US009060976B2

(12) **United States Patent**
Wright et al.

(10) **Patent No.: US 9,060,976 B2**
(45) **Date of Patent: Jun. 23, 2015**

(54) **PHARMACEUTICAL FORMULATION CONTAINING GELLING AGENT**

(71) Applicant: **Purdue Pharma L.P.**, Stamford, CT (US)

(72) Inventors: **Curtis Wright**, Rockport, MA (US); **Benjamin Oshlack**, Boca Raton, FL (US); **Christopher Breder**, Greenwich, CT (US)

(73) Assignees: **Purdue Pharma L.P.**, Stamford, CT (US); **The P.F. Laboratories, Inc.**, Totowa, NJ (US); **Purdue Pharmaceuticals L.P.**, Wilson, NC (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **13/726,324**

(22) Filed: **Dec. 24, 2012**

(65) **Prior Publication Data**

US 2013/0217716 A1 Aug. 22, 2013

Related U.S. Application Data

(63) Continuation of application No. 13/349,449, filed on Jan. 12, 2012, now Pat. No. 8,337,888, which is a continuation of application No. 12/653,115, filed on Dec. 8, 2009, now abandoned, which is a continuation of application No. 10/214,412, filed on Aug. 6, 2002.

(60) Provisional application No. 60/310,534, filed on Aug. 6, 2001.

(51) **Int. Cl.**

A61K 31/439	(2006.01)
A61K 31/485	(2006.01)
A61K 31/167	(2006.01)
A61K 9/20	(2006.01)
A61K 9/00	(2006.01)
A61K 47/38	(2006.01)
A61K 47/36	(2006.01)
A61K 47/10	(2006.01)
A61K 45/06	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/167*** (2013.01); ***A61K 9/2013*** (2013.01); ***A61K 9/205*** (2013.01); ***A61K 9/2054*** (2013.01); ***A61K 9/0002*** (2013.01); ***A61K 31/439*** (2013.01); ***A61K 31/485*** (2013.01); ***A61K 47/38*** (2013.01); ***A61K 47/36*** (2013.01); ***A61K 47/10*** (2013.01); ***A61K 45/06*** (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,065,143	A	11/1962	Christenson et al.
3,133,132	A	5/1964	Loeb et al.
3,173,876	A	3/1965	Zobrist et al.
3,260,646	A	7/1966	Paulsen et al.
3,276,586	A	10/1966	Rosaen
3,541,005	A	11/1970	Strathmann et al.
3,541,006	A	11/1970	Bixler et al.
3,546,876	A	12/1970	Fokker et al.
3,845,770	A	11/1974	Theeuwes et al.
3,916,889	A	11/1975	Russell
3,965,256	A	6/1976	Leslie
3,980,766	A	9/1976	Shaw et al.
4,063,064	A	12/1977	Saunders et al.
4,070,494	A	1/1978	Hoffmeister et al.
4,088,864	A	5/1978	Theeuwes et al.
4,160,020	A	7/1979	Ayer et al.
4,175,119	A	11/1979	Porter
4,200,098	A	4/1980	Ayer et al.
4,235,870	A	11/1980	Leslie
4,285,987	A	8/1981	Ayer et al.
4,293,539	A	10/1981	Ludwig et al.
4,366,310	A	12/1982	Leslie
4,385,057	A	5/1983	Bjork et al.
4,389,393	A	6/1983	Schor et al.
4,424,205	A	1/1984	LaHann et al.
4,443,428	A	4/1984	Oshlack et al.
4,457,933	A	7/1984	Gordon et al.
4,459,278	A	7/1984	Porter
4,588,580	A	5/1986	Gale et al.
4,599,342	A	7/1986	LaHann

(Continued)

FOREIGN PATENT DOCUMENTS

EP	0318262	A1	5/1989
EP	0661045		7/1995

(Continued)

OTHER PUBLICATIONS

Moroni, et al., "Application of Poly(oxyethylene) Homopolymers in Sustained Release Solid Formulations", Drug Dev. and Indus. Pharmacy, 21(12), 1411-28 (1995).

