CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

211230Orig1s000
211230Orig2s000

Trade Name:	Sunosi Tablets, 75mg and 150 mg
Generic or Proper Name:	solriamfetol
Sponsor:	Jazz Pharmaceuticals Ireland Limited
Approval Date:	March 20, 2019
Indication:	• NDA 211230 Original 1 - to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy • NDA 211230 Original 2 - to improve wakefulness in adult patients with excessive daytime sleepiness associated with obstructive sleep apnea (OSA)

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211230Orig1s000
211230Orig2s000

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APPLICATION NUMBER:

211230Orig1s000
211230Orig2s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 211230/Original 1
NDA 211230/Original 2

NDA APPROVAL

Jazz Pharmaceuticals Ireland Limited
C/O Jazz Pharmaceuticals, Inc.
Attention: Lily Gong
Director, Regulatory Affairs
3180 Porter Drive
Palo Alto, CA 94304

Dear Ms. Gong:

Please refer to your New Drug Application (NDA) dated and received December 20, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sunosi (solriamfetol) Tablets, 75mg and 150 mg.

We acknowledge receipt of your major amendment dated December 19, 2018, which extended the goal date by three months.

This new drug application provides for the use of Sunosi (solriamfetol) Tablets for the following indications which, for administrative purposes, we have designated as follows:

- NDA 211230 Original 1 - to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy
- NDA 211230 Original 2 - to improve wakefulness in adult patients with excessive daytime sleepiness associated with obstructive sleep apnea (OSA)

APPROVAL & LABELING

We have completed our review of NDA 211230/Original 1 and NDA 211230/Original 2, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTROLLED SUBSTANCE SCHEDULING

You were previously informed that FDA intends to recommend scheduling of Sunosi under the Controlled Substances Act (CSA). The scheduling of this product in accordance with the CSA (21 U.S.C. 811) is not yet complete as of the date of this letter. Therefore, in accordance with the FDCA (21 U.S.C. 355(x)), the date of approval for Sunosi shall be the date on which the

Drug Enforcement Administration (DEA) publishes a notice in the Federal Register announcing the interim final scheduling of solriamfetol.

We note that, when the drug is scheduled by the DEA, you will need to make appropriate revisions to the Prescribing Information, Medication Guide, and carton and container labeling by submitting a supplement to your NDA. This would include the statements in the labeling detailing the scheduling of solriamfetol, as the scheduled substance in Sunosi, as required under 21 CFR 201.57(a)(2) and (c)(10)(i). Therefore, Sunosi may be marketed only after DEA has published the notice in the Federal Register announcing the interim final scheduling of solriamfetol and you submit a supplement to your NDA to revise all applicable drug labeling to reflect the drug scheduling described in the notice. For changes to the Prescribing Information, Medication Guide, carton and container labeling to describe the scheduling of solriamfetol, you can submit a Changes Being Effected supplement described in 21 CFR 314.70(c)(6). Permission to use a Changes Being Effected supplement for this purpose reflects a waiver by the Agency, pursuant to 21 CFR 314.90, of the requirement to submit a Prior Approval Supplement for changes to reflect the scheduling to the Highlights of Prescribing Information for Sunosi described in 21 CFR 314.70(b)(2)(v)(C) and changes to the Medication Guide described in 21 CFR 314.70(b)(2)(v)(B).

We note that Sunosi will be listed in the Orange Book upon the date of approval in accordance with 21 U.S.C. 355(x). With respect to the submission of patent information, as required under 21 CFR 314.53(c)(2)(ii), we note that you must submit Form FDA 3542 within 30 days after the date on which DEA has published the notice in the Federal Register announcing the interim final scheduling of solriamfetol.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on December 7, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for

industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 211230**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Sunosi was not referred to an FDA advisory committee because the efficacy and safety data were readily interpretable and not controversial, and there was experience with other drugs in this class.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the indication to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy has orphan drug designation, you are exempt from this requirement.

We are waiving the pediatric study requirement for the indication to improve wakefulness in adult patients with excessive daytime sleepiness associated with OSA because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients **and** is not likely to be used in a substantial number of pediatric patients. Clinical practice guidelines, published literature, claims data, and clinical experts recommend surgical and/or mechanical therapies to treat the underlying airway obstruction in pediatric patients. Stimulants and alerting agents do not form part of the treatment algorithm for OSA in any pediatric age group.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of pregnancy complications, effects on the developing fetus and neonate, and effects on the breastfed infant during lactation.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

3475-1 A prospective, registry based observational exposure cohort study that compares the maternal, fetal, and infant outcomes of women exposed to solriamfetol during pregnancy to an unexposed control population. The registry will detect and record major and minor congenital malformations, spontaneous abortions, stillbirths, elective terminations, small for gestational age, preterm birth, and any other adverse pregnancy outcomes. These outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

The timetable you submitted on January 15, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/19
Study Completion:	09/29
Final Report Submission:	09/30

3475-2 An additional pregnancy study that uses a different design from the Pregnancy Registry (for example a retrospective cohort study using claims or electronic medical record data with outcome validation or a case control study) to assess major congenital malformations, spontaneous abortions, stillbirths, and small for gestational age and preterm birth in women exposed to solriamfetol during pregnancy compared to an unexposed control population.

The timetable you submitted on January 15, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/19
Study Completion:	09/24
Final Report Submission:	09/25

3475-3 Perform a lactation study (milk only) in lactating women who have received therapeutic doses of solriamfetol using a validated assay to assess concentrations of solriamfetol in breast milk and the effects on the breastfed infant.

The timetable you submitted on January 15, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/19
Study Completion:	09/20
Final Report Submission:	09/21

Submit clinical protocol(s) to your INDs 107203 and 122590 with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312 or FDA's regulations under 21 CFR parts 50 (Protection of Human Subjects) and 56 (Institutional Review Boards).

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

You must comply with the reporting requirements described in 21 CFR 314.80(c)(1) (e.g., 15-day alert reports) beginning on the date of **this** letter. The due dates for the periodic (including quarterly) adverse drug experience reports described in 21 CFR 314.80(c)(2) should be calculated from the date of this letter. Annual reports described in 21 CFR 314.81(b)(2) are due within 60 days of the anniversary of the date of approval in accordance with 21 U.S.C. 355(x).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, contact CDR Sarah Seung, Regulatory Project Manager, at sarah.seung@fda.hhs.gov or (240) 402-3879.

Sincerely,

{See appended electronic signature page}

Ellis F. Unger, MD
Director
Office of Drug Evaluation I
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):
- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ELLIS F UNGER
03/20/2019 05:28:00 PM