NDA 215498/S-005

SUPPLEMENT APPROVAL AND FULFILLMENT OF POSTMARKETING COMMITMENTS

Ipsen Biopharmaceuticals, Inc.
Attention: Arden Tesmer, MS Regulatory Affairs
Senior Manager, Global Regulatory Affairs, Rare Diseases Therapeutic Area
One Main Street, 7th Floor
Cambridge, MA, 02142

Dear Arden Tesmer:

Please refer to your supplemental new drug application (sNDA) dated February 20, 2025, received February 20, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bylvay (odevixibat) capsules and oral pellets.

This Prior Approval sNDA provides for changes to the prescribing information to reflect safety and efficacy data from the following studies:

- A4250-008, titled, *An Open-label Extension Study to Evaluate Long-term Efficacy and Safety of A4250 in Children with Progressive Familial Intrahepatic Cholestasis Types 1 and 2 (PEDFIC 2)* to address postmarketing commitment (PMC) 4109-2 cited in the approval letter dated July 20, 2021

- A4250-015, titled, *An Open Label Study to Evaluate the Long-term Safety and Efficacy of Odevixibat (A4250) in Patients with Alagille Syndrome (ASSERT-EXT) to* address postmarketing commitment (PMC) 4444-1 cited in the approval letter dated June 13, 2023

- A4250-022, titled, *A Phase 1, Open Label, Fixed-Sequence, Crossover Study to Evaluate the Interaction of Multiple Dose Odevixibat on the Pharmacokinetics of Single Dose Combined Oral Contraceptive Steroids in Healthy Female Subjects*

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.

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).

FULFILLMENT OF POSTMARKETING COMMITMENTS

We have received your submissions dated September 24 and December 3, 2024, containing the final reports for the following postmarketing commitments listed in the July 20, 2021 and June 13, 2023 approval letters for the original NDA and supplemental NDA 215498/S-003, respectively:

4109-2	Conduct a prospective, long-term, observational study of patients aged 3 months or older with progressive familial intrahepatic cholestasis (PFIC) in order to assess the long-term safety of treatment with BYLVAY (odevixibat) over a 72-week treatment period.
4444-1	Conduct a prospective, long-term, observational study of patients aged 12 months or older with Alagille syndrome in order to assess the long-term safety of treatment with BYLVAY (odevixibat) over a 72-week treatment period.

[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.

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

We remind you that there are postmarketing requirement and postmarketing commitments listed in the July 20, 2021 and June 13, 2023 approval letters that are still open.

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.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

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).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, contact Kirti Patel, Senior Regulatory Project Manager, at Kirti.Patel@fda.hhs.gov or (301) 796-1082.

Sincerely,

{See appended electronic signature page}

Frank A. Anania, MD, FACP, AGAF, FAASLD
Director
Division of Hepatology and Nutrition
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information

outcome data in women taking BYLVAY during pregnancy. Pregnant women exposed to BYLVAY, or their healthcare providers, should report BYLVAY exposure by calling 1-855-463-5127 *[see Use in Specific Populations (8.1)]*.

Manufactured for:

Ipsen Biopharmaceuticals, Inc.
One Main Street
Cambridge, MA 02142

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/

FRANK A ANANIA
12/19/2025 03:27:35 PM