Apicella, et al., "Poly(ethylene oxide) (PEO) Constant Release Monolithic Devices," Polymers in Medicine: Biomedical and Pharmaceutical Applications, Chapter 3 (1992).

(Continued)

Primary Examiner — Robert A Wax
Assistant Examiner — Olga V Tcherkasskaya
(74) *Attorney, Agent, or Firm* — Lowenstein Sandler LLP

(57) **ABSTRACT**

Disclosed in certain embodiments is a controlled release oral dosage form comprising a therapeutically effective amount of a drug susceptible to abuse together with one or more pharmaceutically acceptable excipients; the dosage form further including a gelling agent in an effective amount to impart a viscosity unsuitable for administration selected from the group consisting of parenteral and nasal administration to a solubilized mixture formed when the dosage form is crushed and mixed with from about 0.5 to about 10 ml of an aqueous liquid; the dosage form providing a therapeutic effect for at least about 12 hours when orally administered to a human patient.

1 Claim, No Drawings

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,610,870	A	9/1986	Jain et al.	
4,612,008	A	9/1986	Wong et al.	
4,666,705	A	5/1987	DeCrosta et al.	
4,764,378	A	8/1988	Keith et al.	
4,765,989	A	8/1988	Wong et al.	
4,769,372	A	9/1988	Kreek	
4,785,000	A	11/1988	Kreek et al.	
4,806,341	A	2/1989	Chien et al.	
4,812,446	A	3/1989	Brand	
4,834,984	A	5/1989	Goldie et al.	
4,844,909	A	7/1989	Goldie et al.	
4,861,598	A	8/1989	Oshlack	
4,957,681	A	9/1990	Klimesch et al.	
4,970,075	A	11/1990	Oshlack	
4,990,341	A	2/1991	Goldie et al.	
5,026,556	A	6/1991	Drust et al.	
5,059,600	A	10/1991	Gawin et al.	
5,069,909	A	12/1991	Sharma et al.	
5,111,942	A	5/1992	Bernardin	
5,114,942	A	5/1992	Gawin et al.	
5,130,311	A	7/1992	Guillaumet et al.	
5,149,538	A	9/1992	Granger et al.	
5,169,645	A	12/1992	Shukla et al.	
5,202,128	A	4/1993	Morella et al.	
5,215,758	A	6/1993	Krishnamurthy	
5,225,199	A	7/1993	Hidaka et al.	
5,232,934	A	8/1993	Downs	
5,240,711	A	8/1993	Hille et al.	
5,266,331	A	11/1993	Oshlack et al.	
5,273,758	A	12/1993	Royce	
5,273,760	A	12/1993	Oshlack et al.	
5,286,493	A	2/1994	Oshlack et al.	
5,290,816	A	3/1994	Blumberg	
5,321,012	A	6/1994	Mayer et al.	
5,324,351	A	6/1994	Oshlack et al.	
5,330,766	A	7/1994	Morella et al.	
5,356,467	A	10/1994	Oshlack et al.	
5,368,852	A	11/1994	Umemoto et al.	
5,376,705	A	12/1994	Leys et al.	
5,378,474	A	1/1995	Morella et al.	
5,403,868	A	4/1995	Reid et al.	
5,409,944	A	4/1995	Black et al.	
5,411,745	A	5/1995	Oshlack et al.	
5,422,123	A	6/1995	Conte et al.	
5,436,265	A	7/1995	Black et al.	
5,472,712	A	12/1995	Oshlack et al.	
5,472,943	A	12/1995	Crain et al.	
5,474,995	A	12/1995	Ducharme et al.	
5,478,577	A	12/1995	Sackler et al.	
5,500,227	A	3/1996	Oshlack et al.	
5,502,058	A	3/1996	Mayer et al.	
5,505,959	A	4/1996	Tachon et al.	
5,508,042	A	4/1996	Oshlack et al.	
5,510,368	A	4/1996	Lau et al.	
5,514,680	A	5/1996	Weber et al.	
5,521,213	A	5/1996	Prasit et al.	
5,536,752	A	7/1996	Ducharme et al.	
5,549,912	A	8/1996	Oshlack et al.	
5,550,142	A	8/1996	Ducharme et al.	
5,552,422	A	9/1996	Gauthier et al.	
5,556,838	A	9/1996	Mayer et al.	
5,580,578	A	12/1996	Oshlack et al.	
5,593,695	A	1/1997	Merrill et al.	
