Effective Date **8/15/2023**
Next Review Date… **8/15/2024**
Coverage Policy Number **IP0332**

Denosumab (Xgeva®)

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Related Coverage Resources

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. 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

This policy supports medical necessity review for denosumab (**Xgeva®**).

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

Initial Approval Criteria

Denosumab (Xgeva) is considered medically necessary for the prevention of skeletal-related events in individuals with bone metastases from solid tumors when the individual meets ALL of the following criteria:

1. Age 18 years or older
2. Has bone metastases
3. Individuals with prostate cancer must have castration-resistant prostate cancer (CRPC)
4. Documentation of **ONE** of the following:

a. Failure, contraindication, or intolerance to zoledronic acid [only applies to Employer and Individual and Family Plans]
b. Is currently receiving denosumab (Xgeva) and has demonstrated a beneficial clinical response
c. Individual has prostate cancer with bone metastases

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

Dosing. The recommended dose is 120 mg administered as a subcutaneous (SC) injection up to once every 4 weeks

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Denosumab (Xgeva) is considered medically necessary for the treatment of giant cell tumor of bone when the medication is prescribed by or in consultation with a hematologist or an oncologist

Dosing. The recommended dose is 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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Denosumab (Xgeva) is considered medically necessary for the treatment of hypercalcemia of malignancy when the individual meets ALL of the following criteria:

1. Has a current malignancy
2. Has an albumin-corrected calcium (cCa) greater than or equal to 11.5 mg/dL
3. Medication is prescribed by or in consultation with a hematologist or an oncologist

Dosing. The recommended dose is 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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Denosumab (Xgeva) is considered medically necessary for the prevention of skeletal-related events in individuals with multiple myeloma when the individual meets ALL of the following criteria:

1. Age 18 years or older
2. Documentation of **ONE** of the following:
   a. Failure, contraindication, or intolerance to zoledronic acid [only applies to Employer and Individual and Family Plans]
   b. Is currently receiving denosumab (Xgeva) and has demonstrated a beneficial clinical response
3. Medication is prescribed by or in consultation with a hematologist or an oncologist

Dosing. The recommended dose is 120 mg administered as a subcutaneous (SC) injection up to once every 4 weeks

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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.

Continuation of Therapy Criteria

Continuation of denosumab (Xgeva) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

Conditions Not Covered

Denosumab (Xgeva) is considered experimental, investigational or unproven for **ANY** other use.

Coding Information

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

Background

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.
- **Prostate Cancer:** National Comprehensive Cancer Network (NCCN) guidelines for prostate cancer (version 1.2023 – September 16, 2022) state that if bone antiresorptive therapy is recommended, Xgeva is preferred (category 1) over zoledronic acid (Zometa) [category 2A] if bone metastases are present.[3]

References

1. Xgeva® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; June 2020.
2. Prolia® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; January 2023.
3. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – September 16, 2022). © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 23, 2023.
4. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – February 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 23, 2023.

5. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2023 – December 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 23, 2023.
6. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – February 17, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 23, 2023.
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.