Effective Date: 10/2012
Last P&T Approval/Version: 01/26/2022
Next Review Due By: 01/2023
Policy Number: C8849-A

Xgeva (denosumab)

PRODUCTS AFFECTED

Xgeva (denosumab

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Bone metastases from solid tumors, Giant cell tumor of bone, Hypercalcemia of malignancy, Multiple myeloma

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. HYPERCALCEMIA OF MALIGNANCY:
1. Documented diagnosis of hypercalcemia of malignancy as defined as albumin-correctedserum calcium level greater than 12.5 mg/dL (3.1 mmol/L)dated within the past 30 daysAND
2. Prescriber attestation of a trial and failure or labeled contraindication of Zometa (zoledronic acidSOLN 5MG/100ML) or pamidronate

AND

3. Prescriber attests to NO concurrent use with another RANKL-inhibitor [i.e., combination use of same active ingredient (Prolia)] OR intravenous bisphosphonates

B. GIANT CELL TUMOR OF BONE:
1. Documentation that member has a diagnosis of a giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity AND
2. Member meets one of the following age requirements (a OR b): a) Age ≥ 18 years; OR b) Age 13 through 17 years with skeletal maturity (defined by at least 1 mature long bone, e.g., closed epiphyseal growth plate of the humerus) and a history of body weight ≥ 45 kg; AND
3. Prescriber attestation that member has been counseled to concurrently take calcium (1000 mg) and vitamin D (400-1200 international units) supplements in conjunction with Xgeva (denosumab)

C. PREVENTION OF SKELATAL- RELATED EVENTS IN PATIENTS WITH MULTIPLE MYELOMA OR BONE METASTASES FROM SOLID TUMORS
1. (a) Diagnosis of a solid tumor primary cancer (i.e., breast, bladder, kidney, ovarian, thyroid cancer etc.) AND evidence of ONE (1) or more metastatic bone lesions.
   OR
   (b) Diagnosis of multiple myeloma
   AND
2. Prescriber attests to NO concurrent use with another RANKL-inhibitor [i.e., combination use of same active ingredient (Prolia)] OR intravenous bisphosphonates
   NOTE TO REVIEWER: IF Prescriber attestation not available, check claims history
   AND
3. Prescriber attestation that member has been counseled to concurrently take calcium (1000 mg) and vitamin D (400-1200 international units) supplements in conjunction with Xgeva (denosumab)

CONTINUATION OF THERAPY:

A. HYPERCALCEMIA OF MALIGNANCY:
1. Positive response to therapy with documented objective improvement in symptoms: defined as albumin-corrected serum calcium level of 12.5 mg/dL or less

B. PREVENTION OF SKELATAL- RELATED EVENTS IN PATIENTS WITH MULTIPLE MYELOMA OR BONE METASTASES FROM SOLID TUMORS AND GIANT CELL TUMOR OF BONE:
1. Documented clinically significant improvements in the disease state, stability on the medication, or lack of disease progression
   AND
2. Documentation that member is not having intolerable or unacceptable toxicity

DURATION OF APPROVAL:

Hypercalcemia of Malignancy: Initial authorization: Up to 3 months, Continuation of therapy: 12 months
Giant cell tumor of bone, Multiple Myeloma and Bone Metastases from a Solid Tumor: Initial authorization 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified endocrinologist, oncologist, or other applicable specialist. Submit consultation notes if applicable

AGE RESTRICTIONS:
18 years of age or older (EXCEPTION in GIANT CELL TUMOR OF BONE- see criteria within indication)

QUANTITY:
Bone metastases from solid tumors : 120 mg every 4 weeks
Giant cell tumor of bone: 120 mg once every 4 weeks; during the first month, give an additional 120mg on days 8 and 15
Hypercalcemia of malignancy: 120 mg every 4 weeks; during the first month, give an additional 120mg on days 8 and 15
Multiple myeloma: 120 mg every 4 weeks

Maximum Quantity Limits – << based on FDA label>>

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Xgeva (denosumab). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
RANK Ligand (RANKL) Inhibitors

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Xgeva, a receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor, is indicated for the prevention of skeletal related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. Xgeva is also indicated for the 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. Xgeva is also indicated for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. Another injectable formulation of denosumab is available, Prolia®, but it is not included in this policy. The prescribing information for Xgeva notes that patients receiving Xgeva should not take Prolia. Xgeva is available as a single-use vial that contains 120 mg of denosumab per 1.7 mL (70 mg/mL)

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of XGEVA (denosumab) that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare. XGEVA (denosumab) is contraindicated in members with hypocalcemia.

OTHER SPECIAL CONSIDERATIONS:
None

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

HCPCS CODE	DESCRIPTION
J0897	injection, denosumab,1mg

AVAILABLE DOSAGE FORMS:
Xgeva SOLN 120MG/1.7ML

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
3. Hu MI, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. J Clin Endocrinol Metab. 2014;99: 3144-3152.
4. Hu MI, Glezerman I, Leboulleux S, et al. Denosumab for patients with persistent or relapsed hypercalcemia of malignancy despite recent bisphosphonate treatment. J Natl Cancer Inst. 2013;105(18):1417-1420.
5. Zometa® injection for intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; December 2016.
6. Aredia® injection [prescribing information]. East Hanover, NJ: Novartis; May 2012.
7. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org..
   National Comprehensive Cancer Network. Breast Cancer Version 5.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 20, 2020.

8. National Comprehensive Cancer Network. Prostate Cancer Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 20, 2020.
9. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed August 17, 2020.