BLA 761102/S-003

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
COMMITMENTS

Servier Pharmaceuticals LLC
Attention: Denisa Weinstein, MSc, RAC
Director, Global Regulatory Affairs
200 Pier Four Boulevard
Boston, MA 02210

Dear Ms. Weinstein:

Please refer to your supplemental biologics license application (sBLA), dated December 26, 2019, received December 26, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for ASPARLAS (calaspargase pegol-mknl) intravenous injection.

This Prior Approval supplemental biologics application provides for the following revisions to the United States Prescribing Information: updates to Section 6.2 based on the results from postmarketing commitment (PMC) 3550-2 and updates based on the Pregnancy & Lactation Labeling Rule (PLLR).

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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

[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 via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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(s) 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 COMMITMENTS

The submissions dated January 8, 2019 and December 26, 2019, also contained the final report for the following postmarketing commitments listed in the December 20, 2018, approval letter for BLA 761102.

PMC 3550-1 To develop and validate screening and confirmatory assays for the evaluation of anti calaspargase antibodies. Develop an assay to determine whether any anti-calaspargase antibodies are anti-PEG. The Sponsor will submit final reports in accordance with 21 CFR 601.12.

PMC 3550-2 To reanalyze the remaining immunogenicity samples from Study DFCI 11-001 to determine the incidence of anti-calaspargase pegol and anti-PEG antibodies using the ADA validated assays from PMC 3550-1. For any newly confirmed positive samples, the neutralizing capacity of the anti-calaspargase antibodies will be evaluated with

[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.

the validated integrated binding ADA/serum asparaginase activity assays. The Sponsor will submit the final study report in accordance with 21 CFR 601.12.

We have reviewed your submissions and conclude that the above commitments are fulfilled.

We remind you that there are postmarketing commitments listed in the December 20, 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]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, contact Rosa Lee-Alonzo, Senior Regulatory Health Project Manager, at Rosa.Lee-Alonzo@fda.hhs.gov or (301) 348-3004.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Acting Director
Division of Hematologic Malignancies I
Office of Oncologic Diseases
Center for Drug Evaluation and Research

[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

ENCLOSURE:

- Content of Labeling
    - Prescribing Information

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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/

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