



NDA 215498/S-003

SUPPLEMENT APPROVAL

Albireo AB
c/o Albireo Pharma, Inc.
Attention: Martha J. Carter
Chief Regulatory Officer
53 State Street
19th Floor
Boston, MA 02109

Dear Ms. Carter:

Please refer to your supplemental new drug application (sNDA) dated December 15, 2022, received December 15, 2022, 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 supplemental new drug application provides for expanding the prescribing information to include the treatment of cholestatic pruritus in patients 12 months of age and older with Alagille Syndrome (ALGS).

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).

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

- 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.

The timetable you submitted on June 8, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	07/2023
Final Protocol Submission:	11/2023
Study Completion:	08/2024
Final Report Submission:	02/2025

- 4444-2 Conduct a 5-year registry-based study to collect data on the health of Alagille syndrome patients chronically treated with Bylvay (odevixibat).

Report yearly on the following safety endpoints:

- Incidence of biliary diversion surgery, liver transplantation, and all-cause mortality
- Assessment of growth and development

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>.

- Incidence of fat-soluble vitamin deficiencies and their long-term sequelae

The timetable you submitted on June 8, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	02/2024
Final Protocol Submission:	08/2024
Interim/Other:	11/2025
	11/2026
	11/2027
	11/2028
Study Completion:	11/2029
Final Report Submission:	05/2030

Submit clinical protocols to your IND 145988 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 enrolled 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*.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

[NOTE: The use of the term “new safety-related information” below

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>

includes new safety information (NSI) as described in section 505-1(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) (21 U.S.C. 355-1(b)) and other safety-related information unrelated to section 505(o)(4) of the FDCA.]

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).

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

Sincerely,

{See appended electronic signature page}

Frank A. Anania, MD, FACP, AGAF, FAASLD
(Acting) 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

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
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