5,593,994	A	1/1997	Batt et al.	
5,604,253	A	2/1997	Lau et al.	
5,604,260	A	2/1997	Guay et al.	
5,616,601	A	4/1997	Khanna et al.	
5,639,476	A	6/1997	Oshlack et al.	
5,639,780	A	6/1997	Lau et al.	
5,656,295	A	8/1997	Oshlack et al.	
5,667,805	A	9/1997	Merrill et al.	
5,672,360	A	9/1997	Sackler et al.	
5,679,650	A	10/1997	Fukunaga et al.	
5,681,585	A	10/1997	Oshlack et al.	
5,695,781	A	12/1997	Zhang et al.	
5,730,716	A	3/1998	Beck et al.	
5,741,524	A	4/1998	Staniforth et al.	
5,762,963	A	6/1998	Byas-Smith	
5,843,480	A	12/1998	Miller et al.	
5,849,240	A *	12/1998	Miller et al.	264/460
5,866,164	A	2/1999	Kuczynski et al.	
5,879,705	A	3/1999	Heafield et al.	
5,891,471	A *	4/1999	Miller et al.	424/468
5,891,919	A	4/1999	Blum et al.	
5,914,131	A	6/1999	Merrill et al.	
5,958,452	A	9/1999	Oshlack et al.	
5,958,459	A	9/1999	Chasin et al.	
5,965,161	A	10/1999	Oshlack et al.	
5,965,163	A *	10/1999	Miller et al.	424/468
5,968,551	A	10/1999	Oshlack et al.	
6,024,982	A	2/2000	Oshlack et al.	
6,120,751	A	9/2000	Unger	
6,124,282	A	9/2000	Sellers et al.	
6,136,864	A	10/2000	Nichols et al.	
6,143,322	A	11/2000	Sackler et al.	
6,153,621	A	11/2000	Hamann	
6,162,467	A *	12/2000	Miller et al.	424/468
6,223,075	B1	4/2001	Beck et al.	
6,228,863	B1	5/2001	Palermo et al.	
6,245,357	B1	6/2001	Edgren et al.	
6,277,398	B1	8/2001	Caruso	
6,294,194	B1	9/2001	Horhota et al.	
6,309,668	B1	10/2001	Bastin et al.	
6,348,469	B1 *	2/2002	Seth	514/254.02
6,352,721	B1	3/2002	Faour	
6,375,957	B1 *	4/2002	Kaiko et al.	424/400
6,403,056	B1	6/2002	Unger	
6,419,954	B1	7/2002	Chu	
6,436,441	B1	8/2002	Sako et al.	
6,440,464	B1	8/2002	Hsia et al.	
6,488,963	B1	12/2002	McGinity	
6,491,949	B2	12/2002	Faour et al.	
6,559,159	B2	5/2003	Carroll et al.	
6,572,885	B2	6/2003	Oshlack et al.	
6,593,367	B1	7/2003	Dewey et al.	
6,627,635	B2	9/2003	Palermo et al.	
6,696,088	B2	2/2004	Oshlack et al.	
6,733,783	B2	5/2004	Oshlack et al.	
6,808,720	B2	10/2004	Unger	
6,995,169	B2	2/2006	Chapleo et al.	
7,141,250	B2	11/2006	Oshlack et al.	
7,144,587	B2	12/2006	Oshlack et al.	
7,157,103	B2	1/2007	Sackler	
7,201,920	B2	4/2007	Kumar et al.	
7,332,182	B2	2/2008	Sackler	
7,727,557	B2	6/2010	Sackler	
7,776,314	B2	8/2010	Bartholomaus et al.	
7,842,307	B2 *	11/2010	Oshlack et al.	424/450
7,943,174	B2	5/2011	Oshlack et al.	
8,017,148	B2	9/2011	Sackler	
8,075,872	B2	12/2011	Arkenau-Maric	
8,101,630	B2	1/2012	Kumar et al.	
8,114,383	B2	2/2012	Barthalomaus	
8,114,384	B2	2/2012	Arkenau	
8,192,722	B2	6/2012	Arkenau-Maric	
8,309,060	B2	11/2012	Bartholomaus et al.	
8,337,888	B2	12/2012	Wright et al.	
8,377,453	B2 *	2/2013	Han et al.	424/400
8,389,007	B2	3/2013	Wright et al.	
8,524,275	B2	9/2013	Oshlack et al.	
8,529,948	B1	9/2013	Wright et al.	
8,609,683	B2	12/2013	Wright et al.	
8,652,497	B2	2/2014	Sackler	
8,652,515	B2	2/2014	Sackler	
8,871,265	B2	10/2014	Wright et al.	
2003/0004177	A1 *	1/2003	Kao et al.	514/282
2003/0021841	A1	1/2003	Matharu et al.	
2003/0026838	A1	2/2003	Farrell	
2003/0035839	A1	2/2003	Hirsh et al.	
2003/0054027	A1	3/2003	Unger	
2003/0059471	A1	3/2003	Compton et al.	
2003/0064099	A1	4/2003	Oshlack et al.	
2003/0064122	A1	4/2003	Goldberg et al.	
2003/0068276	A1	4/2003	Hughes et al.	

