Reference number(s)
2390-A

STANDARD MEDICARE PART B MANAGEMENT

PROLIA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures.
2. Treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.
3. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture, who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 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 osteoporosis therapy.
4. 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.
5. Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

B. Compendial Uses
1. Prevention of osteoporosis in osteopenic postmenopausal women
2. Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk
3. Consider in postmenopausal (natural or induced) patients receiving adjuvant aromatase inhibition therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce risk of fractures

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Osteoporosis treatment
Authorization of 12 months may be granted for the treatment of osteoporosis in men or postmenopausal women at high risk for fracture.

B. Osteoporosis prevention
Authorization of 12 months may be granted for the prevention of osteoporosis in osteopenic postmenopausal women.

C. Increasing bone mass in prostate cancer
Authorization of 12 months may be granted to increase bone mass in men at high risk for fracture who are receiving androgen deprivation therapy for prostate cancer.

D. Increasing bone mass in breast cancer
Authorization of 12 months may be granted to increase bone mass in women at high risk for fracture who are receiving adjuvant aromatase inhibition therapy for breast cancer.

E. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture
Authorization of 12 months may be granted to increase bone mass in men and women with glucocorticoid-induced osteoporosis at high risk for fracture.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Prolia
B. The member is receiving the requested medication for an indication listed in Section II
C. The medication has been effective for treating the diagnosis or condition

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Prolia
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Prostate cancer
4. NCCN Guideline: Breast cancer

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Prolia are covered in addition to the following:
A. Prevention of osteoporosis in osteopenic postmenopausal women
B. Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk

C. Maintenance or improvement in bone mineral density in patients receiving adjuvant aromatase inhibition therapy

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Prolia for prevention of osteoporosis in osteopenic postmenopausal women as an approvable indication is evidenced by a multicenter, randomized, placebo-controlled study of 332 postmenopausal women with low bone mineral density (BMD) by Bone et al. Treatment with denosumab given once every 6 months improved BMD from baseline compared with placebo at 2 years. Postmenopausal women (mean age, 59.4 +/- 7.5 years) were eligible for enrollment if they had a lumbar spine (LS)-BMD T-score of -1 to -2.5 (mean T-score, -1.61 +/- 0.42), no history of fracture after age 25 years, and had not received IV bisphosphonates, fluoride, or strontium within the previous 5 years or parathyroid hormone agents (including derivatives), steroids, hormone-replacement therapy, selective estrogen-receptor modulators, calcitonin, or calcitriol within the previous 6 weeks. Patients were randomized to receive either denosumab 60 mg (n=166) or placebo (n=166) given subcutaneously every 6 months. All patients also received oral calcium (1000 mg) and vitamin D (400 to 800 international units or greater) daily. Approximately 86% of patients completed 24 months of study treatment. At 24 months, patients in the denosumab arm had a mean percentage LS-BMD increase over baseline (6.5%; 97.5% CI, 5.8% to 7.2%) and patients in the placebo arm had a mean percentage LS-BMD decrease over baseline (-0.6%; 97.5% CI, -1.2% to 0.1%); additionally, the mean percentage LS-BMD difference between the 2 arms was significant (7%; 97.5% CI, 6.2% to 7.8%; p less than 0.0001). In patients who received denosumab, mean percentage BMDs were all increased from baseline at 24 months for the total hip (3.4%; 97.5% CI, 3% to 3.7%), femoral neck (2.8%; 97.5% CI, 2.3% to 3.3%), trochanter (5.2%; 97.5% CI, 4.7% to 5.6%), and distal third of the radius (1.4%; 97.5% CI, 0.9% to 1.9%), and the mean percent BMD differences compared with placebo were significant (p less than 0.0001). Markers of bone turnover were reduced from baseline in patients receiving denosumab (mean percent reduction: C-telopeptide I, 63% to 88%; tartrate-resistant acid phosphatase 5b, 40% to 50%; intact N-terminal propeptide of type 1 procollagen, 65% to 76%).

Support for using Prolia for the prevention or treatment of osteoporosis during androgen deprivation therapy is found in the National Comprehensive Cancer Network's guideline for prostate cancer. The NCCN Guideline for prostate cancer supports the use of Prolia as prevention or treatment of osteoporosis during androgen deprivation therapy in patients with high fracture risk.

Support for using Prolia to maintain or improve bone mineral density and reduce the risk of fractures in postmenopausal patients receiving adjuvant aromatase inhibition therapy is found in the National Comprehensive Cancer Network's guideline for breast cancer. The NCCN Guideline for breast cancer supports the use of Prolia in postmenopausal (natural or induced) patients receiving adjuvant aromatase inhibition therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce the risk of fractures.

VI. REFERENCES

1. Prolia [package insert]. Thousand Oaks, CA: Amgen Inc.; May 2022.
2. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado. Available at https://www.micromedexsolutions.com Accessed October 18,2022.
3. The NCCN Drugs & Biologics Compendium™ © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 18, 2022.

4. Bone HG, Bolognese MA, Yuen CK, et al: Effects of denosumab on bone mineral density and bone turnover in postmenopausal women. J Clin Endocrinol Metab 2008; 93(6):2149-2157.