



NDA 208700/S-10

SUPPLEMENT APPROVAL

Advanced Accelerator Applications USA, Inc.
Attention: Christopher Jordan, MSHS, RAC
Americas Head, Regulatory Affairs
57 East Willow Street
Millburn, NJ 07041

Dear Mr. Jordan:¹

Please refer to your supplemental new drug application (sNDA) dated and received August 2, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LUTATHERA (lutetium Lu 177 dotatate), 370 MBq/mL solution for infusion.

This Prior Approval supplemental new drug application provides for

- Revisions to Dosage and Administration section (subsections 2.3, 2.4, 2.5, and 2.6) to revise information regarding anti-emetics and provide additional details regarding amino acid solutions; provide additional details regarding LUTATHERA dose modifications; and add the use of infusion pumps as an administration method in case of dose reduction;
- revisions to Warnings and Precautions section (subsections 5.1-5.3) to add clarification to the risks from radiation exposure; revise incidence rate of secondary myelodysplastic syndrome in the ERASMUS study;
- revisions to Adverse Reactions section (subsection 6.1) with corrections to the NETTER-1 Adverse Events and laboratory abnormalities tables (Table 4 and 5), to correct for rounding errors identified;
- revisions to Drug Interactions section (subsection 7.2) to include potential for drug interactions with repeated administration of corticosteroids;
- revisions to Clinical Studies section (subsections 14.1 and 14.2); make corrections to NETTER-1 efficacy table based on identified inconsistencies; and, add proposed revisions to the description and data summary of the ERASMUS study;
- revisions to How Supplied/Storage and Handling section to add “do not freeze” and instructions to store Lutathera in original package; and,

- revisions to Highlights of Prescribing Information and Patient Counseling Information in accordance with the proposed changes.

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

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for

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>.

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.

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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety 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).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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>

If you have any questions, call Nataliya Fesenko, Pharm.D., Regulatory Health Project Manager, at (240) 402-6376.

Sincerely,

{See appended electronic signature page}

Harpreet Singh, M.D.
Director
Division of Oncology 2
Office of Oncologic Diseases
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/

B HARPREET SINGH
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