(56) **References Cited**

U.S. PATENT DOCUMENTS

2003/0068370	A1	4/2003	Sackler	
2003/0068371	A1	4/2003	Oshlack et al.	
2003/0068375	A1*	4/2003	Wright et al.	424/468
2003/0068392	A1	4/2003	Sackler	
2003/0082230	A1	5/2003	Baichwal et al.	
2003/0124061	A1	7/2003	Roberts	
2003/0124185	A1	7/2003	Oshlack et al.	
2003/0125347	A1	7/2003	Anderson et al.	
2003/0126428	A1	7/2003	Liu et al.	
2003/0170181	A1	9/2003	Midha	
2003/0232081	A1	12/2003	Doshl et al.	
2004/0047907	A1	3/2004	Oshlack et al.	
2004/0126428	A1	7/2004	Hughes et al.	
2004/0131552	A1	7/2004	Boehm	
2004/0151791	A1	8/2004	Mayo-Alvarez et al.	
2004/0224020	A1	11/2004	Schoenhard	
2004/0228802	A1	11/2004	Chang et al.	
2004/0241234	A1	12/2004	Vilkov	
2004/0253310	A1*	12/2004	Fischer et al.	424/472
2004/0266807	A1	12/2004	Oshlack et al.	
2005/0020613	A1	1/2005	Boehm et al.	
2005/0031546	A1	2/2005	Bartholomaus et al.	
2005/0063909	A1	3/2005	Wright et al.	
2005/0106249	A1	5/2005	Hwang et al.	
2005/0112067	A1	5/2005	Kumar et al.	
2005/0112201	A1	5/2005	Baichwal et al.	
2005/0118267	A1	6/2005	Baichwal et al.	
2005/0158382	A1*	7/2005	Cruz et al.	424/468
2005/0163717	A1	7/2005	Anderson et al.	
2005/0186139	A1	8/2005	Bartholomaus	
2005/0214223	A1	9/2005	Bartholomaeus et al.	
2005/0236741	A1	10/2005	Arkenau et al.	
2005/0276853	A1	12/2005	Baichwal et al.	
2006/0002860	A1	1/2006	Bartholomaus	
2006/0018837	A1	1/2006	Preston et al.	
2006/0039864	A1	2/2006	Bartholomaus	
2006/0165790	A1*	7/2006	Walden et al.	424/468
2006/0188447	A1	8/2006	Arkenau-Maric	
2006/0193782	A1	8/2006	Bartholomaus	
2006/0251721	A1*	11/2006	Cruz et al.	424/468
2007/0003616	A1	1/2007	Arkenau-Maric	
2007/0003617	A1*	1/2007	Fischer et al.	424/468
2007/0110807	A1	5/2007	Vergnault et al.	
2007/0166234	A1	7/2007	Kumar et al.	
2007/0202049	A1*	8/2007	Guimberteau et al.	424/10.2
2007/0264327	A1	11/2007	Kumar et al.	
2008/0008659	A1*	1/2008	Guimberteau et al.	424/10.1
2008/0063725	A1*	3/2008	Guimberteau et al.	424/492
2008/0095843	A1	4/2008	Nutalapati et al.	
2008/0176955	A1	7/2008	Heck et al.	
2008/0254123	A1*	10/2008	Fischer et al.	424/486
2008/0260815	A1*	10/2008	Hayes et al.	424/455
2009/0004267	A1*	1/2009	Arkenau-Maric et al.	424/465
2009/0011016	A1*	1/2009	Cailly-Dufestel et al.	424/465
2009/0081290	A1*	3/2009	McKenna et al.	424/468
2009/0169587	A1	7/2009	Baichwal et al.	
2009/0215808	A1	8/2009	Yum et al.	
2010/0015222	A1*	1/2010	Han et al.	424/468
2010/0015223	A1*	1/2010	Cailly-Dufestel et al.	424/472
2010/0221293	A1	9/2010	Cruz et al.	
2011/0262532	A1	10/2011	Oshlack et al.	
2012/0164220	A1	6/2012	Huang	

