

Medical Drug Clinical Criteria

Subject:	Denosumab Agents		
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Table of Contents

Overview	Coding	References
Clinical criteria	Document history	

Overview

This document addresses the use of denosumab which is approved for the treatment of individuals with osteoporosis, glucocorticoid-induced osteoporosis, treatment induced bone loss, bone metastases, multiple myeloma, giant cell tumor of the bone, hypercalcemia of malignancy and for all other indications as applicable. Denosumab (Prolia, Xgeva) is a subcutaneous, fully human monoclonal antibody that is specifically designed to target the human receptor activator of nuclear factor kappa-B ligand (RANKL).

The American College of Endocrinology (AAACE/ACE) (2020) osteoporosis treatment guidelines stratify initial treatment based on risk status. For those at high risk/no prior fractures, initial therapy options include bisphosphonates (alendronate, risedronate, or zoledronic acid) or denosumab. For those at very high risk/prior fractures, initial therapy options are denosumab, abaloparatide, teriparatide, romosozumab, or zoledronic acid. The Endocrine Society osteoporosis guideline update (2020) recommends initial therapy with bisphosphonates (alendronate, risedronate, zoledronic acid, or ibandronate) or alternatively denosumab for those at high risk.

Osteoporosis may be diagnosed by bone mineral density (BMD) testing indicating a T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population. It also may be clinically diagnosed based on a history of a fragility fracture (low trauma fracture).

Higher risk for fracture may be defined as:

1. History of osteoporotic fracture; or
2. Multiple risk factors for fractures, including but not limited to: Prior low-trauma fracture as an adult, advanced age, gender, ethnicity, low bone mineral density (T-score -1.0 to -2.5), low body weight (<57.6kg), family history of osteoporosis, use of glucocorticoids (daily dosage equivalent to 5 mg or greater prednisone for at least 3 months), current cigarette smoking, excessive alcohol consumption (3 or more drinks per day), secondary osteoporosis (such as rheumatoid arthritis), early menopause, height loss of kyphosis, fall risk and low calcium intake; or
3. Failure or intolerance to other osteoporosis therapies.

A failure of other osteoporosis therapies, otherwise known as refractory disease, may be defined as a decline in BMD while on therapy ($\geq 5\%$) or a fragility fracture while on therapy.

AAACE/ACE (2020) recommends obtaining a baseline axial (lumber spine and hip; 1/3 radius if indicated) dual-energy X-ray absorptiometry (DXA) and after treatment initiation, repeat DXA every 1 to 2 years until findings are stable. Depending on clinical circumstances, follow-up DXA every 1 to 2 years or less frequently can be continued thereafter. Successful response to osteoporosis therapy is considered when BMD is stable or increasing with no evidence of new fractures or vertebral fracture progression.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Prolia (denosumab)

Initial requests for Prolia (denosumab) may be approved when the following criteria are met:

- I. Individual is 18 years of age or older;
- AND**

- II. Individual is a male or postmenopausal female with a diagnosis of osteoporosis (defined as a bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)); **AND**
- III. Individual has had at least one osteoporotic (minimal trauma) fracture; **OR**
- IV. Individual has two or more risk factors for osteoporotic fracture; **OR**
- V. Individual has failed, is intolerant to or has a medical contraindication to other available osteoporosis therapies (for example, bisphosphonates);

OR

- VI. Individual has glucocorticoid-induced osteoporosis (defined as a bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)) and is initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5mg or greater of prednisone and expected to remain on glucocorticoids for a least 6 months;

AND

- VII. Individual has had at least one osteoporotic (minimal trauma) fracture; **OR**
- VIII. Individual has two or more risk factors for osteoporotic fracture; **OR**
- IX. Individual has failed, is intolerant to or has a medical contraindication to other available osteoporosis therapies (for example, bisphosphonates);

OR

- X. Individual is a postmenopausal (natural or induced) female receiving adjuvant aromatase inhibitor therapy for treatment of breast cancer;

OR

- XI. Individual is a male receiving androgen deprivation therapy for non-metastatic prostate cancer; **AND**
- XII. Individual has had at least one osteoporotic (minimal trauma) fracture; **OR**
- XIII. Individual has one or more additional risk factors for osteoporotic fracture.

Continuation Request for Prolia (denosumab) may be approved if the following criterion is met:

- I. There is clinically significant response to therapy (including but not limited to confirmation of no new fractures or reduction of fractures, or no worsening vertebral fractures, or no clinically significant adverse reaction); **AND**
- II. If individual has been on therapy \geq 24 months of treatment, a repeat BMD demonstrates a stable or increase in BMD.

