Drug Coverage Policy

Effective Date.....6/15/2025
Coverage Policy Number.....IP0332
Policy Title..... Xgeva

Bone Modifiers – Xgeva

- Xgeva® (denosumab subcutaneous injection – Amgen)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Xgeva, a receptor activator of nuclear factor kappa-B ligand inhibitor, is indicated for the following uses:[1]

- **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 of, in patients with multiple myeloma and in those with bone metastases from solid tumors.

Another injectable formulation of denosumab is available, Prolia® (denosumab subcutaneous injection), but it is not included in this policy.[2]

Guidelines
Several guidelines address Xgeva.

- **Cancer:** Various guidelines from the National Comprehensive Cancer Network (e.g., breast cancer, prostate cancer, lung cancer, multiple myeloma) recommend Xgeva for the prevention of skeletal related adverse events.[3-6]
- **Hypercalcemia of Malignancy:** Guidelines from the Endocrine Society for the treatment of hypercalcemia of malignancy in adults (2023) have several recommendations.[7] In adults with hypercalcemia of malignancy, treatment with Xgeva over an intravenous bisphosphonate is recommended.

Medical Necessity Criteria

Policy Statement
Prior Authorization is recommended for prescription benefit coverage of Xgeva. 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 Xgeva as well as the monitoring required for adverse events and long-term efficacy, approval requires Xgeva to be prescribed by a physician who has consulted with or who specializes in the condition.

Xgeva is considered medically necessary when ONE of the following is met (1, 2, 3, or 4)

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, D, and E):

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.

E) Preferred product criteria are met for the product(s) as listed in the below table(s) [Employer Plans, Individual and Family Plans]

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 ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

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

C) Preferred product criteria are met for the product(s) as listed in the below table(s) [Employer Plans, Individual and Family Plans]

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

Employer Plans:

Product	Criteria
Xgeva	**1. Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events.** Approve if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i, ii, iii, or iv): **i.** Patient has had failure, contraindication, or intolerance to zoledronic acid injection (Zometa); OR **ii.** Patient has renal impairment (creatinine clearance < 30 mL/min); OR **iii.** Patient has a previous history of using Xgeva; OR **iv.** Patient has prostate cancer with bone metastases. **2. Giant Cell Tumor of Bone.** Approve if the patient meets the above medical necessity criteria.

Product	Criteria
	3. Hypercalcemia of Malignancy. Approve if the patient meets the above medical necessity criteria. **4. Multiple Myeloma – Prevention of Skeletal-Related Events.** Approve if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i, ii, or iii): **i.** Patient has had failure, contraindication, or intolerance to zoledronic acid injection (Zometa); OR **ii.** Patient has renal impairment (creatinine clearance < 30 mL/min); OR **iii.** Patient has a previous history of using Xgeva.

Individual and Family Plans:

Product	Criteria
Xgeva	**1. Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events.** Approve if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i, ii, iii, or iv): **i.** Patient has had failure, contraindication, or intolerance to zoledronic acid injection (Zometa); OR **ii.** Patient has renal impairment (creatinine clearance < 30 mL/min); OR **iii.** Patient has a previous history of using Xgeva; OR **iv.** Patient has prostate cancer with bone metastases. **2. Giant Cell Tumor of Bone.** Approve if the patient meets the above medical necessity criteria. **3. Hypercalcemia of Malignancy.** Approve if the patient meets the above medical necessity criteria. **4. Multiple Myeloma – Prevention of Skeletal-Related Events.** Approve if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i, ii, or iii): **i.** Patient has had failure, contraindication, or intolerance to zoledronic acid injection (Zometa); OR **ii.** Patient has renal impairment (creatinine clearance < 30 mL/min); OR **iii.** Patient has a previous history of using Xgeva.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0897	Injection, denosumab, 1 mg

References

1. Xgeva® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; June 2020.
2. Prolia® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2024.
3. 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.
4. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – March 5, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 14, 2025.
5. 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.
6. 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.
7. 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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Updated the policy title. **Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events:** Relocated zoledronic acid requirement and the exceptions to a preferred product table and added an additional exception for "Patient has renal impairment (creatinine clearance < 30 mL/min)"; Updated statement "Is currently receiving denosumab (Xgeva) and has demonstrated a beneficial clinical response" to now be "Patient has a previous history of using Xgeva" **Giant Cell Tumor of Bone:** Removed specialist prescriber requirement	6/15/2024

	Hypercalcemia of Malignancy: Updated authorization approval duration to 2 months, was previously 12 months; Removed specialist prescriber requirement **Multiple Myeloma** – **Prevention of Skeletal-Related Events:** Relocated zoledronic acid requirement and the exceptions to a preferred product table and added an additional exception for "Patient has renal impairment (creatinine clearance < 30 mL/min)"; Updated statement "Is currently receiving denosumab (Xgeva) and has demonstrated a beneficial clinical response" to now be "Patient has a previous history of using Xgeva".	
Annual Revision	No criteria changes.	6/15/2025

The policy effective date is in force until updated or retired.