

- POLICY:** Bone Modifiers – Denosumab Products (Xgeva) Utilization Management Medical Policy
- Bilprevda® (denosumab-nxxp) subcutaneous injection – Shanghai Henlius Biotech/Organon)
 - Bomynta® (denosumab-bnht subcutaneous injection – Fresenius)
 - Xbryk™ (denosumab-dssb subcutaneous injection – Samsung Bioepis)

EFFECTIVE DATE: 1/1/2026

LAST REVISIONS DATE: 09/15/2025

COVERAGE CRITERIA FOR: All Aspirus Health Plans

OVERVIEW

Denosumab products (Xgeva, biosimilars) are receptor activator of nuclear factor kappa-B ligand inhibitors indicated for the following uses:¹⁻³

- **Giant cell tumor of bone**, treatment of adults and skeletally mature adolescents with disease that is unresectable or where surgical resection is likely to result in severe morbidity.
- **Hypercalcemia of malignancy**, treatment of, that is refractory to bisphosphonate therapy.
- **Skeletal-related events**, prevention, in patients with multiple myeloma and in those with bone metastases from solid tumors.

Another injectable formulation of denosumab subcutaneous injection is available, Prolia® (biosimilars) but it is not included in this policy.⁴

Guidelines

Several guidelines address denosumab products (Xgeva, biosimilars).

- **Cancer:** Various guidelines from the National Comprehensive Cancer Network (NCCN) [e.g., breast cancer, prostate cancer, lung cancer, multiple myeloma] recommend denosumab products (Xgeva, biosimilars), for the prevention of skeletal related adverse events.⁵⁻⁹
- **Hypercalcemia of Malignancy:** Guidelines from the Endocrine Society for the treatment of hypercalcemia of malignancy in adults (2023) have several recommendations.¹⁰ In adults with hypercalcemia of malignancy, treatment with denosumab products (Xgeva, biosimilars) over an intravenous bisphosphonate is recommended.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of denosumab products (Xgeva, biosimilars). Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with denosumab products (Xgeva, biosimilars) as well as the monitoring required for adverse events and

long-term efficacy, approval requires denosumab products (Xgeva, biosimilars) to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of denosumab products (Xgeva, biosimilars) are recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Xgeva, Osenvelt and Wyost

Non-Preferred Products(s): Bilprevida, Bomynta and Xbryk

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any one of the items listed below (A, B, C, D or E). Chart notes documenting the issue must be provided at time of request:

- A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR
- B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR
- C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR
- D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR
- E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

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- 1. Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

Note: Some examples of cancer in this clinical scenario include breast cancer, prostate cancer, and non-small cell lung cancer.

A) Patient is ≥ 18 years of age; AND

B) Patient has bone metastases; AND

C) Patient with prostate cancer must have castration-resistant prostate cancer; AND

Note: This includes patients who have progressed after treatment with hormonal therapy or after surgical castration (e.g., bilateral orchiectomy). Examples of hormonal therapies for prostate cancer include Lupron Depot (leuprolide for depot suspension), Eligard (leuprolide acetate for injectable suspension), Trelstar (triptorelin pamoate for injectable suspension), or Zoladex (goserelin implant).

D) Medication is prescribed by or in consultation with a hematologist or an oncologist.

Dosing. Approve 120 mg administered as a subcutaneous (SC) injection up to once every 4 weeks.

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- 2. Giant Cell Tumor of Bone.** Approve for 1 year.

Dosing. Approve 120 mg subcutaneous (SC) up to once every 4 weeks with loading doses on Day 8 and Day 15 of Month 1.

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- 3. Hypercalcemia of Malignancy.** Approve for 2 months if the patient meets BOTH of the following (A and B):

A) Patient has a current malignancy; AND

B) Patient has an albumin-corrected calcium (cCa) ≥ 11.5 mg/dL.

Dosing. Approve 120 mg subcutaneous (SC) up to once every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.

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- 4. Multiple Myeloma – Prevention of Skeletal-Related Events.** Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient is ≥ 18 years of age; AND

B) The medication is prescribed by or in consultation with a hematologist or an oncologist.

Dosing. Approve 120 mg administered as a subcutaneous (SC) injection up to once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of denosumab products (Xgeva, biosimilars) are not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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2. Wyost® subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; March 2024.
3. Osenvelt® subcutaneous injection [prescribing information]. Jersey City, NJ: Celltrion; February 2025.
4. Bomynta® subcutaneous injection [prescribing information]. Lake Zurich, IL: Fresenius Kabi; March 2025.
5. Bilpreveda® subcutaneous injection [prescribing information]. Jersey City, NJ: Shanghai Henlius Biotech/Organon; August 2025.
6. Prolia® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2024.
7. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – December 4, 2024). © 2024 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on March 14, 2025.
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9. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 1.2025 – September 17, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 14, 2025.
10. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 14, 2025.
11. Ghada El-Hajj Fuleihan, Clines GA, Hu MI, et al. Treatment of hypercalcemia of malignancy in adults: an Endocrine Society Clinical Practice guideline. *J Clin Endocrinol Metab.* 2023;108(3):507-528.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Aspirus Policy	Policy reviewed and approved by Aspirus P&T committee as a new policy for 1/1/2026.	09/15/2025