CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212690Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 049641

MEETING MINUTES

Jazz Pharmaceuticals
Attention: Paula Hines, PhD.
Senior Director, Global Regulatory Lead
CNS/Sleep Global Regulatory Affairs
3180 Porter Drive
Palo Alto, CA 94304

Dear Dr. Hines:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for JZP258.

We also refer to the pre-NDA meeting between representatives of your firm and the FDA on October 2, 2019.

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

If you have any questions, contact Vandna Kishore, Senior Regulatory Project Manager at vandna.kishore@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Acting Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

MEMORANDUM OF MEETING MINUTES

Meeting Type:	B
Meeting Category:	Pre-NDA
Meeting Date and Time:	October 2, 2019 10 AM
Meeting Location:	FDA White Oak Campus, Building 22, Room 1313
Application Number:	049641
Product Name:	JZP-258
Indication:	Treatment of cataplexy and excessive daytime sleepiness in patients 7 years of age and older with narcolepsy
Sponsor Name:	Jazz Pharmaceuticals
Meeting Chair:	Eric Bastings, MD

FDA ATTENDEES

Billy Dunn, MD, Acting Deputy Office Director
Eric Bastings, MD, Acting Division Director
Ranjit Mani, MD, Clinical Reviewer
Alice Hughes, MD, Director for Safety
Sally Yasuda, PharmD, Team Leader for Safety
Dawei Li, PhD, Clinical Pharmacology Reviewer
Sharon Yan, PhD, Biometrics Reviewer
Martha Heimann, PhD, OPQ CMC Lead
Nandini Bhattacharya, PhD, Microbiology
Xia Xu, PhD, Microbiology Reviewer
Danielle Harris, PharmD, DMEPA Deputy Director
Chad Morris, DMEPA Reviewer
Donella Fitzgerald, DRISK Team Lead
Jamie Wilkins Parker, DRISK
Ingrid Chapman, PharmD, Risk Management Analyst
John Palmer, MD, NIH Fellow
Vandna Kishore, RPh, Regulatory Project Manager

SPONSOR ATTENDEES

(b) (4)	Clinical Pharmacology Consultant
Jed Black, MD	Senior Fellow, Sleep/Neuroscience, Clinical Development
Cuiping Chen, PhD	Senior Director, Clinical Pharmacology
Peng Chen, PhD	Director, Biostatistics

Nicole Damour	Associate Director, Global Regulatory Affairs, Chemistry, Manufacturing, and Controls
Sanja Gauthier, MD	Executive Director, Medical Safety
Paula Hines, PhD	Senior Director, Global Regulatory Lead, Regulatory Strategy
Robert Iannone, MD, MSCE	Executive Vice President, Head of Research and Development
Philip Jochelson, MD	Vice President, Therapeutic Area Head Clinical Development, Sleep and CNS
Gunjan Junnarkar, PhD	Senior Director, Process Development
Sherice Mills	Senior Director, Benefit Risk Management
Patricia Moore	Vice President, Research and Development Quality and Global Regulatory Affairs
Judith Profant, PhD, DBSM	Director, Medical Affairs
(b) (4)	Regulatory Consultant
Jeffrey Silverman, PhD	Vice President, Early Development
Franck Skobieranda, MD	Vice President, Clinical Development, Sleep
Roman Skowronski, MD, PhD	Executive Director, Clinical Development, Sleep and CNS Executive Director, Clinical Development, Sleep and CNS

Appears this way on original

1.0 BACKGROUND

This meeting is for a Pre-New Drug Application (Pre-NDA) discussion for JZP-258, also referred to as "oxybate" and previously referred to as an "oxybate mixed-salt oral solution (OMSOS)." The proposed NDA for JZP-258 is to be submitted under the Section 505(b)(1) pathway.

JZP-258 is an aqueous oral solution containing 0.413 g/mL of oxybate, stated to be equivalent to a 0.5 g/mL mixture of calcium, potassium, magnesium, and sodium oxybate. JZP-258 has been developed as a lower-sodium alternative to Xyrem® (sodium oxybate oral solution [500 mg/mL]), which is notable for its high sodium content.

Xyrem is currently approved for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy in patients 7 years of age and older.

The proposed indications for JZP-258 are the same as those for which Xyrem® is currently approved. The proposed dosing regimen for JZP-258 is (b) (4) that currently recommended in the Prescribing Information for Xyrem.

The proposed NDA for JZP-258 is to contain reports for the following clinical studies, summary data for which are provided in this meeting package.

- Study JZP258-101, an open-label, randomized crossover study investigating the relative bioequivalence and bioavailability of JZP-258 and Xyrem under fasted conditions in healthy subjects.

- Study 13-010, an open-label, randomized crossover study investigating the relative bioequivalence and bioavailability of JZP-258 and Xyrem under fasted and fed conditions in healthy subjects.

- Study 15-003, a randomized, double-blind, placebo-controlled crossover study comparing the taste of JZP-258 with placebo in healthy subjects.

- Study 15-006, a double-blind, placebo-controlled, randomized withdrawal study of the efficacy and safety of JZP-258 in the treatment of cataplexy and excessive daytime sleepiness in narcolepsy.

All clinical studies of JZP-258 have been conducted in adult subjects only.

The clinical, chemistry, nonclinical, and clinical pharmacology data to be included in the proposed NDA for JZP-258 are summarized in this meeting package, as is the format in which those data are to be submitted in that application.

FDA sent Preliminary Comments to Jazz on September 27, 2019.

2. DISCUSSION

Please note the following regarding the text below: the Agency's initial responses to the sponsor's questions are in blue font, the sponsor's pre-meeting responses (dated September 30, 2019) are in purple font, the meeting discussion is summarized in green font, and a single Agency post-meeting comment is in brown font.

2.1. Chemistry, Manufacturing, and Controls

Question 1: Does the Agency agree that the proposed CMC package and control strategy outlined in the meeting package are adequate to support the registration of JZP-258?

FDA Response to Question 1:

In general, your proposed Chemistry, Manufacturing, and Controls (CMC) package and control strategy appear appropriate, pending review of the data provided in the proposed NDA. However, you should address the concerns outlined below in the original NDA submission.

Microbiology:

(b) (4)

For the NDA

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