FOREIGN PATENT DOCUMENTS

EP	1293195	A1	3/2003
WO	01/07950		6/1991
WO	93/10765		5/1993
WO	95/20947		8/1995
WO	WO-95/20947	A1	8/1995
WO	97/37689		10/1997
WO	97/48385		12/1997
WO	97/49384		12/1997
WO	99/32120		7/1999
WO	WO-99/32119	A1	7/1999
WO	00/33835		6/2000
WO	WO-01/58447	A1	8/2001
WO	2002/087558		11/2002
WO	WO-02/094254	A2	11/2002
WO	WO-03/015531	A2	2/2003
WO	2003/024430		3/2003
WO	WO-03/026743	A2	4/2003
WO	2003/035029		5/2003
WO	WO-03/092676	A1	11/2003
WO	WO-2004/026256	A2	1/2004
WO	WO-2004/026283	A1	4/2004
WO	WO-2004/037259	A1	5/2004
WO	WO-2005/053587	A1	6/2005
WO	2010078486		7/2010

OTHER PUBLICATIONS

Apicella, et al., "Poly(ethylene oxide)-Based Delivery Systems", Polymeric Drugs and Drug Administration, ACS Symposium Series 545, Chapter 9 (1994).

Zhang, F, et al., "Properties of Sustained-Release Tablets Prepared by Hot-Melt Extrusion", Pharmaceutical Development and Technology, vol. 4, No. 2, p. 241-250 (1999).

Maggi, L., et al., "Dissolution Behaviour of Hydrophilic Matrix Tablets Containing Two Different Polyethylene Oxides (PEOs) for the Controlled Release of a Water-Soluble Drug", Biomaterials, vol. 23, p. 1113-1119 (2002).

The 1997 Physician's Desk Reference ("PDR") entry for Oxycontin ®.

Paragraph IV Patent Certification Notice for ANDA 202455 (2013).

Complaint 1:13-cv-04606 (Jul. 2, 2013).

Paragraph IV Patent Certification Notice for ANDA 202434 (2011).

Paragraph IV Patent Certification Notice for ANDA 203235 (2011).

Paragraph IV Patent Certification Notice for ANDA 202372 (2011).

Paragraph IV Patent Certification Notice for ANDA 202483 (2011).

Paragraph IV Patent Certification Notice for ANDA 202762 (2011).

