	OR	OFF	2016/10/31 11:58
L5	1	"20150056284".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 12:14
L6	32454	a61k31/496.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:16
L7	71137	c07d417/12.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:16
L8	78904	a61k9/0053,2009,2018,2027,2031,2054,2059,2095.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:17
L9	1909	(l6 or l7) and l8	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:22
L10	193	l9 and ((gelatin$6 or gel$3) with (starch))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:23
L11	0	l10 and (piperazin$2 with benzoisothiazol$2)	US-PGPUB; USPAT; USOCR; FPRS;	OR	OFF	2016/10/31 12:26

			EPO; JPO; DERWENT			
L12	3	l10 and (benzoisothiazol$2)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:26
L13	8784	(l6 or l7) and ((gelatin$6 or gel$3) with (starch))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:27
L14	53	l13 and (piperazin$2 with benzoisothiazol$2)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:27
L15	13	l10 and lurasidone	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:42
L16	11	(("FUJIHARA") near2 ("Kazuyuki")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 12:43
L17	327	(("SUMITOMO") near3 ("DAINIPPON") near3 ("PHARMA") near3 ("CO") near3 ("LTD")).AS.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 12:43
L18	334	L16 or L17	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 12:43
L19	1	l10 and l18	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/31 12:44
L20	6	(("FUJIHARA") near2 ("Kazuyuki")).INV.	EPO; JPO; DERWENT	OR	OFF	2016/10/31 12:44
S1	1	"8883794".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/03 17:40
S2	1	"8729085".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/03 17:40
S3	11	(("FUJIHARA") near2 ("Kazuyuki")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/03 17:41

S4	307	(("SUMITOMO") near3 ("DAINIPPON") near3 ("PHARMA") near3 ("CO") near3 ("LTD")).AS.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/03 17:41
S5	6	(("FUJIHARA") near2 ("Kazuyuki")).INV.	EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:11
S6	3	("20040028741" | "4600579" | "5532372").PN.	US-PGPUB; USPAT	OR	OFF	2016/02/04 10:12
S7	1	("6150366").PN.	US-PGPUB; USPAT	OR	OFF	2016/02/04 10:12
S8	2	("20030203020" | "20050147699").PN.	US-PGPUB; USPAT	OR	OFF	2016/02/04 10:12
S9	7883	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) with tablet$1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:43
S10	235905	tablet$1.ab.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:43
S11	821	S9 and S10	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:44
S12	3166	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) with (improv$6 or benefit$1 or beneficial or advantag$4 or increas$3 or dissolut$3 or availabilit$3 or disintegrat$3 or stabilit$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:45
S13	170	S11 and S12	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:45
S14	2360	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) near25 (improv$6 or benefit$1 or beneficial or advantag$4 or increas$3 or dissolut$3 or availabilit$3 or disintegrat$3 or stabilit$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:51
S15	650	S9 and S14	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:51
S16	4637	((pregelatiniz$3 or pregelatinis$3) near4 (starch)).ab.	US-PGPUB;	OR	OFF	2016/02/04 10:51

			USPAT; USOCR; EPO; JPO; DERWENT			
S17	82	S15 and S16	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 10:51
S18	15	(pregelatin$7 near10 ratio) and S17	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:04
S19	28	(pregelatin$7 near10 ratio) and S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:08
S20	13	S19 not S18	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:08
S21	4232	starch near2 ("1500")	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:11
S22	73	S15 and S21	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 11:11
S23	1	"9119820".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 13:26
S24	62	lurasidone with (amount$1 or dose$1 or dosage$1)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 14:23
S25	46	tablet$1 and S24	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 14:23
S26	7	"1535616".PN.	EPO; JPO; DERWENT	OR	OFF	2016/02/04 14:27
S28	8649	a61k31/496.cpc.	US-PGPUB;	OR	OFF	2016/02/04 15:23

			USPAT; USOCR; EPO; JPO; DERWENT			
S29	16298	a61k9/0053,2009,2018,2027,2031,2054,2059,2095.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:23
S30	15704	c07d417/12.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:24
S31	16298	S29 and S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:24
S32	3089	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) and S31	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:24
S33	0	(benzoisothiazol with piperazinyl with isoindole) and S32	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:26
S34	0	(benzisothiazol with piperazinyl with isoindole) and S32	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:27
S35	23	lurasidone and S32	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:27
S36	373	S28 and S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:28
S37	70	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) and S36	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:28
S38	0	(benzisothiazol with piperazinyl with isoindole) and S37	US-PGPUB;	OR	OFF	2016/02/04 15:28

			USPAT; USOCR; EPO; JPO; DERWENT			
S39	15	lurasidone and S37	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:28
S40	63	S29 and S30	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:28
S41	12	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) and S40	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/02/04 15:29
S42	11	(("FUJIHARA") near2 ("Kazuyuki")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:30
S43	307	(("SUMITOMO") near3 ("DAINIPPON") near3 ("PHARMA") near3 ("CO") near3 ("LTD")).AS.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:30
S44	314	S42 or S43	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:30
S45	6	S44 and (S36 or S40)	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:31
S46	6	((pregelatiniz$3 or pregelatinis$3) near4 (starch)) and S45	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:31
S47	1	"7727553".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/04 15:39
S48	1	"20040186105".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/10/27 15:44
S49	71123	c07d417/12.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/27 16:07
S50	32441	a61k31/496.cpc.	US-PGPUB; USPAT;	OR	OFF	2016/10/27 16:07

