



BLA 125320/S-185

SUPPLEMENT APPROVAL

Amgen, Inc.
Attention: Vandana Pathak, RAC
Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop 28-2-D
Thousand Oaks, CA 91320-1799

Dear Ms. Pathak:

Please refer to your Supplemental Biologics License Application (sBLA), dated July 21, 2017, received July 21, 2017, submitted under section 351(a) of the Public Health Service Act for Xgeva® (denosumab) Injection, 70mg/mL.

This Prior Approval supplemental biologics application adds the following to Warnings & Precautions section of labeling; Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation, changes to Patient Counseling, and minor editorial edits.

APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, 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. Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

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 MS Word format that includes the changes approved in this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

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

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 3333-1 Perform a retrospective analysis in Metastatic-Related and Non Metastatic-Related Fractures in clinical trials 20050136, 20050244 and 20050103, leading to Xgeva approval in patients with bone metastases from solid tumors, during the active treatment period, and characterize the non-metastatic fractures. Submit the final report with labeling.

The timetable you submitted on 1/24/2018, states that you will conduct this study according to the following schedule:

Draft protocol Submission:	05/2018
Final Protocol Submission:	12/2018
Final Report Submission:	06/2019

Submit clinical protocols to your IND 9838 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol,**” “**Postmarketing Commitment Final Report,**” or “**Postmarketing Commitment Correspondence.**”

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, call Christina Marshall, Safety Regulatory Project Manager, at (301) 796-3099.

Sincerely,

{See appended electronic signature page}

Katherine Fedenko, MS, CRNP
Deputy Director, Safety
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KATHERINE M FEDENKO
01/24/2018