



NDA 220482

NDA APPROVAL

Haisco-USA Pharmaceuticals, Inc
1200 US Highway 22E
Suite 2000
Bridgewater, NJ 08807

Attention: Rong Zhou, PhD
Vice General Manager

Dear Dr. Zhou:

Please refer to your new drug application (NDA) received May 30, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for CYPSEDO (cipepofol) Injection, 50 mg/ 20 mL.

This NDA provides for the use of CYPSEDO (cipepofol) injection for induction of general anesthesia in adults undergoing surgery.

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.

CONTROLLED SUBSTANCE SCHEDULING

You were previously informed that FDA intends to recommend scheduling of CYPSEDO under the Controlled Substances Act (CSA). The scheduling of this product in accordance with the CSA (21 U.S.C. 811) is not yet complete as of the date of this letter. Therefore, in accordance with the FDCA (21 U.S.C. 355(x)), the date of approval for CYPSEDO shall be the date on which the Drug Enforcement Administration (DEA) publishes a notice in the Federal Register announcing the interim final scheduling of cipepofol.

We note that, when the drug is scheduled by the DEA, you will need to make appropriate revisions to the Prescribing Information and carton and container labeling by submitting a supplement to your NDA. This would include the statements in the labeling detailing the scheduling of cipepofol, as the scheduled substance in CYPSEDO, as required under 21 CFR 201.57(a)(2) and (c)(10)(i). Therefore, CYPSEDO may be marketed only after DEA has published the notice in the Federal Register announcing the interim final scheduling of cipepofol and you submit a

supplement to your NDA to revise all applicable drug labeling to reflect the drug scheduling described in the notice. For changes to the Prescribing Information and carton and container labeling to describe the scheduling of CYPSEDO, you can submit a Changes Being Effected supplement described in 21 CFR 314.70(c)(6). Permission to use a Changes Being Effected supplement for this purpose reflects a waiver by the Agency, pursuant to 21 CFR 314.90, of the requirement to submit a Prior Approval Supplement for changes to reflect the scheduling to the Highlights of Prescribing Information for CYPSEDO described in 21 CFR 314.70(b)(2)(v)(C).

We note that CYPSEDO will be listed in the Orange Book upon the date of approval in accordance with 21 U.S.C. 355(x). With respect to the submission of patent information, as required under 21 CFR 314.53(c)(2)(ii), we note that you must submit Form FDA 3542 within 30 days after the date on which DEA has published the notice in the Federal Register announcing the interim final scheduling of cipepofol.

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 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 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 220482.**” Approval of this submission by FDA is not required before the labeling is used.

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>.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for CYPSEDO (cipepofol) Injection shall be 36 months from the date of manufacture when stored at 2°C-25 °C.

ADVISORY COMMITTEE

Your application for CYPSEDO was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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 deferring submission of your pediatric studies according to the timetables listed below, because this product is ready for approval for use in adults and adequate pediatric studies have not been completed.

Your deferred pediatric studies required under 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.

5003-1 Conduct a randomized, double-blinded, multicenter, active-controlled study evaluating pharmacokinetics, safety, and efficacy of cipepofol in pediatric patients from 3 to less than 17 years of age.

Final Protocol Submission: 05/2026 (completed)

Study Completion: 03/2028

Final Report Submission: 09/2028

5003-2 Conduct a juvenile animal study in rats to support the initiation of clinical studies in pediatric patients from birth to less than 3 years of age. This study will evaluate the effect of cipepofol on growth and development, specifically reproductive performance/sexual maturation and brain

development, including central nervous system histopathology and long-term behavioral effects.

Final Protocol Submission: 11/2025 (completed)
Study Completion: 06/2027
Final Report Submission: 09/2027

5003-3 Conduct an acute neurotoxicity study in neonatal rats evaluating the impact of cipepofol on neuronal development to support clinical pediatric studies in pediatric patients from birth to less than 3 years of age. This study will evaluate the effect of cipepofol on neuroapoptosis and central nervous system histopathology in neonatal rats during the peak of synaptogenesis.

Final Protocol Submission: 11/2026
Study Completion: 06/2027
Final Report Submission: 09/2027

5003-4 Conduct a randomized, double-blinded, multicenter, active-controlled study evaluating pharmacokinetics, safety, and efficacy of cipepofol in pediatric patients from birth to less than 3 years of age.

Draft Protocol Submission: 11/2028
Final Protocol Submission: 02/2029
Study Completion: 06/2030
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. See guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act*³.

Submit the protocols to your IND 141001, 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.

³ <https://www.fda.gov/media/131980/download>

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.

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

You must comply with the reporting requirements described in 21 CFR 314.80(c)(1) (e.g., 15-day alert reports) beginning on the date of **this** letter. The due dates for the periodic (including quarterly) adverse drug experience reports described in 21 CFR 314.80(c)(2) should be calculated from the date of this letter. Annual reports described in 21 CFR 314.81(b)(2) are due within 60 days of the anniversary of the date of approval in accordance with 21 U.S.C. 355(x).

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

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

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

official USP monographs. More information on the USP-NF is available on USP's website⁶.

If you have any questions, contact Christopher Wolff, PharmD, Regulatory Project Manager, at christopher.wolff@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Teresa Buracchio, MD
Director
Office of Neuroscience
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
- Carton and Container Labeling

⁶ <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/

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