

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

216190Orig1s000

Trade Name: Ontralfy oral solution

Generic or Proper Name: tizanidine

Sponsor: Fidelity Biopharma Co.

Approval Date: December 12, 2024

Indication: For the treatment of spasticity in adults.

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APPROVAL LETTER



NDA 216190

NDA APPROVAL

Fidelity BioPharma Co.
Attention: Song Lin, Chief Executive Officer
157 Church Street, Suite 1915
New Haven, CT 06510

Dear Song Lin:

Please refer to your new drug application (NDA) dated May 31, 2023, received May 31, 2023, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ontralfy (tizanidine) oral solution.

We acknowledge receipt of your amendment dated June 12, 2024, which constituted a complete response to our March 29, 2024, action letter.

This NDA provides for the use of Ontralfy (tizanidine) oral solution for the treatment of spasticity in adults.

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.

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.

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>.

CONTAINER LABELING

Submit the final printed container label that is identical to the container label submitted on December 4, 2024, as soon as it is available, but no more than 30 days after it is printed. Please submit this 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 Container Labeling for approved NDA 216190**”. 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 Ontralfy (tizanidine) oral solution shall be 24 months from the date of manufacture when stored at controlled room temperature, 20°C 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 ages 0 to less than 2 years because necessary studies are impossible or highly impracticable. This is because the product (1) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and (2) is not likely to be used by a substantial number of pediatric patients in this age group (section 505B(a)(4)(B)(iii) of the Act)..

We are deferring submission of your pediatric studies for ages 2 to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act/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 Federal Food, Drug, and Cosmetic Act/FDCA. These required studies are listed below.

- 4749-1 An open-label pharmacokinetic (PK) and safety study of tizanidine in pediatric patients 2-17 years of age with spasticity. Patients will be enrolled from the following age groups: 2 to 5 years, 6 to 11 years, and 12 to 17 years, and each group will be adequately represented.

Draft Protocol Submission: 04/2025

Final Protocol Submission: 07/2025

Study Completion: 12/2027

Final Report Submission: 06/2028

- 4749-2 An open-label observational safety study in pediatric patients 2 to 17 years of age with spasticity to evaluate for potential short-term and long-term effects of tizanidine in the pediatric population on physical and neurocognitive development. Patients will be enrolled from the following age groups: 2 to 5 years, 6 to 11 years, and 12 to 17 years, and each group will be adequately represented.

Draft Protocol Submission: 01/2028

Final Protocol Submission: 04/2028

Study Completion: 07/2030

Final Report Submission: 12/2030

FDA considers the term *final* to mean that the 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 protocol(s) to your IND 156316, 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

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,

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>.

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 website⁷.

If you have any questions, contact Amy Bolger, PharmD, Regulatory Health Project Manager, by email at Amy.Bolger@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Laura Jawidzik, MD
Deputy Director
Division of Neurology 1
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
 - Prescribing Information

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/>

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/

LAURA A JAWIDZIK
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