



NDA 217759/S-005

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENTS**

Pharming Technologies B.V.
Attention: Jennifer Knicley
Senior Director, Global Regulatory Affairs
10 Independence Boulevard, Suite 401
Warren, NJ 07059

Dear Jennifer Knicley:

Please refer to your supplemental new drug application (sNDA) dated and received December 23, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Joenja (leniolisib) tablet.

This Prior Approval sNDA provides for updates to Sections 7 Drug Interactions, 8 Use in Specific Populations, 12 Clinical Pharmacology, and 13 Nonclinical Toxicology of the Prescribing Information (PI) to include results of studies conducted in response to postmarketing requirements (PMR) 4407-1, -3, and -4, listed below. This sNDA also provides labeling changes to Section 5 Warnings and Precautions to include hypersensitivity reactions, including anaphylaxis, and Section 6 Adverse Reactions to include weight increase.

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), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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.

Because none of these criteria apply to your supplemental application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submissions dated April 28, 2023, and November 8, 2024, containing the final reports for the following postmarketing requirements listed in the March 24, 2023 approval letter for NDA 217759.

- 4407-1 Conduct a 6 month carcinogenicity study in transgenic (rasH2) mice.
- 4407-3 Conduct a pre- and post-natal development study in rats.
- 4407-4 Conduct a cocktail drug-drug interaction (DDI) clinical study to assess the effect of leniolisib on the pharmacokinetics of CYP1A2 substrate (caffeine), CYP3A4 substrate (midazolam), BCRP/OATB1B1/1B3 substrate (rosuvastatin), and MATE/OCT2 substrate (metformin).

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>.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there are postmarketing requirements and a postmarketing commitment listed in the March 24, 2023, approval letter that are still open.

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Elaine Sit, Regulatory Project Manager, at (301) 796-5073.

Sincerely,

{See appended electronic signature page}

Robert Lim, MD
Deputy Director for Safety
Division of Pulmonology, Allergy, and Critical Care
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
 - Prescribing Information

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/

ROBERT H LIM
05/28/2025 11:55:29 AM