Paragraph IV Patent Certification Notice for Amendment to ANDA 202762 (2011).

Paragraph IV Patent Certification Notice for ANDA 202455 (2011).

Paragraph IV Patent Certification Notice for ANDA 202352 (2011).

Woodburn, K.R., et al., "Vascular Complications of Injecting Drug Misuse", British Journal of Surgery, 1996, vol. 83, p. 1329-1334.

Kim, C., "Drug Release from Compressed Hydrophilic POLYOX-WSR Tablets", Journal of Pharmaceutical Sciences, vol. 84, No. 3, Mar. 1995, p. 303-306.

Apicella, A., "Poly(ethylene oxide) (PEO) and Different Molecular Weight PEO Blends Monolithic Devices for Drug Release", Biomaterials, vol. 14, No. 2, 1993, p. 83-90.

Deighan, C.J., et al., "Rhabdomyolysis and Acute Renal Failure Resulting From Alcohol and Drug Abuse", QJ Med, vol. 93, 2000, p. 29-33.

Kalant, H., et al., "Death in Amphetamine Users: Causes and Rates", CMA Journal, vol. 112, Feb. 8, 1975, p. 299-304.

U.S. Pharmacopeia, p. 2206, 1995.

Complaint 1:13-cv-01272-SHS (Feb. 25, 2013).

Answer and Counterclaims 1:13-cv-01272-SHS (Mar. 8, 2013).

Answer to Counterclaims 1:13-cv-01272-SHS (Apr. 1, 2013).

Consent Judgement :13-cv-01272-SHS (May 1, 2013).

Complaint 1:13-cv-03188-SHS (May 10, 2013).

Answer; Affirmative Defenses and Counterclaims 1:13-cv-03188-SHS (Jun. 7, 2013).

Complaint 1:13-cv-03374-SHS (May 17, 2013).

Answer and Counterclaims 1:13-cv-03374-SHS (Jun. 3, 2013).

Complaint 1:13-cv-03372-SHS (May 17, 2013).

Written Opinion and International Search Report for International Patent Application No. PCT/IB2011/003152 issued Sep. 19, 2012.

U.S. Appl. No. 13/333,560—Non-Final Rejection dated Jan. 29, 2013.

U.S. Appl. No. 13/333,560—Amendment/Response dated Apr. 29, 2013.

Paragraph IV Patent Certification Notice for ANDA 202352 (2013).

Paragraph IV Patent Certification Notice for ANDA 202372 (2013).

Paragraph IV Patent Certification Notice for ANDA 202434 (2013).

