CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

207202Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 115927

MEETING MINUTES

Otsuka Pharmaceutical Development &
Commercialization, Inc.
Attention: Jeffrey Yuan, Ph.D.
Director, Global Regulatory Affairs
508 Carnegie Center
Princeton, New Jersey 08540

Dear Dr. Yuan:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for aripiprazole tablet with an ingestible event marker (IEM) from Proteus® (the Proteus Ingestible Sensor).

We also refer to the meeting between representatives of your firm and the FDA on May 5, 2015. The purpose of the meeting was to gain alignment with us on the proposed NDA structure and content, on the handling of packaging and environmental assessment, on the acceptability of the human factors validation data for review, on the proposed labeling, and on the handling of the Otsuka Medical Software in the NDA.

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, please email Simran Parihar, PharmD, Regulatory Health Project Manager, at simran.parihar@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell Mathis, M.D.
CAPT, USPHS
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes
Sponsor's Slide Presentation

FOOD AND DRUG ADMINISTRATION
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MEMORANDUM OF MEETING MINUTES

Meeting Type:	Type B
Meeting Category:	Pre-NDA
Meeting Date and Time:	Tuesday, May 5, 2015 9:00 -10:30 AM (ET)
Meeting Location:	White Oak Building 22, Conference Room: 1315
Application Number:	IND 115927
Product Name:	aripiprazole tablet + ingestible event marker (IEM)
Indication:	Schizophrenia
Sponsor/Applicant Name:	Otsuka Pharmaceutical Development & Commercialization, Inc.

FDA ATTENDEES

Mitchell Mathis, M.D.	Director, Division of Psychiatry Products (DPP)
Tiffany Farchione, M.D.	Deputy Director, DPP
Jing Zhang, M.D.	Clinical Team Leader
Aisar Atrakchi, Ph.D.	Pharmacology/Toxicology Supervisor
David Claffey, Ph.D.	CMC Team Leader, Office of Pharmaceutical Quality (OPQ)
Ashley Boam, MSBE	Director (acting), Office of Policy for Pharmaceutical Quality (OPQ)
Richard Lostritto, Ph.D.	Deputy Director (Acting), Science and Policy
Irene Z. Chan, Pharm.D., BCPS	Associate Director, Division of Medication Error Prevention and Analysis (DMEPA)
Loretta Holmes, BSN, Pharm.D.	Safety Evaluator, DMEPA
Danielle Harris, Pharm.D., BCPS	Team Leader, DMEPA
Ariane Conrad. Pharm.D.	FDA/ISMP Safe Medication Management Fellow, DMEPA
Katelyn Brown, Pharm.D.	Regulatory Pharmaceutical Fellow, Medication Safety, DMEPA
Patricia Love, M.D.	Deputy Director, Office of Combination Products (OCP), Office of Commissioner (OC)
Bindi Nikhar, MD	Clinical Associate Director, OCP/OC
Shawn Forrest, MS	Branch Chief (Acting), Cardiac Diagnostic Devices Branch, CDRH
Mitchell Shein, MS	Deputy Director, Cardiac Diagnostic Devices Branch, CDRH
Luke Ralston	Lead Reviewer, 513(g)
Simran Parihar, Pharm.D.	Regulatory Health Project Manager, DPP

SPONSOR ATTENDEES

Otsuka Pharmaceutical Co., Ltd

Janet Ahn	Director of Product Management Digital Health
Michael Fahmy, M.S.	Director of Labeling, Global Regulatory Affairs
Elora Gupta, Ph.D.	Senior Director of Global Regulatory Affairs
Kenji Tomikawa	Manager, Medical Regulatory Affairs
David Unger, Ph.D.	Senior Director, Pharmaceutical Technology
Tim Peters-Strickland, M.D.	Senior Director, Global Clinical Development
Jeffery Yuan, Ph.D.	Director of Global Regulatory Affairs
Henrietta Ukwu, M.D.	Senior Vice President of Global Regulatory Affairs
Yukako Tsuzaki, M.A.	Language Services Specialist

