NDA 217006

NDA APPROVAL

Otsuka Pharmaceutical Company, Ltd.
c/o Otsuka Pharmaceutical Development & Commercialization, Inc.
Attention: Michelle Hillsman, MS
508 Carnegie Center Drive
Princeton, NJ 08540

Dear Ms. Hillsman:

Please refer to your new drug application (NDA) dated and received June 27, 2022, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Abilify Asimtufii (aripiprazole) extended-release injectable suspension.

This NDA provides for the use of Abilify Asimtufii (aripiprazole) extended-release injectable suspension, for intramuscular use, for the treatment of schizophrenia in adults and as maintenance monotherapy treatment of bipolar I disorder 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

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Prescribing Information, Medication Guide, and Instructions for Use) 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 26, 2023, submission containing final printed carton and container labeling.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Abilify Asimtufii (aripiprazole) extended-release injectable suspension shall be 24 months from the date of manufacture when stored at 20 to 25°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.

We are waiving the pediatric studies requirement for this application on the basis that studies would be unfeasible or highly impractical for both indications (schizophrenia and maintenance monotherapy treatment of bipolar I disorder). In pediatric patients 0 to 9 years of age with bipolar I disorder, and 0 to 12 years of age with schizophrenia the condition has a very low prevalence. In pediatric patients 10 to 17 years of age with bipolar I disorder, and 13 to 17 years of age with schizophrenia, long-acting antipsychotic injections are unlikely to be used in a substantial number of pediatric patients; therefore, it is not feasible to conduct necessary studies in a sufficient number of pediatric patients.

[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:

4438-1 The Minimum Quantitation Limit (MQL) for the current leachables methods are greater than the revised AET of (b) (4) mcg/mL. Revalidate the leachables methods such that the MQL is below the revised AET of (b) (4) mcg/mL. Repeat the leachables study on the first three batches of each strength manufactured for commercial marketing and use the revalidated method. Test leachables at the timepoints as recommended in ICH Q1A.

The timetable you submitted on April 25, 2023, states that you will conduct each study according to the following schedule:

A. Revalidation of the leachables method with LOQ below the AET of (b) (4) mcg/mL.

   Leachables testing at the initial timepoint of first commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

   Final Report Submission: 07/2024

B. Leachables testing up to 12 months for first commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

   Leachables testing at the initial timepoint for second commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

   Final Report Submission: 07/2025

C. Leachables testing up to 24 months for first commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

   Leachables testing up to 12 months for second commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A

   Leachables testing at the Initial timepoint of third commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

   Final Report Submission: 07/2026

D. Leachables testing up to 24 months for second commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

Leachables testing up to 12 months for third commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

Final Report Submission: 07/2027

E. Leachables testing up to 24 months for third commercially manufactured batch. Testing will occur at the timepoints as recommended in ICH Q1A.

Final Report Submission: 07/2028

4438-2 Identify compounds from the extractables studies with unknown structural formula that are above the revised AET of (b) (4) mcg/mL. Note simulation studies will not be considered accurate identification.

The timetable you submitted on April 25, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 07/2024

4438-3 No forced degradation studies have been provided to prove the analytical methods are stability indicating. Provide data from forced degradation studies for the formulation in this NDA. Use conditions including acid, base, oxidative, heat, light.

The timetable you submitted on April 25, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 07/2024

Submit clinical protocols to your IND 134612 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]

If you have any questions, contact Tiffanie Taylor, Regulatory Project Manager, at Tiffanie.Taylor@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

[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

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- 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
04/27/2023 06:41:05 PM