Mass General Brigham
Health Plan

Prolia (denosumab)
Xgeva (denosumab)
Effective 04/01/2023

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☒ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	These medications have been designated specialty and must be filled at a contracted specialty pharmacy when obtained through the pharmacy benefit.		
Contact Information	**Medical and Specialty Medications**		
	All Plans	Phone: 877-519-1908	Fax: 855-540-3693
	Non-Specialty Medications		
	All Plans	Phone: 800-711-4555	Fax: 844-403-1029
Exceptions	N/A		

Overview
Denosumab is a type of monoclonal antibody used to treat osteoporosis and prevention of bone issues caused by certain cancers. Denosumab is available as two branded products (Prolia and Xgeva), each with specific FDA indications.

Approval Diagnosis:

- Treatment/prevention of postmenopausal osteoporosis in women (Prolia®)
- Treatment of osteoporosis in men (Prolia®)
  Treatment/prevention of glucocorticoid-induced osteoporosis in men and women (Prolia®)
- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer (Prolia®)
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer (Prolia®)
- Prevention of skeletal-related events secondary to bone metastases in cancer related to solid tumors and in multiple myeloma (Xgeva®)
- Treatment of giant cell tumor of the bone (Xgeva®)
- Treatment of hypercalcemia of malignancy (Xgeva®)

Coverage Guidelines
Authorization may be granted for members who are new to the plan currently receiving treatment with Prolia or Xgeva excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization may be granted for members when all the following drug-specific criteria are met, and documentation is provided:

Treatment/prevention of osteoporosis

Prolia® (denosumab)
Prescriber provides documentation of **ALL** of the following:

1. Appropriate diagnosis
2. **ONE** of the following:
    a. Physician attestation of inadequate response to an adequate trial or adverse reaction to **ONE** oral bisphosphonate (see appendix for details)
    b. Contraindication to **ALL** oral bisphosphonates (see appendix for details)
    c. Member is at very high risk for fracture indicated by at least **ONE** of the following: a. History of fracture within the past 12 months
        i. History of fractures while on osteoporosis therapy
        ii. History of multiple fractures
        iii. History of fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids)
        iv. T-score less than −3.0
        v. High risk for falls
        vi. History of injurious falls
        vii. Very high fracture probability by FRAX® (fracture risk assessment tool) or other validated fracture risk algorithm

<u>Treatment/prevention of glucocorticoid-induced osteoporosis</u>
Prolia® (denosumab):
Prescriber provides documentation of **ALL** of the following:

1. **ONE** of the following:
    a. Appropriate diagnosis
    b. Chronic glucocorticoid use determined by claims for >5 mg of prednisone equivalent for ≥ 3 months in claims history
2. **ONE** of the following:
    a. Physician attestation of inadequate response to an adequate trial or adverse reaction to **ONE** oral bisphosphonate (see appendix for details)
    b. Contraindication to oral bisphosphonates (see appendix for details)
    c. Member is at very high risk for fracture indicated by at least **ONE** of the following: a. History of fracture within the past 12 months
        i. History of fractures while on osteoporosis therapy
        ii. History of multiple fractures
        iii. History of fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids)
        iv. T-score less than −3.0
        v. High risk for falls
        vi. History of injurious falls
        vii. Very high fracture probability by FRAX® (fracture risk assessment tool) or other validated fracture risk algorithm

<u>Prevention of skeletal-related events secondary to bone metastases in cancer related to solid tumors and in multiple myeloma;</u>
<u>Treatment of hypercalcemia of malignancy;</u>
<u>Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer;</u>

Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer

Prolia® (denosumab):

1. Appropriate diagnosis
2. **ONE** of the following:
    a. Physician attestation of inadequate response to an adequate trial or adverse reaction to **ONE** bisphosphonate (see appendix for details)
    b. Contraindication to **ALL** oral and injectable bisphosphonates

Xgeva® (denosumab):

