



NDA 213702/S-004

## **SUPPLEMENT APPROVAL**

Jazz Pharmaceuticals Ireland Limited  
Attention: Elysia Tusavitz  
Senior Director, Global Regulatory Lead  
One Commerce Square  
2005 Market Street, Suite 2100  
Philadelphia, PA 19103

Dear Tusavitz:

Please refer to your supplemental new drug application (sNDA) dated and received October 1, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zepzelca (lurbinectedin) injection.

This “Changes Being Effected” sNDA provides for the following changes to the US Prescribing Information:

- Update to subsection 2.2 (Dosage Modifications for Adverse Reactions)
- Updates to subsection 2.4 (Preparation, Administration and Storage) to include information about the incompatibility of reconstituted Zepzelca with Nylon membrane filters when Normal Saline Solution (NSS) is used as the IV diluent
- Updates to section 5 (WARNINGS AND PRECAUTIONS) to include subsections 5.3 (Extravasation Resulting in Tissue Necrosis) and 5.4 (Rhabdomyolysis)
- Addition of extravasation resulting in tissue necrosis, rhabdomyolysis, and tumor lysis syndrome to the newly created section 6.2 (Postmarketing Experience)
- Updates to section 17 (PATIENT COUNSELING INFORMATION)
- Updates to the Patient Package Insert to reflect changes made to the Prescribing Information
- Updates to the vial and carton labels to change the trademark symbol from “™” to “®”, and to update the barcode to a vertically stacked style on the vial label to improve machine readability.

### **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.

## **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

## **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](http://FDA.gov).<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and 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*.<sup>2</sup>

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).

## **CARTON AND CONTAINER LABELING**

We acknowledge your March 30, 2022, submission containing final printed carton and container labeling.

## **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

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

<sup>2</sup> 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>.

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.

### **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 Kwadwo Korsah, Pharm.D., Regulatory Health Project Manager, at (301) 796-6630.

Sincerely,

*{See appended electronic signature page}*

Martha Donoghue, M.D.  
Deputy Director  
Division of Oncology 2  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### **ENCLOSURE(S):**

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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**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.**  
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/s/  
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MARTHA B DONOGHUE  
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