			USOCR; FPRS; EPO; JPO; DERWENT			
S51	78856	a61k9/2095,2009,2027,2031,2054,0053,2018,2059.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/10/27 16:08

10/31/2016 12:45:53 PM
C:\Users\spihonak\Documents\EAST\Workspaces\14512189.wsp

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	**Art Unit**
	SARAH PIHONAK	1627

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	02/04/2016	11/02/2016							
	1	-	-							
	2	-	-							
	3	-	-							
	4	-	-							
	5	-	-							
	6	-	-							
	7	-	-							
	8	-	-							
	9	-	-							
	10	-	-							
	11	-	-							
	12	-	-							
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	21	-	-							
	22	-	-							
	23	-	-							
	24	-	-							
1	25	✓	=							
2	26	✓	=							
3	27	✓	=							
4	28	✓	=							
5	29	✓	=							
6	30	✓	=							
7	31	✓	=							
8	32	✓	=							
9	33	✓	=							
10	34	✓	=							
11	35	✓	=							
12	36	✓	=							

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	**Art Unit**
	SARAH PIHONAK	1627

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	02/04/2016	11/02/2016							
13	37	✓	=							
14	38	✓	=							
15	39	✓	=							
16	40	✓	=							
17	41	✓	=							
18	42	✓	=							
19	43	✓	=							
20	44	✓	=							
21	45	✓	=							
22	46	✓	=							
23	47	✓	=							
24	48	✓	=							
25	49	✓	=							
26	50	✓	=							
27	51	✓	=							
28	52	✓	=							
29	53	✓	=							
30	54	✓	=							
31	55	✓	=							
32	56	✓	=							
33	57	✓	=							
	58	N	-							
34	59	N	=							

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14512189	FUJIHARA, KAZUYUKI
	Examiner	Art Unit
	SARAH PIHONAK	1627

CPC- SEARCHED		
Symbol	Date	Examiner
a61k31/496	2/4/16	s.p.
a61k9/0053,2009,2018,2027,2031,2054,2059,2095	2/4/16	s.p.
c07d417/12	2/4/16	s.p.
a61k31/496	10/31/16	s.p.
c07d417/12	10/31/16	s.p.
a61k9/0053,2009,2018,2027,2031,2054,2059,2095	10/31/16	s.p.

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
invention and claims search in stn, east	2/4/16	s.p.
inventor and assignee search in east, palm	2/4/16	s.p.
updated inventor and assignee search in palm, east	10/31/16	s.p.
updated invention and claims search in stn, east	10/31/16	s.p.

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
a61k	31/496	10/31/16	s.p.
c07d	417/12	10/31/16	s.p.
a61k	9/0053,2009,2018,2027,2031,2054,2059,2095	10/31/16	s.p.

	/SARAH PIHONAK/ Primary Examiner.Art Unit 1627

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

CUSTOMER NUMBER

22850

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	10/10/2014	Kazuyuki FUJIHARA	472299US40CONT	5575

TITLE OF INVENTION: PHARMACEUTICAL COMPOSITION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	02/07/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
PIHONAK, SARAH	1627	514-254040

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Oblon, McClelland,

2 Maier & Neustadt, L.L.P.

3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: SUMITOMO DAINIPPON PHARMA CO., LTD.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Osaka, JAPAN

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☒ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☑ Payment by credit card. Transmitted via EFS-Web

☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 15-0030 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☐ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Maki Saitoh/ Date 12/14/2016

Typed or printed name Maki Saitoh Registration No. 72,208

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Par Pharm., Inc.
Exhibit 1013
Page 368

Electronic Patent Application Fee Transmittal

Application Number:	14512189
Filing Date:	10-Oct-2014
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Filer:	Bradley Davis Lytle/Mimi Chanthaphone
Attorney Docket Number:	472299US40CONT

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
UTILITY APPL ISSUE FEE	1501	1	960	960

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**960**

Electronic Acknowledgement Receipt	
EFS ID:	27794958
Application Number:	14512189
International Application Number:	
Confirmation Number:	5575
Title of Invention:	PHARMACEUTICAL COMPOSITION
First Named Inventor/Applicant Name:	Kazuyuki FUJIHARA
Customer Number:	22850
Filer:	Bradley Davis Lytle/Mimi Chanthaphone
Filer Authorized By:	Bradley Davis Lytle
Attorney Docket Number:	472299US40CONT
Receipt Date:	14-DEC-2016
Filing Date:	10-OCT-2014
Time Stamp:	16:00:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$960
RAM confirmation Number	121516INTEFSW16030600
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	472299us.pdf	1661313 6192a2ef8c3699fabc6608f276784dd5a18054b7	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30759 dc7da5cb9ffd0a17848a9f0372f2ed260d337f9f	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1692072		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/512,189	01/31/2017	9555027	472299US40CONT	5575

22850 7590 01/11/2017

OBLON, MCCLELLAND, MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Kazuyuki FUJIHARA, Suzuka-shi, JAPAN;
SUMITOMO DAINIPPON PHARMA CO., LTD, Osaka, JAPAN;

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