Effective Date **2/1/2022**
Next Review Date… **2/1/2023**
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®).

Medical Necessity Criteria

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

1. **Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events.** Individual meets **ALL** of the following criteria (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. Individual is ≥ 18 years of age
   B. Individual has bone metastases
   C. Individuals with prostate cancer must have received at least **ONE** hormonal therapy (for example Lupron Depot® (leuprolide for depot suspension), Eligard® (leuprolide acetate for injectable

suspension), Trelstar® (triptorelin pamoate for injectable suspension), or Zoladex® (goserelin implant)

D. Documentation of **ONE** of the following (i, ii, or iii):
   i. Individual has had an inadequate response to zoledronic acid
   ii. Individual has a contraindication per FDA label, significant intolerance, or is not a candidate* for zoledronic acid.
   iii. Individual has a history of beneficial clinical response with denosumab (Xgeva)

**Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], or other attributes/conditions or is unable to administer and requires this dosage formulation*

E. The medication is being prescribed by, or in consultation with, a hematologist or an oncologist

2. **Giant Cell Tumor of Bone - Treatment.** Individual meets the following criteria:
   A. The medication is prescribed by, or in consultation with, a hematologist or an oncologist

3. **Hypercalcemia of Malignancy.** Individual meets **ALL** of the following criteria (A, B, C, and D):
   A. Individual has a current malignancy
   B. Individual meets **ONE** of the following (i or ii)
      i. Documentation of **ONE** of the following (a or b):
         a. Individual has had an inadequate response to at least **ONE** intravenous bisphosphonate therapy [for example, zoledronic acid injection (Zometa) or pamidronate injection (Aredia)]
         b. Individual has a contraindication per FDA label, significant intolerance, or is not a candidate* for intravenous bisphosphonate therapy

            **Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], or other attributes/conditions or is unable to administer and requires this dosage formulation*

      ii. Individual has an estimated calculated creatinine clearance (CrCl) < 30 mL/min

   C. Individual has an albumin-corrected calcium (cCa) ≥ 11.5 mg/dL
   D. The medication is prescribed by, or in consultation with, a hematologist or an oncologist

4. **Multiple Myeloma – Prevention of Skeletal-Related Events.** Individual meets **ALL** of the following criteria (A, B, and C):
   A. Individual is ≥ 18 years of age
   B. Documentation of **ONE** of the following (i, ii, or iii):
      i. Individual has had an inadequate response to zoledronic acid
      ii. Individual has a contraindication per FDA label, significant intolerance, or is not a candidate* for zoledronic acid.

         **Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], or other attributes/conditions or is unable to administer and requires this dosage formulation*

      iii. Individual has a history of beneficial clinical response with denosumab (Xgeva)

   C. The medication is prescribed by, or in consultation with, a hematologist or an oncologist

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.

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

Reauthorization Criteria

Denosumab (Xgeva) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

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 / Billing 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

Background

OVERVIEW
Xgeva, a receptor activator of nuclear factor kappa-B ligand (RANKL) 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 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.

Dosing Information and Availability
Xgeva is intended for subcutaneous route only and should not be administered intravenously, intramuscularly, or intradermally.

- Multiple Myeloma and Bone Metastasis from Solid Tumors
  The recommended dose of Xgeva is 120 mg administered as a subcutaneous injection every 4 weeks. Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia.

- Giant Cell Tumor of Bone

The recommended dose of Xgeva is 120 mg administered every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen. Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia.

- Hypercalcemia of Malignancy
  The recommended dose of Xgeva is 120 mg administered every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen.

Xgeva is supplied in a single-use vial as 120 mg/1.7 mL (70 mg/mL) (1 vial per carton).[1]

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

References

1. Xgeva® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; June 2020.
2. Prolia® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; March 2020.