Xgeva (denosumab)

Requests for Xgeva (denosumab) may be approved when the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Individual is using for the prevention of skeletal-related events with one of the following conditions:
 - A. Multiple myeloma; **OR**
 - B. Bone metastases from solid tumor other than prostate cancer; **OR**
 - C. Bone metastases from castration resistant/recurrent prostate cancer;

OR

- III. Individual is 18 years of age or older; **AND**
- IV. Individual is using for the treatment of hypercalcemia of malignancy (defined as an albumin-corrected serum calcium level greater than 12.5 mg/dL (3.1 mmol/L)) and is refractory to recent (within last 30 days) treatment with intravenous bisphosphonate therapy (such as pamidronate or zoledronic acid);

OR

- V. Individual is using for the treatment of localized or metastatic giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity; **AND**
 - A. Individual is 18 years of age or older; **OR**
 - B. Individual is a skeletally mature adolescent (defined by at least one mature long bone [for example; closed epiphyseal growth plate of the humerus]).

Request for denosumab agents (Prolia, Xgeva) may not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Denosumab Agents Quantity Limit

Drug	Limit
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Prolia (denosumab) 60 mg/1 mL prefilled syringe	60 mg (1 prefilled syringe) every 6 months
Xgeva (denosumab) 120 mg/1.7 mL vial*	1 vial per 28 days
Override Criteria	
*Xgeva (denosumab): Requests for increased quantities may be approved for one (1) month, only during the first month of therapy for two (2) additional 120 mg doses for the diagnosis of Giant Cell Tumor of Bone or Hypercalcemia of Malignancy	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0897 Injection, denosumab, 1 mg [Prolia, Xgeva]

ICD-10 Diagnosis

C00.0-C39.9	Malignant neoplasms
C40.00-C41.9	Malignant neoplasm of bone and articular cartilage
C43.0-C60.9	Malignant neoplasms
C61	Malignant neoplasm of prostate
C62.00-C75.9	Malignant neoplasms
C76.0-C76.8	Malignant neoplasm of other and ill-defined sites
C79.51	Secondary malignant neoplasm of bone
C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage [specified as GCTB]
E83.52	Hypercalcemia
M81.0-M81.8	Osteoporosis without current pathological fracture
M85.80-M85.9	Other specified disorders of bone density and structure [osteopenia]
N95.1	Menopausal and female climacteric states
Z08	Encounter for follow-up examination after completed treatment for malignant neoplasm
Z51.11-Z51.12	Encounter for antineoplastic chemotherapy and immunotherapy
Z78.0	Postmenopausal status NOS
Z79.51-Z79.52	Long term (current) use of steroids
Z79.811	Long term (current) use of aromatase inhibitors
Z79.899	Other long term (current) drug therapy [prophylactic drug therapy]
Z85.00-Z85.45	Personal history of malignant neoplasms
Z85.46	Personal history of malignant neoplasm of prostate
Z85.47-Z85.59	Personal history of malignant neoplasms
Z85.810-Z85.9	Personal history of malignant neoplasms
Z87.310	Personal history of (healed) osteoporosis fracture
M80.00XA- M80.88XS	Osteoporosis with current pathological fracture

Document History

Revised: 08/18/2023

Document History:

- 08/18/2023 – Annual Review: Change document name, Wording changes. Coding Reviewed: No changes.
- 08/19/2022- Annual Review: No changes. Coding Reviewed: Added ICD-10-CM Z78.0.
- 09/13/2021- Annual Review: Reformat Prolia Quantity Limit. Coding reviewed: No changes.

- 08/20/2021- Annual Review: Add continuation Criteria, formatting changes. Coding reviewed: No changes.
- 02/21/2021 – Select Review: Wording and formatting updates. Coding Reviewed: No changes.
- 12/21/2020 – Add quantity limits for Prolia and Xgeva.
- 08/21/2020 – Annual Review: No Changes. Coding Reviewed: No changes.
- 12/09/2019 – Select Review: Clarify Xgeva use in prostate cancer; formatting changes for clarity. Coding reviewed: No changes.
- 08/16/2019 – Annual Review: Clarify Prolia PA definition of osteoporosis for consistency with other agents in the class. Wording and formatting changes for clarity.
- 11/08/2018 – Code review: no changes. Added X80.00XA-M80.88XS.
- 08/17/2018 – Annual Review: Initial review of CG-DRUG-73. Update Prolia PA to delete specific examples of fracture risk factors for consistency with other agents in the class review and as they are available in the overview section. Wording and formatting changes for clarity.

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 - a. Bone Cancer. V3.2023. Revised April 4, 2023.
 - b. Breast Cancer. V4.2023. Revised March 23, 2023.
 - c. Kidney Cancer. V4.2023. Revised January 18, 2023.
 - d. Multiple Myeloma. V3.2023. Revised December 8, 2022.
 - e. Non-Small Cell Lung Cancer. V3.2023. Revised April 13, 2023.
 - f. Prostate Cancer. V1.2023. Revised September 16, 2022.
 - g. Systemic Mastocytosis. V3.2023. Revised June 23, 2023.
 - h. Thyroid Cancer. V2.2023. Revised May 18, 2023.

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