NDA 217645

NDA APPROVAL

Tris Pharma, Inc.
Attention: Rashmi Aravind
Director, Regulatory Affairs
2033 Route 130
Monmouth Junction, NJ 08852

Dear Rashmi Aravind:

Please refer to your new drug application (NDA) dated and received July 24, 2023, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Onyda XR (clonidine hydrochloride) extended-release oral suspension.

This NDA provides for the use of Onyda XR (clonidine hydrochloride) extended-release oral suspension for treatment of attention-deficit/hyperactivity disorder (ADHD) as monotherapy or as adjunctive therapy to stimulant medication.

APPROVAL & LABELING

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

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, Patient Package Insert, 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.

[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.

CARTON AND CONTAINER LABELING

We acknowledge your May 24, 2024, submission containing final printed carton and container labeling.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Onyda XR (clonidine hydrochloride) extended-release oral suspension shall be 24 months from the date of manufacture when stored at 20 to 25 °C.

ADVISORY COMMITTEE

Your application for Onyda XR was not referred to an FDA advisory committee because this drug is not the first in its class and evaluation of the data did not raise significant, unexpected safety or efficacy issues.

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 ages 0 to 4 years because necessary studies are impossible or highly impracticable. This is because there are no validated diagnostic criteria and assessment measures for diagnosing ADHD in children younger than 4 years of age, assessment measures for determining treatment effect in children younger than 4 years of age are not well defined, and non-medication interventions are preferred treatment for behavioral disorders such as ADHD in very young children (e.g., <4 years of age).

We are deferring submission of your pediatric studies for patients 4 years to younger than 6 years of age for this application because this product is ready for approval for use in patients 6 years of age and older and pediatric studies in younger children have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

PMR 4636-1 Conduct an adequate and well-controlled study to evaluate the safety and effectiveness of clonidine hydrochloride extended-release oral suspension in pediatric patients 4 years to <6 years of age with attention-deficit/hyperactivity disorder

Final Protocol Re-Submission: July 2024
Study Completion: July 2025
Final Report Submission: January 2026

PMR 4636-2 Conduct a long-term, open-label study to evaluate the safety and tolerability of clonidine hydrochloride extended-release oral suspension in pediatric patients 4 years to <6 years of age with attention-deficit/hyperactivity disorder

Final Protocol Submission: July 2024
Study Completion: August 2026
Final Report Submission: January 2027

FDA considers the term “final” to mean that an applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocols to your IND 128004 with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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.*[4]

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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.[7]

If you have any questions, contact Iram Baig, Regulatory Project Manager, at Iram.Baig@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

[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[7] https://www.uspnf.com/

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - 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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