CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

216755Orig1s000

Trade Name:	LIKMEZ
Generic or Proper Name:	Metronidazole, oral suspension
Sponsor:	Saptalis Pharmaceuticals, LLC
Approval Date:	September 22, 2023
Indication:	LIKMEZ is a nitroimidazole antimicrobial indicated for • Trichomoniasis in adults • Amebiasis in adults and pediatric patients • Anaerobic Bacterial Infections in adults

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APPROVAL LETTER

NDA 216755

NDA APPROVAL

Saptalis Pharmaceuticals, LLC
Attention: Rekha Kallam
Director, Regulatory Affairs
45 Davids Drive
Hauppauge, NY 11788

Dear Rekha Kallam:

Please refer to your new drug application (NDA) dated and received November 23, 2022, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Likmez (metronidazole) oral suspension, 500 mg/5 mL.

This NDA provides for the use of Likmez (metronidazole) oral suspension for the treatment of:

- trichomoniasis in adults,
- amebiasis in adults and pediatric patients, and
- anaerobic bacterial infections 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.

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

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Prescribing Information and Patient Package Insert) 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.

CONTAINER LABEL

Submit the final printed container label that is identical to the enclosed container label, as soon as it is available, but no more than 30 days after it is printed. Please submit this label 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 Label for approved NDA 216755**. Approval of this submission by FDA is not required before the label is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Likmez (metronidazole) oral suspension, 500 mg/5 mL shall be 24 months at 20°C to 25°C (68°F to 77°F). Brief exposure to 15°C to 30°C (59°F to 86°F) permitted [see USP Controlled Room Temperature].

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 the treatment of trichomoniasis in pediatric patients from birth to < 12 years of age because necessary studies are impossible or highly impracticable.

We are deferring submission of your planned pediatric studies (i.e., a phase 2 PK and safety study in pediatric patients 12 months to < 4 years of age for the treatment of anaerobic bacterial infections, a study in pediatric patients birth to < 12 months and 4 years to < 18 years of age for the treatment of anaerobic bacterial infections, and a study in pediatric patients 12 years to < 18 years of age for trichomoniasis) because this

[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.

product is ready for approval for use in adults and pediatric studies have not been completed.

Your deferred pediatric studies required under 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 FDCA. These required studies are listed below.

4502-1 Conduct a phase 2, open-label, single-arm, pharmacokinetic, and safety study in pediatric patients aged 12 months to < 4 years with anaerobic bacterial infections.

Draft Study Protocol Submission	12/2023
Final Study Protocol Submission	03/2024
Study Completion	01/2026
Final Report Submission	06/2026

4502-2 Conduct a search and provide a summary of the published literature assessing dosing, safety, efficacy of metronidazole, and the effect of disease state on metronidazole pharmacokinetics in pediatric patients to support an indication for the treatment of anaerobic bacterial infections in pediatric patients from birth to < 12 months and 4 years to < 18 years of age.

Final Report Submission	06/2025

In your summary, clearly identify/specify the pediatric extrapolation plan including identifying a reference adult patient population, targeted exposures, and a justification of the selected exposure target ranges. If you rely on pharmacokinetic (PK) information from healthy adults to select a target exposure range, additional information will be needed with respect to the disease effect on the drug's PK.

4502-3 Conduct a search and provide a summary of the published literature assessing dosing, safety, efficacy of metronidazole, and the effect of disease state on metronidazole pharmacokinetics in pediatric patients to support an indication for the treatment of trichomoniasis in pediatric patients aged 12 years to < 18 years.

Final Report Submission	06/2025

In your summary, clearly identify/specify the pediatric extrapolation plan including identifying a reference adult patient population, targeted exposures, and a justification of the selected exposure target ranges. If you rely on pharmacokinetic (PK) information from healthy adults to select a target exposure range, additional information will be needed with respect to the disease effect on the drug's PK.

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 protocols to your IND 132217, 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, 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

[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) at* 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.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, call Sheel Shah, PharmD, Regulatory Project Manager, at 240-402-3968.

Sincerely,

{See appended electronic signature page}

Peter Kim, MD, MS
Director
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

[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/

PETER W KIM
09/22/2023 03:17:03 PM