denosumab (Prolia®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO120

Description

Denosumab (Prolia) is a monocloncal antibody that activates nuclear factor kappa-B ligand (RANKL) inhibitors which prevent the formation, function, and survival of osteoclasts resulting in decreased bone resorption.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
denosumab (Prolia)	60 mg/mL syringe	Post-menopausal Osteoporosis in Women Osteoporosis in Men Increase Bone Mass in Women with Breast Cancer receiving Aromatase Inhibitor Therapy Increase Bone Mass in Men with Non-metastatic Prostate Cancer receiving Androgen Deprivation Therapy Glucocorticoid-induced Osteoporosis	60 mg/mL (1 syringe) per 180 days

Initial Evaluation

I. Denosumab (Prolia) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. **Not** used in combination with other osteoporotic agents [e.g., bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid injection), calcitonin nasal spray, parathyroid hormones (teriparatide, abaloparatide), raloxifene, Xgeva, or Evenity]; **AND**
   C. Documentation of treatment failure or ineffective response to a minimum 12 month trial of previous therapy with bisphosphonates (oral or IV) such as alendronate, risedronate, ibandronate, or zoledronic acid; **OR**
   D. Member has a documented contraindication or intolerance to BOTH oral bisphosphonates AND intravenous (IV) bisphosphonates such as alendronate, risedronate, ibandronate, or zoledronic acid; **AND**

E. A diagnosis of one of the following:
    1. **Post-menopausal Osteoporosis in Women or Osteoporosis in Men; AND**
        i. Member has hip DXA (femoral neck or total hip) or lumbar spine T-score ≤-2.5 **or** forearm DXA 33% (one-third) radius; **OR**
        ii. Member has a T-score ≤-1 or low bone mass and a history of fragility fracture to the hip or spine; **OR**
        iii. Member has a T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **OR**
    2. **Women with Breast Cancer receiving Aromatase Inhibitor Therapy (e.g., anastrozole, letrozole); OR**
    3. **Men with Non-metastatic Prostate Cancer receiving Androgen Deprivation Therapy (e.g., leuprolide, goserelin, histrelin); OR**
    4. **Glucocorticoid-induced Osteoporosis; AND**
        i. Member is taking ≥ 7.5 mg prednisone or oral steroids daily with an anticipated duration of ≥ 6 months.

II. Denosumab (Prolia) is considered not medically necessary when criteria above are not met and/or when used for:
    A. Prevention of skeletal complications of bone metastases from solid tumor cancers
    B. Treatment of giant cell tumor of the bone
    C. Hypercalcemia of malignancy

III. Denosumab (Prolia) is considered investigational when used for all other conditions, including but not limited to:
    A. Prevention of osteoporosis

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. **Not** used in combination with other osteoporotic agents [e.g., bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid injection), calcitonin nasal spray, parathyroid hormones (teriparatide, abaloparatide), or raloxifene]; **AND**
IV. Member has demonstrated clinical improvement [e.g., improved bone mineral density, absence in fracture(s)] with denosumab (Prolia).

Supporting Evidence

I. In the pivotal trials for denosumab (Prolia), the participants were adults.
II. According to the American Society of Clinical Oncology, both bisphosphonates and denosumab (Prolia) are appropriate treatment for increasing bone mass in women with breast cancer who

are receiving an aromatase inhibitor, or men with non-metastatic breast cancer who are receiving ADT.

III. For the treatment of osteoporosis in postmenopausal women, the safety and efficacy of denosumab (Prolia) was studied in a three year, randomized, double-blind, placebo-controlled trial. The primary efficacy outcome was the incidence of new morphometric (radiologically-diagnosed) vertebral fractures at three years; the absolute risk reduction was 4.8% in favor of denosumab (Prolia) [95% CI (3.9, 5.8)].

IV. For the treatment to increase bone mass in men with osteoporosis, the safety and efficacy of denosumab (Prolia) was demonstrated in a one year, double-blind, placebo-controlled trial. The primary efficacy outcome was percent change in lumbar spine bone mass density (BMD) from baseline to one year. Treatment with denosumab (Prolia) increased BMD at one year with a treatment difference of 4.8% [95% CI (4.0, 5.6)].

