

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214697Orig1s000

Trade Name: NEFFY®

Generic or Proper Name: epinephrine nasal spray

Sponsor: ARS Pharmaceuticals Operations, Inc.

Approval Date: August 09, 2024

Indication: Neffy is an alpha and beta-adrenergic receptor agonist indicated for emergency treatment of type I allergic reactions, including anaphylaxis, in adult and pediatric patients who weigh 30 kg or greater.

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APPROVAL LETTER

NDA 214697

NDA APPROVAL

ARS Pharmaceuticals Operations, Inc.
C/O Pacific Link Consulting
Attention: Richard Lowenthal
President, Pacific-Link Consulting
11682 El Camino Real
Suite 120
San Diego, CA 92130

Dear Richard Lowenthal:

Please refer to your new drug application (NDA) dated August 19, 2022, received August 19, 2022, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for neffy (epinephrine nasal spray), 2 mg/0.1 mL.

We acknowledge receipt of your amendment dated April 2, 2024, which constituted a complete response to our September 19, 2023, action letter.

This NDA provides for the use of neffy (epinephrine nasal spray) for the emergency treatment of type I allergic reactions, including anaphylaxis, in adults and pediatric patients who weigh 30 kg or greater.

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, 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.

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 214697.**” 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 neffy (epinephrine nasal spray), 2 mg/0.1 mL, shall be 24 months from the date of manufacture when stored at 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 study requirement for ages <4 years because necessary studies are impossible or highly impracticable.

We are deferring submission of your pediatric study for pediatric patients between 15 to <30 kg for this application because this product is ready for approval for use in adults and pediatric patients who weigh 30 kg or greater.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually

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>.

according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. This required study is listed below.

- 4671-1 Conduct a single-dose, pharmacokinetic and pharmacodynamics study of neffy (ARS-1) in pediatric patients ≥ 4 years of age and between 15 to <30 kg with Type I allergies that require prescription of an epinephrine product.

The timetable you submitted on June 13, 2024, amended July 31, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 11/2024

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 139091, with a cross-reference letter to this NDA. Reports of this required pediatric postmarketing study 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 this study. 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 4671-2 Conduct a registry-based study in high volume oral food challenge and allergen immunotherapy clinics in which subjects would use either neffy (ARS-1) or an epinephrine injection product for treatment of anaphylaxis. Collect initial symptoms along with clinical outcome data comparing neffy (ARS-1) to epinephrine injection, including time to symptom resolution, adverse events, and whether a repeat dose is needed.

The timetable you submitted on June 13, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2024
Final Protocol Submission: 02/2025
Study Completion: 02/2026

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>.

Final Report Submission: 06/2026

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 139091 for this product. Submit all protocols nonclinical and chemistry, manufacturing, and controls protocols and 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*.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, 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).

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.⁷

⁴ For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/media/128163/download>.

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.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

If you have any questions, call Ji Hyun LaRose, Regulatory Project Manager, at (301) 796-9017.

Sincerely,

{See appended electronic signature page}

Kelly Stone, MD, PhD
Associate Director for Therapeutic Review
Division of Pulmonology, Allergy, and Critical Care
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

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/

KELLY D STONE
08/09/2024 10:44:47 AM