(56) **References Cited**

OTHER PUBLICATIONS

Paragraph IV Patent Certification Notice for ANDA 202483 (2013).
Paragraph IV Patent Certification Notice for ANDA 203235 (2013).
Ortho-McNeil-Janssen Pharmaceuticals, Inc. (2010). Prescribing Information for Concerta Extended-Release Tablets.
Findings of Fact and Conclusions of Law, In re: Oxycontin Antitrust Litigation, Case 1:04-md-01603-SHS, Jan. 14, 2014.
Opinion & Order filed May 27, 2014, Case 1:04-md-01603-SHS, 24 pgs.
USPTO Non-Final Rejection for U.S. Appl. No. 13/765,368 dated Oct. 4, 2013.
USPTO Response for U.S. Appl. No. 13/765,368 dated Jan. 6, 2014.
USPTO Final Rejection for U.S. Appl. No. 13/765,368 dated Mar. 12, 2014.
USPTO Response for U.S. Appl. No. 13/765,368 dated Jun. 12, 202014.
USPTO Advisory Action for U.S. Appl. No. 13/765,368 dated Jul. 1, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 13/890,874 dated Dec. 18, 2013.
USPTO Response for U.S. Appl. No. 13/890,874 dated Feb. 28, 2014.
USPTO Final Rejection for U.S. Appl. No. 13/890,874 dated Mar. 11, 2014.
USPTO Response for U.S. Appl. No. 13/890,874 dated Jun. 11, 2014.
USPTO Advisory Action for U.S. Appl. No. 13/890,874 dated Jun. 19, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 13/946,418 dated Sep. 12, 2013.
USPTO Response for U.S. Appl. No. 13/946,418 dated Dec. 12, 2013.
USPTO Final Rejection for U.S. Appl. No. 13/946,418 dated Apr. 10, 2014.
USPTO Response for U.S. Appl. No. 13/946,418 dated Jun. 10, 2014.
USPTO Advisory Action for U.S. Appl. No. 13/946,418 dated Jun. 23, 2014.
Bettini et al., "Translocation of drug particles in HPMC matrix gel layer: effect of drug solubility and influence on release rate," Journal of Controlled Release, vol. 70, No. 3, Feb. 2001, pp. 383-391.
Sarkar, N., "Kinetics of thermal gelation of methylcellulose and hydroxypropylmethylcellulose in aqueous solutions," Carbohydrate Polymers, vol. 26, No. 3, Jan. 1995, pp. 195-203.
Wilkins, Jeffrey, N., "Pharmacotherapy of Schizophrenia Patients with Comorbid Substance Abuse", Schizophrenia Bulletin, vol. 23, No. 2, 1997, http://schizophreniabulletin.oxfordjournals.org pp. 215-228.
Yang, et al., "Characterization of Compressibility and Compactibility of Poly(ethylene oxide) Polymers for Modified Release Application by Compaction Simulator", Journal of Pharmaceutical Sciences, vol. 85, No. 10, Oct. 1996 pp. 1085-1086.
Paragraph IV Patent Certification Notice for ANDA 203915 (Jul. 26, 2013).
USPTO Non-Final Rejection for U.S. Appl. No. 14/243,580, dated Oct. 2, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 14/460,134, dated Oct. 2, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 14/460,170, dated Oct. 2, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 14/470,631, dated Oct. 21, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 14/470,662, dated Nov. 4, 2014.
USPTO Non-Final Rejection for U.S. Appl. No. 14/484,077, dated Oct. 22, 2014.
Sarkar, N., "Thermal Gelation Properties of Methyl and Hydroxypropyl Methylcellulose," Journal of Applied Polymer Science, vol. 24, No. 4, Aug. 1979, pp. 1073-1087.
Findings of Fact and Conclusions of Law, In re: Oxycontin Antitrust Litigation, Case 1:04-md-01603-SHS, Apr. 8, 2015, pp. 1-69.

* cited by examiner

PHARMACEUTICAL FORMULATION CONTAINING GELLING AGENT

RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 13/349,449, filed Jan. 12, 2012, which is a continuation of U.S. patent application Ser. No. 12/653,115, filed Dec. 8, 2009, which is a continuation of U.S. patent application Ser. No. 10/214,412, filed Aug. 6, 2002, which claims the benefit of U.S. Provisional Application No. 60/310,534, filed Aug. 6, 2001. The contents of these applications are hereby incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

Opioid analgesics are sometimes the subject of abuse. Typically, a particular dose of an opioid analgesic is more potent when administered parenterally as compared to the same dose administered orally. Therefore, one popular mode of abuse of oral opioid formulations involves the extraction of the opioid from the dosage form, and the subsequent injection of the opioid (using any "suitable" vehicle for injection) in order to achieve a "high." Also, some formulations can be tampered with in order to provide the opioid agonist contained therein better available for illicit use. For example, a controlled release opioid agonist formulation can be crushed in order to provide the opioid contained therein available for immediate release upon oral or nasal administration. An opioid formulation can also be abusable by administration of more than the prescribed dose of the drug.

Opioid antagonists have been combined with certain opioid agonists in order to deter the parenteral abuse of opioid agonists. In the prior art, the combination of immediate release pentazocine and naloxone has been utilized in tablets available in the United States, commercially available as Talwin® Nx from Sanofi-Winthrop. Talwin® Nx contains immediate release pentazocine hydrochloride equivalent to 50 mg base and naloxone hydrochloride equivalent to 0.5 mg base. A fixed combination therapy comprising tilidine (50 mg) and naloxone (4 mg) has been available in Germany for the management of pain since 1978 (Valoron® N, Goedecke). A fixed combination of buprenorphine and naloxone was introduced in 1991 in New Zealand (Temgesic® Nx, Reckitt & Colman) for the treatment of pain.

