Clinical Policy: Denosumab (Prolia, Xgeva)

Reference Number: PA.CP.PHAR.58
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

Description
Denosumab (Prolia®, Xgeva®) is a receptor activator of nuclear factor kappa-B ligand inhibitor.

FDA Approved Indication(s)
Prolia is indicated:

- For the treatment of postmenopausal women with osteoporosis (OP) at high risk for fracture*, or patients who have failed or are intolerant to other available OP therapy. In postmenopausal women with OP, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures
- For the treatment to increase bone mass in men with OP at high risk for fracture*, or patients who have failed or are intolerant to other available OP 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.
- For the treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture* who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to ≥ 7.5 mg of prednisone and expected to remain on glucocorticoids for ≥ 6 months.

**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 OP 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 ≥ 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, geriatrician, 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. Failure of a 12-month trial of zoledronic acid (Reclast®) unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for zoledronic acid*
7. Member is not using Xgeva concomitantly;
8. 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 [i.e., anastrozole (Arimidex®), exemestane (Aromasin®) or letrozole (Femara®)];
   b. Male with nonmetastatic prostate cancer receiving androgen deprivation therapy [i.e., leuprolide (Lupron®), bicalutamide (Casodex®) or Nilandron®];
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses;
5. Member is not using Xgeva concomitantly;
6. 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 member with multiple myeloma or in a member with bone metastases from solid tumors and both (i and ii):
      i. Age ≥ 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 ≥ 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 ≥ 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 ≥ 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.PMN.53.

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 (PA.LTSS.PHAR.01) 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 (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53**.**

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
OP: osteoporosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
alendronate (Fosamax®)	**Osteoporosis** 10 mg PO QD or 70 mg PO q week **Glucocorticoid-induced osteoporosis** 5 mg PO QD or 10 mg PO QD (in postmenopausal women not receiving estrogen) **Osteoporosis prophylaxis** 5 mg PO QD or 35 mg PO q week	Osteoporosis 10 mg/day or 70 mg/week Glucocorticoid-induced osteoporosis 5 mg/day or 10 mg/day (in postmenopausal women not receiving estrogen) Osteoporosis prophylaxis 5 mg/day or 35 mg/week
Fosamax® Plus D (alendronate/ cholecalciferol)	**Osteoporosis** 70 mg alendronate/2,800 units cholecalciferol or 70 mg alendronate/5,600 units cholecalciferol PO q week	70 mg alendronate/5,600 units cholecalciferol/week
risedronate (Actonel®, Atelvia®)	**Osteoporosis (including prophylaxis)** 5 mg PO QD or 35 mg PO q week or 75 mg PO QD for 2 consecutive days for 2 doses/month or 150 mg PO q month **Glucocorticoid-induced osteoporosis** 5 mg PO QD	Osteoporosis (including prophylaxis) 5 mg/day or 35 mg/week or 75 mg/day for 2 days per month or 150 mg/month Glucocorticoid-induced osteoporosis 5 mg/day
ibandronate (Boniva®)	**Osteoporosis (including prophylaxis)** 150 mg PO q month	150 mg/month
zoledronic acid (Reclast®)	**Postmenopausal Osteoporosis, Men with Osteoporosis, Glucocorticoid-induced Osteoporosis** 5 mg IV q year **Postmenopausal Osteoporosis prophylaxis** 5 mg IV q 2 years **Paget's Disease of Bone** 5 mg IV once; may re-treat in patients who have relapsed or who have symptoms	Postmenopausal Osteoporosis, Men with Osteoporosis, Glucocorticoid-induced Osteoporosis 5 mg/year Postmenopausal Osteoporosis Prophylaxis 5 mg/2 years

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		Paget's Disease of Bone 5 mg

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Prolia: hypocalcemia, pregnancy, and known hypersensitivity to Prolia
  - Xgeva: hypocalcemia and known clinically significant hypersensitivity to Xgeva
- Boxed warning(s): none reported

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Denosumab (Prolia)	Postmenopausal women with osteoporosis	60 mg SC once every 6 months	60 mg/dose
	Men with osteoporosis		
	Men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer		
	Women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer		
	Glucocorticoid-induced osteoporosis		
Denosumab (Xgeva)	Multiple myeloma and bone metastasis from solid tumors	120 mg SC once every 4 weeks	120 mg/dose
	Giant cell tumor of bone	120 mg SC every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy only	120 mg/dose
	Hypercalcemia of malignancy		

V. Product Availability

Drug Name	Availability
Denosumab (Prolia)	Injection (single-use prefilled syringe): 60 mg/mL
Denosumab (Xgeva)	Injection (single-use vial): 120 mg/1.7 mL (70 mg/mL)

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	
2Q 2019 annual review: added geriatrician as a prescriber specialist option for osteoporosis; references reviewed and updated.	04.17.19	

References

1. Prolia Prescribing Information. Thousand Oaks, CA: Amgen Inc.; June 2018. Available at: http://www.prolia.com. Accessed February 26, 2019.
2. FRAX: WHO Fracture Risk Assessment Tool. Available at http://www.shef.ac.uk/FRAX/. Accessed June 19, 2017.
3. Xgeva Prescribing Information. Thousand Oaks, CA: Amgen Inc.; June 2018. Available at: http://www.xgeva.com. Accessed February 26, 2019.
4. National Comprehensive Cancer Network. Prostate Cancer Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed February 26, 2019.
5. National Comprehensive Cancer Network. Breast Cancer Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed February 26, 2019.
6. Gralow JR, Biermann JS, Farooki A, et al. NCCN task force report: bone health in cancer care. Journal of the NCCN. 2013; 11(S3): S1-S50.
7. Cosman F, de Beur SJ, LeBoff MS, et al. Position paper: clinician's guide to prevention and treatment of osteoporosis. Osteoporosis Int. 2014; 25(10): 2359-2381.
8. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology practice guidelines for the

diagnosis and treatment of postmenopausal osteoporosis – 2016. Endocrin Pract. 2016; 22(Suppl 4).
9. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012; 97(6): 1802-1822.
10. Denosumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed February 8, 2018.
11. Buckley L, Guyatt G, Fink HA, et al. American College of Rheumatologist guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. 2017; Arthritis & Rheumatology: 69(8):1521-1537 DOI 10.1002/art.40137