1. Diagnosis is **ONE** of the following:
    a. Prevention of skeletal-related events secondary to bone metastases in cancer related to solid tumors
    b. Prevention of skeletal-related events secondary to multiple myeloma
    c. Treatment of hypercalcemia of malignancy
2. Prescriber is an oncologist, hematologist, or orthopedic specialist or has provided consult notes from an oncologist, hematologist, or orthopedic specialist
3. Appropriate dosing

Treatment of Giant Cell Tumor of the bone (GCTB)

Xgeva® (denosumab):

1. Appropriate diagnosis
2. **ONE** of the following:
    a. Documentation that the tumor or metastases are unresectable
    b. Documentation that surgical resection is likely to result in severe morbidity
    c. Documentation that surgery is not an option at this time
3. Dose and frequency are appropriate for GCTB

Continuation of Therapy

Resubmission by prescriber will infer positive response to therapy.

Limitations

1. Approvals will be granted for 1 year.

Appendix

Adverse reactions to oral bisphosphonates

- Upper gastrointestinal effects (i.e. dysphagia, esophagitis, esophageal or gastric ulcers)
    - A gastrointestinal adverse event to any oral bisphosphonate will be considered as having met the trial requirement for oral alendronate where noted.
- Hypersensitivity to any component

Contraindications to oral bisphosphonates

- Abnormalities of esophagus which delay esophageal emptying (i.e. stricture, achalasia, erosive esophagitis, gastric ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- A diagnosis of GERD is not a contraindication to oral bisphosphonate use; however, severe esophagitis, Barrett's esophagus and esophageal ulcerations are reasons to by-pass a trial.

Contraindications/Precautions to ALL (oral and IV) bisphosphonates
Rationale to bypass a trial of bisphosphonates include:

- Severe renal impairment (CrCl < 35 ml/min)
- Severe dental disease (with or without frequent dental extractions)
- Severe gastrointestinal disorders (i.e. severe ulcerative colitis or Crohn's disease)

References

1. Prolia (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; March 2020.
2. Xgeva (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; June 2020
3. Hu MI, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. J Clin Endocrinol Metab 2014; 99:3144.
4. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. Menopause 2021; 28:973
5. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab 2019; 104:1595
6. Terpos E, Zamagni E, Lentzsch S, et al. Treatment of multiple myeloma-related bone disease: recommendations from the Bone Working Group of the International Myeloma Working Group. Lancet Oncol 2021; 22:e119
7. Terpos E, Zamagni E, Lentzsch S, et al. Treatment of multiple myeloma-related bone disease: recommendations from the Bone Working Group of the International Myeloma Working Group. Lancet Oncol 2021; 22:e119
8. Salagame U, Kliewer EV, Demers A, et al. Trends in Prescribing Menopausal Hormone Therapy and Bisphosphonates in Australia and Manitoba, Canada and Adherence to Recommendations. J Womens Health (Larchmt) 2020; 29:177
9. Saag KG, Pannacciulli N, Geusens P, et al. Denosumab Versus Risedronate in Glucocorticoid-Induced Osteoporosis: Final Results of a Twenty-Four-Month Randomized, Double-Blind, Double-Dummy Trial. Arthritis Rheumatol 2019; 71:1174
10. Ishiguro S, Ito K, Nakagawa S, et al. The clinical benefits of denosumab for prophylaxis of steroid-induced osteoporosis in patients with pulmonary disease. Arch Osteoporos 2017; 12:44
11. Chawla S, Henshaw R, Seeger L, et al. Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol 2013; 14:901

Review History
06/22/2022: Created and Reviewed June P&T, switched from CVS Standard to Custom criteria, updated approval duration for Prolia to 24 months; combined Prolia & Xgeva to single document. Effective 09/01/2022.
03/15/23 - Reviewed and updated for Mar P&T. Matched MH UPPL criteria. Effective 4/1/23.