NDA 210365/S-023

SUPPLEMENT APPROVAL

Jazz Pharmaceuticals Research UK Limited
c/o Jazz Pharmaceuticals, Inc.
Attention: Kelly Gough, PharmD, MS
Senior Manager, Global Regulatory Affairs
3170 Porter Drive
Palo Alto, CA 94304

Dear Dr. Gough:

Refer to your supplemental new drug application (sNDA) and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA Number/Supplement Number	Product Name	Date of Submission	Date of Receipt
NDA 210365/S-023	Epidiolex (cannabidiol) oral solution	November 15, 2024	November 15, 2024

This Prior Approval sNDA provides for updates to the clinical pharmacology labeling information in Section 7 Drug Interactions and Section 12.3 Pharmacokinetics of the Prescribing Information (PI).

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, Instructions for Use, and Medication Guide), with the addition of

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

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 REQUIREMENTS

We refer to your sNDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Epidiolex (cannabidiol) oral solution.

We have received your submissions dated October 16, 2024, and November 6, 2024, containing the final reports for the following postmarketing requirements listed in the June 25, 2018, approval letter.

3429-10 A drug-drug interaction trial to evaluate the effects of Epidiolex on the pharmacokinetics of a sensitive CYP2B6 substrate in healthy volunteers. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled "Clinical Drug Interaction Studies —Study Design, Data Analysis, and Clinical Implications."

3429-11 A drug-drug interaction trial to evaluate the effects of Epidiolex on the pharmacokinetics of a sensitive CYP2C9 substrate in healthy volunteers. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled "Clinical Drug Interaction Studies —Study Design, Data Analysis, and Clinical Implications."

3429-15 A drug-drug interaction trial to evaluate the effects of Epidiolex on the pharmacokinetics of a sensitive UGT1A9 substrate in healthy volunteers. Design and conduct the trial in accordance with the FDA Guidance for

[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.

Industry entitled “Clinical Drug Interaction Studies —Study Design, Data Analysis, and Clinical Implications.”

3429-16 A drug-drug interaction trial to evaluate the effects of Epidiolex on the pharmacokinetics of a sensitive UGTB7 substrate in healthy volunteers. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled “Clinical Drug Interaction Studies —Study Design, Data Analysis, and Clinical Implications.”

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

We remind you that there are postmarketing requirements listed in the June 25, 2018, approval letter 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

[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

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 Kelly Ross, Regulatory Health Project Manager via email at Kelly.Ross@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Emily Freilich, MD
Director
Division of Neurology 1
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

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/

EMILY R FREILICH
06/26/2025 09:42:07 AM
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