

Subject:	Denosumab Agents		
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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 (AACE/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, low body weight, family history of osteoporosis, use of glucocorticoids (daily dosage equivalent to 5 mg or greater prednisone for at least 3 months), cigarette smoking, excessive alcohol consumption (3 or more drinks per day), secondary osteoporosis (such as, rheumatoid arthritis), early menopause, height loss or 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.

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)

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.

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

Miscellaneous Osteoporosis Agents Quantity Limit

Drug	Limit
Prolia (denosumab) 60 mg/1 mL prefilled syringe	2 injections per year
Xgeva (denosumab) 120 mg/1.7 mL vial*	1 vial per 28 days
<u>Override Criteria</u>	
<u>*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</u>	

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]
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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
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

Reviewed: 08/21/2020

Document History:

- 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.

References

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4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
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6. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 5, May 2019, Pages 1595–1622, <https://doi.org/10.1210/jc.2019-00221>.
7. Shoback D, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Guideline Update, *The Journal of Clinical Endocrinology & Metabolism*, Volume 105, Issue 3, March 2020, Pages 587-594.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2020; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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