V. For the treatment of glucocorticoid-induced osteoporosis, the safety and efficacy of denosumab (Prolia) was studied in the 12-month primary analysis of a two year, randomized, multicenter, double-blind, parallel-group, active controlled study. Patients were randomized (1:1) to receive either an oral daily bisphosphonate or denosumab (Prolia). At the 12-month primary analysis, denosumab (Prolia) significantly increased lumbar spine BMD compared to the active control (3.8% vs 0.8%, respectively).

VI. For the treatment of bone loss in men with non-metastatic prostate cancer receiving androgen deprivation therapy (ADT), the safety and efficacy of denosumab (Prolia) was studied in a three year, randomized (1:1) double-blind, placebo controlled, multinational study. The primary efficacy outcome was percent change in lumbar spine BMD from baseline to month 24, which denosumab (Prolia) demonstrated a higher lumbar spine BMD compared to placebo; the treatment difference was 6.7% [95% CI (6.2, 7.1); $p < 0.0001$].

VII. For the treatment of bone loss in women with breast cancer receiving aromatase inhibitor therapy, the safety and efficacy studied in a one year, randomized, placebo controlled trial. In the denosumab (Prolia) treated arm, the percent change in lumbar spine BMD from baseline to month 12 was 4.8% vs -0.7% in the placebo arm.

VIII. According to the American Society of Clinical Oncology (ASCO), the recommended therapies for delaying or preventing osteoporosis in men with non-metastatic prostate cancer receiving ADT and women with breast cancer receiving aromatase inhibitor therapy are bisphosphonates and denosumab (Prolia).

Investigational or Not Medically Necessary Uses

I. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy of denosumab (Prolia) in the following settings:
   A. Prevention of skeletal complications of bone metastases from solid tumor cancers
   B. Treatment of giant cell tumor of the bone
   C. Hypercalcemia of malignancy
   D. Prevention of osteoporosis.

References

1. Prolia [Prescribing Information]. Thousand Oaks, CA: Amgen, Inc. October 2019.
2. Camacho PM, Petak SM, Binkley N, et al. American Association Of Clinical Endocrinologists And American College Of Endocrinology Clinical Practice Guidelines For The Diagnosis And Treatment Of Postmenopausal Osteoporosis. September 2016. Available at: https://doi.org/10.4158/EP161435.GL.
3. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 97, Issue 6, June 2012, Pages 1802–1822. Available at: https://doi.org/10.1210/jc.2011-3045
4. Buckley L, Guyatt G, Fink HA, et al. American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. American College of Rheumatology, Volume 69, Issue 8, August 2017, Pages 1521-1537. Available at: https://www.rheumatology.org/Portals/0/Files/Guideline-for-the-Prevention-and-Treatment-of-GIOP.pdf
5. Cavallo J. Bone-Targeted Therapies for Men with Prostate Cancer Receiving Androgen Deprivation Therapy. The American Society of Clinical Oncology Post. August 2017. Available at: https://www.ascopost.com/News/57907
6. Joint Position Statement on Management of Aromatase Inhibitor-Associated Bone Loss in Postmenopausal Women with hormone-Sensitive Breast Cancer. The American Society of Clinical Oncology Post. April 2017. Available at: https://ascopost.com/News/55553

Policy Implementation/Update:

Date Created	October 2011
Date Effective	October 2011
Last Updated	November 2019
Last Reviewed	01/2016, 11/2019

Action and Summary of Changes	**Date**
Criteria Transitioned into policy with the following updates: supporting evidence added, investigational section added, guidelines for the specific denosumab (Prolia) indications have been reviewed for therapy appropriateness, the requirement to trial/fail bisphosphonates have been extended to all denosumab (Prolia) indications per guidelines, specific inclusion criteria around glucocorticoid-induced osteoporosis has been added; lastly, for osteoporosis prevention in men and women the trial/fail therapies have been updated to include all agents [bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid injection), calcitonin nasal spray, parathyroid hormones (teriparatide, abaloparatide), raloxifene] that are appropriate in those settings.	11/2019