Proteus Digital Health

George Savage, M.D.	Cofounder and Chief Medical Officer
Jafar Shenasa	Head, Regulatory Affairs

1.0 BACKGROUND

The sponsor, Otsuka Pharmaceutical Co., Ltd (Otsuka), is developing a combination drug-device that consists of an aripiprazole tablet plus an embedded ingestible event marker (IEM) from Proteus® (the Proteus Ingestible Sensor), which is also referred to as aripiprazole + IEM, under the Investigational New Drug (IND) 115927. IND 115927 was allowed to proceed on Oct 24, 2013. The purpose of the aripiprazole + IEM tablet is to be used in conjunction with a system to (b) (4).

The sponsor's agenda for this meeting is to gain concurrence with FDA that adequate evidence is available to file a NDA for TRADEMARK. The proposed claim is "TRADEMARK (b) (4) The sponsor requests concurrence with the FDA that the preliminary results from the Human Factors Validation study provide sufficient support for the claim that the NDA may be filed and approved. The Human Factors Validation study included 36 patients from three different diagnostic groups (schizophrenia, major depressive disorder, bipolar 1 disorder) who were divided between two conditions of use (assisted and unassisted).

No new treatment indication is proposed for the aripiprazole + IEM combination beyond those currently approved for Abilify (aripiprazole) in the adult oral tablet formulation:

- Schizophrenia; acute and maintenance treatment
- Acute treatment of manic and mixed episodes associated with bipolar I disorder, and as monotherapy or adjunctive for maintenance treatment
- Adjunctive treatment of major depressive disorder

The Sponsor states that TRADEMARK is not intended to address the treatment of the disease (i.e., schizophrenia, bipolar I disorder, or MDD), because that has been demonstrated by approval of the aripiprazole oral tablet (NDA 21-436).

The sponsor plans not to submit an integrated summary of efficacy or safety in the proposed NDA, since the efficacy and safety of the components have already been demonstrated and the indications for TRADEMARK are the same as those for the Abilify oral tablet in adults. At the Feb 4, 2015 Type C meeting, the sponsor indicated that clinical safety data from trials that used the TRADEMARK product would be provided.

2. DISCUSSION

2.1. General

Question 1: As discussed at the 04 Feb 2015 Type C meeting, the TRADEMARK product consists of the following 4 components: aripiprazole + IEM tablet; Proteus Patch + MDDS; Patient Component of the Otsuka Medical Software; and Healthcare Provider and Caregiver Web Portals of the Otsuka Medical Software. Based on previous meetings with the Agency on the TRADEMARK development program and requirements for registration (see minutes from meetings on 29 Sep 2012, 13 Aug 2013, 10 Feb 2014, and 04 Feb 2015) and International Conference on Harmonisation M4 "Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use," the NDA will consist of chemistry, manufacturing, and control, human factors validation data, safety data from trials using TRADEMARK, and proposed labeling. Appropriate cross-references to the already approved and cleared components of TRADEMARK will be made in the NDA.

The proposed content and structure of the NDA will include a summary of clinical safety and a clinical overview. As previously indicated, the sponsor will cross-reference the Abilify NDAs and Proteus 510(k)s for the efficacy and safety of the drug and device components, as appropriate, and will not provide an integrated summary of efficacy in this NDA.

Does the Agency agree with the proposed structure and table of contents for the NDA?

FDA Response to Question 1:
From clinical point of view, the proposed structure and table of contents for the NDA appears acceptable.

We agree with your proposal to cross-reference the drug substance information to NDA 21436, but request that you, at minimum, include the current drug substance specification in Section 3.2.S.

Discussion at meeting: *There was no further discussion.*

Question 2: The TRADEMARK NDA will be reviewed as a non-new molecular entity (NME) original NDA, as confirmed by the FDA at the pre-IND Meeting, 14 Aug 2013.

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