

NDA 213702/S-010

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT**

Jazz Pharmaceuticals Ireland, Ltd.
Attention: Nina Moore, MS
Associate Director, Regulatory Affairs
2005 Market Street, Suite 2100
Philadelphia, PA 19103

Dear Nina Moore:

Please refer to your supplemental new drug application (sNDA) dated October 31, 2024, received October 31, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zepzelca (lurbinectedin) injection.

This Prior Approval sNDA provides for the following changes to the US Prescribing Information:

- Updates to DOSAGE AND ADMINISTRATION section (revision to subsection 2.3 *Dosage Modifications for Use with Strong and Moderate CYP3A Inhibitors*, addition of subsection 2.4 *Dosage Modifications for Patients with Severe and Moderate Hepatic Impairment*).
- Updates to DRUG INTERACTIONS section (revised subsection 7.1 *Effect of Other Drugs on Zepzelca*).
- Updates to USE IN SPECIFIC POPULATIONS section (revision to subsection 8.6 *Hepatic Impairment*).
- Updates to CLINICAL PHARMACOLOGY section (revision to subsection 12.3 *Pharmacokinetics*).

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, Patient Package Insert), 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(I)(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 application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submission dated October 31, 2024, containing the final reports for the following postmarketing requirements listed in the June 15, 2020, approval letter.

- 3831-2 Submit the final report of a physiologically-based pharmacokinetic modeling with the results from the drug interaction trial with a strong CYP3A4 inhibitor, to assess the effect of concomitant administration of a moderate CYP3A inhibitor on lurbinedin exposure, that will determine the magnitude of increase in the exposure of lurbinedin and appropriate

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>.

dosage recommendation for patients receiving concomitant medications that are moderate CYP3A inhibitors, that may inform labeling. Design and conduct the trial in accordance with the FDA Guidance for Industry titled; *“Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications.”*

- 3831-3 Submit the analysis and datasets with the final report from a hepatic impairment clinical trial to evaluate the pharmacokinetics and safety of lurbinectedin in patients with mild, moderate, or severe hepatic impairment and determine the magnitude of increase exposure and appropriate dosage recommendations, that may inform product labeling. Design and conduct the trial in accordance with the FDA Guidance for Industry titled: *“Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling.”*

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

We remind you that accelerated approval PMR 3831-7 and PMR 3831-8 listed in the October 24, 2022, postapproval postmarketing requirement letter are still open. Pursuant to 21 CFR 314.510 (Subpart H), continued approval of the drug is contingent upon verification and description of clinical benefit and completion of the clinical trial for PMR 3831-7 and PMR 3831-8.

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 Jeffrey Ingalls, Senior Regulatory Health Project Manager, at 301-796-4444 or via email at Jeffrey.Ingalls@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Erin Larkins, MD
Director (Acting)
Division of Oncology 2
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

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/

PAZ J VELLANKI

04/30/2025 03:50:42 PM

I am the Acting Supervisory Associate Director for the Division of Oncology 2 (DO2), signing on behalf of Dr. Erin Larkins, the Acting Division Director of DO2.