NDA 216655

NDA APPROVAL

Xiamen LP Pharmaceutical Co., Ltd.
C/O LP Pharmaceuticals, Inc. (USA)
Attention: Matthew Nieder, PhD
President
LP Pharmaceuticals, Inc
1633 Bayshore Hwy, Suite 280
Burlingame, CA 94010

Dear Dr. Nieder:

Please refer to your new drug application (NDA) dated and received September 19, 2023, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Opipza (aripiprazole) oral film.

This NDA provides for the use of Opipza (aripiprazole) oral film for the following indications:

- Treatment of schizophrenia in patients ages 13 years and older
- Adjunctive treatment of major depressive disorder in adults
- Irritability associated with autistic disorder in pediatric patients 6 years and older
- Treatment of Tourette's disorder in pediatric patients 6 years and older

APPROVAL & 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, Instructions for Use, 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.*[2]

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 enclosed carton and container labeling, 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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 216655**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Opipza aripiprazole oral soluble film shall be 36 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 study requirement for adjunctive treatment of major depressive disorder (MDD) because necessary studies are impossible or highly impracticable. Adjunctive treatment of MDD is listed on the FDA "Automatic Full Waivers" list for adult-related conditions that qualify for a waiver on the basis that pediatric studies would be 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.

We are waiving the pediatric study requirement for schizophrenia for ages 0 to younger than 13 years because necessary studies are impossible or highly impracticable. This is because the number of pediatric patients with schizophrenia is too small in the 0 to younger than 13-year-old age group for clinical studies. Specifically, onset of schizophrenia in pediatric patients younger than age 13 is extremely rare. It is generally accepted that the incidence of childhood-onset schizophrenia is less than 0.04% based on the observations from the National Institutes of Mental Health (NIMH) cohort. Therefore, studies in this age group are highly impracticable.

We are waiving the pediatric study requirement for irritability associated with autistic disorder for ages 0 to younger than 6 years because necessary studies are impossible or highly impracticable. This is because in the American Academy of Pediatrics 2020 guideline of autistic disorder: Identification, evaluation, and management of children with autism spectrum disorder, applied behavior analysis and developmental relationship–focused interventions are recommended for pediatric patients of 0 to 6 years old with autistic disorder. There was no specific recommendation on pharmacology treatments for patients ages 0 to 6 years. The drug is not likely to be used in a substantial number of pediatric patients with autistic disorder in the 0 to younger than 6-year-old age group and studies in this age group are highly impracticable.

We are waiving the pediatric study requirement for Tourette's disorder for ages 0 to younger than 6 years because necessary studies are impossible or highly impracticable. This is because in the American Academy of Neurology (AAN) 2019 guideline: The Treatment of Tics in People with Tourette Syndrome and Chronic Tic Disorders, behavioral treatments are recommended for pediatric patients under 6 years old with Tourette's disorder. No evidence of therapeutic benefit for medications in the 0 to <6-year-old age group was reported. The drug is not likely to be used in a substantial number of pediatric patients with Tourette's disorder in the 0 to younger than 6-year-old age group and studies in this age group are highly impracticable.

This product is appropriately labeled for use in ages 13 to 17 years for the schizophrenia indication. Therefore, no additional studies are needed in this pediatric group.

This product is appropriately labeled for use in ages 6 to 17 years for the irritability associated with autistic disorder and Tourette's disorder indications. Therefore, no additional studies are needed in this pediatric group.

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).

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website.[6]

If you have any questions, contact Shin-Ye (Sandy) Chang, Senior Regulatory Project Manager at shinye.chang@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Bernard Fischer, MD
Deputy Director
Division of Psychiatry
Office of Neuroscience

[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.uspnf.com/

Center for Drug Evaluation and Research

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
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