NDA 217900

CORRECTED NDA APPROVAL

Sun Pharmaceutical Industries, Inc.
Attention: Christine Boisclair
SVP Regulatory Affairs & Quality Assurance
65 Hayden Avenue, Suite 3000N
Lexington, MA 02421

Dear Christine Boisclair:

Please refer to your new drug application (NDA) dated and received July 28, 2023, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Leqselvi (deuruxolitinib) tablets.

This NDA provides for the use of Leqselvi (deuruxolitinib) tablets for the treatment of adults with severe alopecia areata.

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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- A bullet point has been added before the phrase “complete any necessary immunizations, including…” under Section 2.1 of the USPI.

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 (Prescribing Information, Patient Package Insert, and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using

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

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 217900".** 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 Leqselvi (deuruxolitinib) tablets shall be 30 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F) and excursions permitted to 15°C to 30°C (59°F to 86°F).

ADVISORY COMMITTEE

Your application for Leqselvi (deuruxolitinib) tablets was not referred to an FDA advisory committee because there were no issues that warranted an 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 waiving the pediatric study requirement for ages 0 to less than 6 years of age because necessary studies are impossible or highly impracticable.

We are deferring submission of your pediatric studies for ages 6 to 17 years of age for this application because pediatric studies should be delayed until additional safety or effectiveness data have been collected and reviewed.

[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.

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

4655-1 Conduct a juvenile toxicity study to evaluate the potential toxicity of deuruxolitinib, including the potential effects on growth, development, and reproduction, when administered orally to juvenile rats.

Final Protocol Submission: Complete (01/2024)
Study Completion: 08/2025
Final Report Submission: 02/2026

4655-2 Conduct a randomized, controlled trial to evaluate the safety, efficacy, and pharmacokinetics of deuruxolitinib in the adolescent population (12 years to less than 18 years) with severe alopecia areata. Evaluate at least 300 subjects exposed to deuruxolitinib for a minimum of 52 weeks.

Draft Protocol Submission: 08/2024
Final Protocol Submission: 02/2025
Study/Trial Completion: 04/2029
Final Report Submission: 10/2029

4655-3 Conduct a randomized, controlled trial to evaluate the safety, efficacy, and pharmacokinetics of deuruxolitinib in the pediatric population (6 years to less than 12 years) with severe alopecia areata. Evaluate at least 100 subjects exposed to deuruxolitinib for a minimum of 52 weeks.

This trial should not be initiated until you have submitted for review clinical data from your trial in subjects 12 years to less than 18 years and nonclinical data from your juvenile toxicity study.

Draft Protocol Submission: 04/2030
Final Protocol Submission: 10/2030
Study/Trial Completion: 01/2035
Final Report Submission: 07/2035

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.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of maternal, fetal and infant toxicity and to assess a known serious risk of increased systemic exposure to deuruxolitinib in patients who are CYP2C9 poor or intermediate metabolizers.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4655-4 Prospective pregnancy registry study:

Collect global data from prospective pregnancy exposure registry/registries, preferably disease-based multiproduct pregnancy registry/registries, using a registry-based cohort study design to compare the maternal, fetal, and infant outcomes of women with Alopecia Areata exposed to deuruxolitinib during pregnancy with unexposed comparator population(s).The registry will identify and record pregnancy complications, major and minor congenital malformations, spontaneous abortion, stillbirths, pregnancy terminations, preterm births, small for-gestational-age births, and any other adverse outcomes, including postnatal growth and development. These outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

Draft Protocol Submission: 01/2025
Final Protocol Submission: 01/2026
Study/Trial Completion: 01/2036
Final Report Submission: 01/2037

4655-5 Retrospective cohort study for pregnancy outcomes:

Conduct an additional pregnancy study that uses a different design from the pregnancy exposure registry (for example a retrospective cohort study using claims or electronic medical record data or a case control study) to

assess major congenital malformations, spontaneous abortions, stillbirths, pregnancy terminations, preterm births, and small for gestational age infants in women exposed to deuruxolitinib during pregnancy compared to an unexposed comparator population(s).

Draft Protocol Submission: 01/2025
Final Protocol Submission: 01/2026
Study/Trial Completion: 01/2036
Final Report Submission: 01/2037

4655-6 Clinical Pharmacology:

Conduct a PK study in subjects who are CYP2C9 Normal Metabolizers (NM), Intermediate Metabolizers (IM), and Poor Metabolizers (PM) in order to characterize the systemic exposure of deuruxolitinib in these subgroups.

Draft Protocol Submission: 10/2024
Final Protocol Submission: 04/2025
Study/Trial Completion: 04/2026
Final Report Submission: 10/2026

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 clinical protocol(s) to your IND 131423 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.
Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as

[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.

21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii) We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4655-7 Establish an in-vitro diagnostic device to guide the use of deuruxolitinib in patients with severe alopecia areata. The device should detect, at a minimum, the presence of the nonfunctional alleles in cytochrome P450 2C9 (CYP2C9) relevant to the US population.

The timetable you submitted on July 19, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 03/2026
Final Protocol Submission: 03/2027
Study/Trial Completion: 03/2030
Final Report Submission: 03/2031

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 131423 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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).

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 official USP monographs. More information on the USP-NF is available on USP's website[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.uspnf.com/

If you have any questions, contact Qianyiren Song, Regulatory Project Manager, at 301-796-2581 or qianyiren.song@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Nikolay P. Nikolov, MD
Director
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- 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/

NIKOLAY P NIKOLOV
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