NDA 213586

NDA APPROVAL

Teva Neuroscience
Attention: Levana Volovsky
Director, Regulatory Affairs
145 Brandywine Parkway
West Chester, PA 19380

Dear Ms. Volovsky:

Please refer to your new drug application (NDA) dated and received June 17, 2021, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Uzedy (risperidone) extended-release injectable suspension.

We acknowledge receipt of your amendment dated October 28, 2022, which constituted a complete response to our April 15, 2022, action letter.

This NDA provides for the use of Uzedy (risperidone) extended-release injectable suspension, for subcutaneous use, for treatment of schizophrenia in adults.

APPROVAL AND LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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

FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information) 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.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

We acknowledge your April 24, 2023, submission containing final printed carton and container labeling.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Uzedy (risperidone) extended-release injectable suspension shall be 24 months from the date of manufacture when stored at 2° to 8°C.

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.

Studies in adolescents would unlikely be successful given the effort the Applicant has made to enroll adolescents in trials, therefore we are waiving the pediatric studies requirement for this application on the basis that necessary studies are impossible or highly impracticable.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4237-2 Study Dissolution method/acceptance criteria and IVIVC deficiency: To aid in the regulatory decision making in terms of acceptability of the proposed IVIVC model, submit the following information/data in a prior-approval supplement (PAS):

A modeling summary report, which provides an overview of the modeling strategy and details of the modeling procedures, including model development, model verification/modification, and model application in a step-by-step process. Inclusion of a flow chart, decision tree, or other similar representation is preferred for clarity.

Generally, for the IVIVC development of immediate release drug products, at least 3 batches of the proposed drug product that differ in the in vivo PK and in vitro dissolution profiles should be used. As part of the validation steps, follow the "leave-one out" cross validation approach in the construction and validation of your model to challenge its robustness.

Submit the executable project files (e.g., .phxproj, .xlsx or .xls, .sas) for the IVIVC model development and internal/external validation. Provide all relevant input including complete in vitro and in vivo data (i.e., individual, mean, % CV, profiles, in .csv, .xlsx or .xls, or .xpt format) and output files used in the construction and validation of the IVIVC model.

Provide definition file(s) listing all input and output files, and the use or purpose of each of this files in an appropriate format (e.g., .pdf, .xpt, .xls). In addition, provide the hyperlinks for each data file and instructions for extracting these files.

Provide the IVIVC predictions including the output files and summary table supporting your proposed dissolution acceptance criterion.

The timetable you agreed to on March 15, 2022, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/31/2023

Submit clinical protocols to your IND 124384 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The

status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," **or** "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

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 FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.[6]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[6] https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

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

Sincerely,

{See appended electronic signature page}

Bernard Fischer, MD
Deputy Director
Division of Psychiatry
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- 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/

BERNARD A FISCHER
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