Purdue Pharma EP currently markets sustained-release oxycodone in dosage forms containing 10, 20, 40, and 80 mg oxycodone hydrochloride under the tradename OxyContin.

U.S. Pat. Nos. 5,266,331; 5,508,042; 5,549,912 and 5,656,295 disclose sustained release oxycodone formulations.

U.S. Pat. Nos. 4,769,372 and 4,785,000 to Kreek describe methods of treating patients suffering from chronic pain or chronic cough without provoking intestinal dysmotility by administering 1 to 2 dosage units comprising from about 1.5 to about 100 mg of opioid analgesic or antitussive and from about 1 to about 18 mg of an opioid antagonist having little to no systemic antagonist activity when administered orally, from 1 to 5 times daily.

U.S. Pat. No. 6,228,863 to Palermo et al. describes compositions and methods of preventing abuse of opioid dosage forms.

WO 99/32119 to Kaiko et al. describes compositions and methods of preventing abuse of opioid dosage forms.

U.S. Pat. No. 5,472,943 to Crain et al. describes methods of enhancing the analgesic potency of bimodally acting opioid agonists by administering the agonist with an opioid antagonist.

U.S. Pat. No. 3,980,766 to Shaw et al., is related to drugs which are suitable for therapy in the treatment of narcotic drug addiction by oral use, e.g., methadone, formulated to prevent injection abuse through concentration of the active component in aqueous solution by incorporating in a solid dosage or tablet form of such drug an ingestible solid having thickening properties which cause rapid increase in viscosity upon concentration of an aqueous solution thereof.

However, there still exists a need for a safe and effective treatment of pain with opioid analgesic dosage forms which are less subject to abuse than current therapies.

All documents cited herein, including the foregoing, art incorporated by reference in their entireties for all purposes.

OBJECTS AND SUMMARY OF THE INVENTION

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less parenteral abuse than other dosage forms.

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less intranasal abuse than other dosage forms.

It is an object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less oral abuse than other dosage forms.

It is a further object of certain embodiments of the invention to provide an oral dosage form of an opioid analgesic which is subject to less diversion than other dosage forms.

It is a further object of certain embodiments of the invention to provide a method of treating pain in human patients with an oral dosage form of an opioid analgesic while reducing the abuse potential of the dosage form.

It is a further object of certain embodiments of the invention to provide a method of manufacturing an oral dosage form of an opioid analgesic such that it has less abuse potential.

These objects and others are achieved by the present invention, which is directed in part to an oral dosage form comprising an opioid analgesic; and at least one aversive agent for reducing the abuse of the opioid analgesic.

In certain embodiments of the present invention, the oral dosage forms of the present invention comprising an opioid analgesic; and an aversive agent or agents as a component(s) of the dosage form helps to prevent injection, inhalation, and/or oral abuse by decreasing the "attractiveness" of the dosage form to a potential abuser.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as a bittering agent to discourage an abuser from tampering with the dosage form and thereafter inhaling or swallowing the tampered dosage form. Preferably, the bittering agent is released when the dosage form is tampered with and provides an unpleasant taste to the abuser upon inhalation and/or swallowing of the tampered dosage form.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as an irritant to discourage an abuser from tampering with the dosage form and thereafter inhaling, injecting, or swallowing the tampered dosage form. Preferably, the irritant is released when the dosage form is tampered with and provides a burning or irritating effect to the abuser upon inhalation, injection, and/or swallowing of the tampered dosage form.

In certain embodiments of the present invention, the dosage form comprises an aversive agent such as a gelling agent to discourage an abuser from tampering with the dosage form and thereafter inhaling, injecting, and/or swallowing the tam-

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.