Mass General Brigham
Health Plan

Prolia (denosumab)
Xgeva (denosumab)
Effective 09/01/2022

Plan	☐ MassHealth UPPL ☒Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
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.

Submission of the following information is necessary to initiate the prior authorization review for Prolia: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

Coverage Guidelines
Authorization may be granted for members who are 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:

Prolia:

Postmenopausal osteoporosis

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
    a. Member has indicators of very high fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3], or increased fall risk)
    b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo, Bonsity], abaloparatide [Tymlos])
    c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

Osteoporosis in men

1. Member has a history of an osteoporotic vertebral or hip fracture[10]
2. Member meets BOTH of the following criteria:
    a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)[10]
    b. Member has had an oral OR injectable bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with a bisphosphonate (See Appendix A)

Glucocorticoid-induced osteoporosis

1. Member is currently receiving or will be initiating glucocorticoid therapy at an equivalent prednisone dose of ≥ 2.5 mg/day for ≥ 3 months.
2. Member has had an oral OR injectable bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with a bisphosphonate (See Appendix A)
3. Member meets ANY of the following criteria:

a. Member has a history of a fragility fracture
b. Member has a pre-treatment T-score less than or equal to -2.5
c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

Breast cancer

Authorization may be granted to members who are receiving adjuvant aromatase inhibition therapy for breast cancer.

Prostate cancer

Authorization may be granted to members who are receiving androgen deprivation therapy for prostate cancer.

Xgeva:

Multiple myeloma

Authorization may be granted for prevention of skeletal-related events in members with multiple myeloma.

Bone Metastases

Authorization may be granted when ONE of the following are met:

1. For the prevention of skeletal-related events in members with bone metastases from a solid tumor
2. As palliative care for bone metastases from thyroid carcinoma

Giant Cell Tumor of Bone

Authorization of 12 months may be granted for treatment of giant cell tumor of bone

Hypercalcemia of Malignancy

Initial authorization of 2 months may be granted for treatment of hypercalcemia of malignancy that is refractory to intravenous (IV) bisphosphonate therapy OR there is a clinical reason to avoid IV bisphosphonate therapy (See Appendix).

Systemic Mastocytosis

Authorization of 12 months may be granted for second-line therapy for osteopenia or osteoporosis in members with systemic mastocytosis that have not responded to therapy with bisphosphonates or for patients who are not candidates for bisphosphonates because of renal insufficiency.

Continuation of Therapy

Resubmission by prescriber when ONE of the following is met:

1. Member has experienced clinical benefit (e.g., no new fracture seen on radiography) and has not experienced clinically significant adverse events during therapy.
2. Member has experienced clinical benefit as evidenced by a bone mass measurement showing an improvement or stabilization in T-score compared with the previous bone mass measurement and member has not experienced any adverse effects.

Limitations

1. For Prolia: Initial and reauthorization approvals for all diagnoses will be granted for 24 months.
2. For Xgeva:
    a. Initial and reauthorizations approvals for Hypercalcemia of malignancy will be granted for 2 months.
    b. All other diagnosis: Initial and reauthorizations approvals will be granted for 12 months

Appendix

Appendix A.

Clinical reasons to avoid IV bisphosphonate therapy

- Renal insufficiency (creatinine clearance <35ml/min
- Acute renal impairment
- History of intolerance to an IV bisphosphonate

Clinical reasons to avoid oral bisphosphonate therapy

- Presence of anatomic or functional esophageal abnormalities that might delay transit of the tablet (e.g., achalasia, stricture, or dysmotility
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Presence of documented or potential gastrointestinal malabsorption (e.g., gastric bypass procedures, celiac disease, Crohn's disease, infiltrative disorders, etc.)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10-year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture (including fractures of the spine (clinical), hip, wrist, or humerus) and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg (prednisone equivalent) per day.

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

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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
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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.