

Clinical Policy: Denosumab (Prolia, Xgeva)

Reference Number: PA.CP.PHAR.58

Effective Date: 01/18

Last Review Date: 04/18

[Coding Implications](#)

[Revision Log](#)

Description

The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness[®] clinical policy for denosumab (Prolia[®] and Xgeva[®]).

FDA Approved Indication(s)

Prolia is indicated:

- For the treatment of postmenopausal women with osteoporosis at high risk for fracture*. In postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures
- For the treatment to increase bone mass in men with osteoporosis at high risk for fracture*, or patients who have failed or are intolerant to other available osteoporosis therapy
- For treatment to increase bone mass in men at high risk for fracture* receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures
- For treatment to increase bone mass in women at high risk for fracture* receiving adjuvant aromatase inhibitor therapy for breast cancer

**High risk of fracture is defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.*

Xgeva is indicated:

- For the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors
- 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
- For the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

Policy/Criteria

It is the policy of health plans affiliated with Pennsylvania Health and Wellness[®] that Prolia and Xgeva are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Osteoporosis (must meet all):

1. Request is for Prolia;
2. Diagnosis of osteoporosis;
3. If female, member is postmenopausal;
4. Age \geq 18 years or documentation of closed epiphyses;
5. Member meets one of the following (a or b):
 - a. Prescribed by or in consultation with one of the following specialists: a gynecologist, endocrinologist, rheumatologist, orthopedist, or physiatrist;

- b. Failure of a 12-month trial of an oral bisphosphonate (*alendronate is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Member is not using Xgeva concomitantly;
7. Dose does not exceed 60 mg every 6 months.

Approval duration: 12 months

B. Prostate or Breast Cancer Treatment – Induced Bone Loss (must meet all):

1. Request is for Prolia;
2. Diagnosis of one of the following (a or b):
 - a. Female with breast cancer receiving adjuvant aromatase inhibitor therapy;
 - b. Male with nonmetastatic prostate cancer receiving androgen deprivation therapy;
3. Age \geq 18 years or documentation of closed epiphyses;
4. Member is not using Xgeva concomitantly;
5. Dose does not exceed 60 mg every 6 months.

Approval duration: 12 months

C. Bone Metastases, Giant Cell Tumor of Bone, Hypercalcemia of Malignancy (must meet all):

1. Request is for Xgeva for one of the following purposes (a, b, or c):
 - a. Prevention of skeletal-related events in the presence of bone metastases from solid tumors (does not include multiple myeloma), and both (i and ii):
 - i. Age \geq 18 years or documentation of closed epiphyses;
 - ii. Dose does not exceed 120 mg every 4 weeks;
 - b. 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, and both (i and ii):
 - i. Meets one of the following age requirements (a or b):
 - a) Age \geq 18 years;
 - 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 \geq 45 kg;
 - ii. Dose does not exceed 120 mg every 4 weeks with additional 120 mg doses on days 8 and 15 of the first month of therapy;
 - c. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy, and all of the following (i, ii, and iii):
 - i. Age \geq 18 years or documentation of closed epiphyses;
 - ii. Albumin-corrected calcium $>$ 12.5 mg/dL despite treatment with intravenous bisphosphonate therapy in the 30 days prior to initiation of Xgeva therapy;
 - iii. Dose does not exceed 120 mg every 4 weeks with additional 120 mg doses on days 8 and 15 of the first month of therapy;
2. At the time of request, member is not using Prolia concomitantly;

Approval duration: 6 months

D. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. All Indications Specified in Section I (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria, or Continuity of Care policy applies;
2. Member is responding positively to therapy (if hypercalcemia of malignancy, has not achieved complete response as indicated by corrected serum calcium < 10.8 mg/dL);
3. If request is for a dose increase, new dose does not exceed:
 - a. Prolia: 60 mg every 6 months;
 - b. Xgeva: 120 mg every 4 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or Continuity of Care policy applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Prolia (denosumab) is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL (receptor activator of nuclear factor kappa-B ligand). Prolia binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption. Prolia prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone.

Xgeva (denosumab) is a human IgG2 monoclonal antibody that binds to human RANKL. Denosumab has an approximate molecular weight of 147 kDa and is produced in genetically engineered mammalian (Chinese hamster ovary) cells. Xgeva binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption, thereby modulating calcium release from bone. Increased osteoclast activity, stimulated by RANKL, is a mediator of bone pathology in solid tumors with osseous metastases. Similarly, giant cell tumors of bone consist of stromal cells expressing RANKL and osteoclast-like giant cells expressing RANK receptor, and signaling through the RANK receptor contributes to osteolysis and tumor growth. Xgeva prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts, their precursors, and osteoclast-like giant cells.

FDA Approved Indications:

Prolia (denosumab) is a RANKL inhibitor/subcutaneous injectable solution indicated for:

- Treatment of postmenopausal women with osteoporosis at high risk for fracture*. In postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures;
- Treatment to increase bone mass in men with osteoporosis at high risk for fracture*, or patients who have failed or are intolerant to other available osteoporosis therapy;
- Treatment to increase bone mass in men at high risk for fracture* receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures;
- Treatment to increase bone mass in women at high risk for fracture* receiving adjuvant aromatase inhibitor therapy for breast cancer.

**High risk of fracture is defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.*

Xgeva (denosumab) is a RANK ligand (RANKL) inhibitor/subcutaneous injection indicated for:

- Prevention of skeletal-related events in patients with bone metastases from solid tumors. Limitation of use: Xgeva is not indicated for the prevention of skeletal-related events in patients with multiple myeloma.
- 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.
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

Appendices

Appendix A: Abbreviation Key

BMD: bone mineral density	RANK: receptor activator of nuclear factor kappa-B
BMI: body mass index	RANKL: RANK ligand
DXA: dual energy X-ray absorptiometry	WHO: World Health Organization
FDA: Food and Drug Administration	
FRAX: Fracture Risk Assessment Tool	

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0897	Injection, denosumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
2Q2018 annual review: removed requirements related to pregnancy (for Prolia) and hypocalcemia monitoring; allowed COC for oncology related indications on re-auth; Osteoporosis: Modified diagnosis criterion by removing requirement for evidence of diagnosis; removed requirements pertaining to Reclast; added specialist requirement as an option in lieu of bisphosphonate trial; Prostate and breast cancer treatments: removed T-score and risk factors; Criteria added for new FDA indication: multiple myeloma; references reviewed and updated.	02.20 .18	

References

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