BLA 125320/S-203

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENT/COMMITMENT

Amgen, Incorporated
Attention: Wade M. Tokushige
Manager, Regulatory Affairs; Global Regulatory Affairs and Safety
One Amgen Center Drive; Mail Stop: 27-3-A
Thousand Oaks, CA 91320-1799

Dear Mr. Tokushige:

Please refer to your supplemental biologics license application (sBLA), dated August 9, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for XGEVA (denosumab) injection for subcutaneous use.

This Prior Approval supplemental biologics application provides for updates to the Prescribing Information (PI) based on the results in the final study report, Study 20062004.

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, 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 Package Insert) 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 REQUIREMENT/COMMITMENT

We have received your submission dated August 9, 2019, containing the final report for the following postmarketing requirement and commitment listed in the June 13, 2013, approval letter for BLA 125320/S-094.

2799-1 Submit a final report of follow-up safety data of Xgeva (denosumab) in patients with giant cell tumor of bone enrolled in the ongoing single arm trial through November 2012 for a minimum of five years or until death or lost to follow-up, whichever comes first. Comprehensively collect information regarding survival status, disease progression, serious adverse events, and adverse events of special interest including osteonecrosis of the jaw, pregnancy-related complications, atypical fractures, malignant transformation of giant cell tumor of bone, and secondary malignancies. Perform descriptive analyses of these safety

[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.

data, including a subset analysis comparing the long-term safety of denosumab in adolescent and adult patients.

2799-2 Submit the final report including primary datasets, derived datasets, and analysis programs used to generate the safety and efficacy results for the ongoing single arm multicenter trial of denosumab in patients with giant cell tumor of bone. Include an analysis of radiographic response as determined by the local investigator in evaluable patients who received at least one dose of denosumab and underwent at least one postbaseline Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) tumor assessment during the trial. The primary analysis should be conducted after patients enrolled through November 2012 have had the opportunity to complete 12 months of treatment.

We have reviewed your submission and conclude that the above requirement and commitment was fulfilled.

This completes your postmarketing requirement and all of your postmarketing commitments acknowledged in our June 13, 2013, approval letter.

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).

[3] For the most recent version of a guidance, check the FDA guidance web page athttps://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 Norma Griffin, Lead Regulatory Health Project Manager, at 301-796-4255.

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:

- 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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