BLA 761457

BLA APPROVAL

Amneal Pharmaceuticals, LLC
Attention: Ravi Harapanhalli, PhD
Senior Vice President, Global Regulatory Affairs
21 Colonial Drive
Piscataway, New Jersey 08854

Dear Dr. Harapanhalli:

Please refer to your biologics license application (BLA) received September 27, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Oziltus (denosumab-mobz) injection, for subcutaneous use.

We acknowledge receipt of your resubmission dated December 30, 2024, which was submitted in response to our November 22, 2024, refuse-to-file letter.

This BLA seeks licensure of:

> Oziltus (denosumab-mobz) 120 mg/1.7 mL (70 mg/mL) injection for subcutaneous use in a single-dose vial as biosimilar to and interchangeable with US-Xgeva (denosumab) 120 mg/1.7 mL (70 mg/mL) injection for subcutaneous use in a single-dose vial.

LICENSING

We have approved your BLA for Oziltus (denosumab-mobz) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Oziltus under your existing Department of Health and Human Services U.S. License No. 2241.

Oziltus is indicated for:

- Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors.
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture denosumab-mobz drug substance (b) (4) The final formulated drug product will be manufactured, filled, labeled, and packaged at Universal Farma S.L., Guadalajara, Spain. You may label your product with the proprietary name, Oziltus, and market it in 1.7 mL solution for injection in a single-dose vial containing 120 mg of denosumab-mobz.

DATING PERIOD

The dating period for Oziltus shall be 36 months from the date of manufacture when stored at 5 ± 3°C with storage at room temperature (up to 25°C) once removed from the refrigerator for a maximum of 14 days in the original carton to protect from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Oziltus (denosumab-mobz) to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Oziltus, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information).

[1] See 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 (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761457**." Approval of this submission by FDA is not required before the labeling is used.

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.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4949-1 Finalization of acceptance criteria for secondary reference standards (SRS).

The timetable you submitted on August 20, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2029

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

4949-2 Winter-time shipping validation study for MB09 drug product (DP) in pre-filled syringes (PFS) and vials will be performed in the upcoming winter.

The timetable you submitted on August 20, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 04/2026

4949-3 To perform additional low endotoxin recovery (LER) study on two more batches of MB09 drug product.

The timetable you submitted on December 8, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2026

4949-4 To perform the repeated capping validation study for drug product vials using appropriate controls.

The timetable you submitted on December 8, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2026

Submit clinical protocols to your IND 153335 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/subjects 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**."

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 601.12(f)(4)]. 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

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

[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, contact Rashida Redd, Senior Regulatory Project Manager, at 301-796-5489 or Rashida.Redd@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Christy Osgood, MD
Supervisory Associate Director
Division of Oncology 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- Carton and Container Labeling

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/

CHRISTY L OSGOOD
12/19/2025 05:06:22 PM