

BLA 125320/S-213

SUPPLEMENT APPROVAL

Amgen Inc.
Attention: Dohan Weeraratne, MS
Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop: 38-4D
Thousand Oaks, CA 91320-1799

Dear Dohan Weeraratne:

Please refer to your supplemental biologics license application (sBLA), dated and received May 5, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Prolia (denosumab) injection.

This supplemental application provides for the following changes:

- Additions to Section 8.4 (Pediatric Use) of the Prescribing Information (PI) based on terminated studies 20130173¹ and 20170534.²
- Updates to the Immunogenicity section of the PI, including moving the text from Section 6.3 to Section 12.6 as per FDA's draft guidance for industry *Immunogenicity Information in Human Prescription Therapeutic Protein and Select Drug Product Labeling*.³
- Additional editorial changes were made to align with current labeling practices.

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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- The revision date in the PI was updated to reflect the date of approval of this supplement.

¹ *Prospective, Multicenter, Single-arm Study to Evaluate Efficacy, Safety, and Pharmacokinetics of Denosumab in Children With Osteogenesis Imperfecta*

² *Multicenter, Single-arm Open-label Extension Study to Assess Long-term Safety and Efficacy of Current or Prior Treatment With Denosumab in Children/Young Adults With Osteogenesis Imperfecta*

³ 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>.

WAIVER OF HIGHLIGHTS 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, 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,⁴ that is identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) 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 *SPL Standard for Content of Labeling Technical Qs and As*.⁵

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 supplemental application, you are exempt from this requirement.

⁴ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

⁵ 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>.

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*.⁶

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.⁷ Information and Instructions for completing the form can be found at FDA.gov.⁸

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).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, call Elisabeth Hanan, Chief, Project Management Staff, at 240-402-0350.

Sincerely,

{See appended electronic signature page}

Theresa E. Kehoe, M.D.
Director
Division of General Endocrinology
Office of Cardiology, Hematology, Endocrinology,
and Nephrology
Center for Drug Evaluation and Research

⁶ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁷ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁸ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide (version approved January 19, 2024)

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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