denosumab (Prolia)

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: METABOLIC BONE DISEASE AGENTS
Mechanism of Action: Monoclonal antibody that inhibits RANK ligand activity and prevents osteoclast formation
HCPCS:
J0897:Injection, denosumab, 1 mg
How Supplied:

- 60 mg/mL in a single-dose prefilled syringe

Condition(s) listed in policy (see coverage criteria for details)

- Increase BMD in Patients with Hormone-Responsive Breast Cancer undergoing Hormone Ablation Therapy
- Increase BMD in Patients with Prostate Cancer undergoing Androgen Deprivation Therapy
- Osteoporosis

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Increase BMD in Patients with Hormone-Responsive Breast Cancer undergoing Hormone Ablation Therapy

Meets medical necessity if all the following are met:

1. Patient is currently taking an aromatase inhibitor, tamoxifen, or GNRH agonist
2. Meets ONE of the following:

a. Patient is unable to take an oral bisphosphonate and has intolerance or contraindication to an IV bisphosphonate
b. Patient experienced a non-traumatic fracture while on a bisphosphonate
c. Patient has had intolerable gastric side effects to a monthly oral bisphosphonate regimen that would cause him/her to discontinue therapy
d. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate

3. Not being used in combination with other drug therapy for osteoporosis (e.g., Forteo, Evenity, teriparatide, Tymlos)

Covered Doses:
60 mg given subcutaneously once every 6 months

Coverage Period:
one year

ICD-10:
(X = numbers 0-6, 8, 9) C50.X11, C50.X12, C50.X19; (X=numbers 1-6, 8, 9) C50.X21, C50.X22, C50.X29; Z85.3

Increase BMD in Patients with Prostate Cancer undergoing Androgen Deprivation Therapy
Meets medical necessity if all the following are met:

1. Patient is currently taking androgen deprivation therapy [e.g., gonadotropin-releasing hormone (GnRH) agonists such as leuprolide (Lupron)] or has had surgical castration
2. Meets ONE of the following:
   a. Patient is unable to take an oral bisphosphonate and has intolerance or contraindication to an IV bisphosphonate
   b. Patient experienced a non-traumatic fracture while on a bisphosphonate
   c. Patient has had intolerable gastric side effects to a monthly oral bisphosphonate regimen that would cause him/her to discontinue therapy
   d. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate
3. Not being used in combination with other drug therapy for osteoporosis (e.g., Forteo, Evenity, teriparatide, Tymlos)

Covered Doses:
60 mg given subcutaneously once every 6 months

Coverage Period:
one year

ICD-10:
C61

Osteoporosis
Meets medical necessity if all the following are met:

1. ONE of the following:

1. One or more non-traumatic fractures
2. T-scores less than -2.5 S.D
3. T-score is between -1.0 and -2.5 and patient is at high risk for fracture *[e.g. multiple risk factors, 10-year hip fracture probability >/= 3%, a 10-year major osteoporosis-related fracture probability >/= 20% based on USA-adapted WHO absolute fracture risk model (FRAX risk assessment)]*

2. ONE of the following:
   1. Intolerance to prior oral and IV bisphosphonate therapy that would cause discontinuation, or contraindication to oral and IV bisphosphonates
   2. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate
   3. Patient is initiating or continuing long-term glucocorticoid treatment (≥3 months)
   4. Patient is at very high risk of fracture by meeting at least ONE of the following:
      1. Fracture while taking a bisphosphonate
      2. Patient has experienced a recent fracture (within the past 12 months) or history of multiple fractures
      3. Patient experienced a fracture while on long-term glucocorticoid therapy
      4. T-score less than −3.0
      5. Patient is at high risk for falls
      6. 10-year hip fracture probability of > 4.5% based on FRAX score
      7. 10-year major osteoporosis-related fracture probability > 30% based on FRAX score
3. Not being used in combination with other drug therapy for osteoporosis (e.g., Forteo, Evenity, teriparatide, Tymlos)

Covered Doses:
60 mg SC given subcutaneously once every 6 months

Coverage Period:
yearly

ICD-10:
M80.0-M81.9

Additional Information

Summary of Evidence

The contents of this policy were created after examining the following resources:
1. The prescribing information for Prolia
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text
   c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
   d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A"

e. Clinical Pharmacology - supportive narrative text
3. ACOG Committee on Clinical Practice Guidelines–Gynecology. Management of Postmenopausal Osteoporosis: ACOG Clinical Practice Guideline No. 2 (2022)
4. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2020 UPDATE
5. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Guideline Update (2020)
6. NCCN Guideline: Prostate Cancer
7. 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:

- Prevention of osteoporosis in osteopenic postmenopausal women
- Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk
- Maintenance or improvement in bone mineral density in patients receiving adjuvant aromatase inhibition therapy

Explanation of Rationale

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- 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.
- Support for using bisphosphonates or Prolia for osteoporosis at high risk for bone fracture is found in several treatment guideline:
    - The 2022 ACOG Clinical Practice Guideline on the Management of Postmenopausal Osteoporosis supports the use of antiresorptive agents (i.e., bisphosphonates and denosumab), which have broad-spectrum antifracture efficacy, as first-line therapy for most patients with osteoporosis and elevated fracture risk.
    - The 2020 AACE/ACE Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis states that alendronate, denosumab, risedronate, and zoledronate are appropriate as initial therapy for most osteoporotic patients with high fracture risk.
    - The 2020 Endocrine Society Guideline Update on the Pharmacological Management of Osteoporosis in Postmenopausal Women recommends bisphosphonates as initial

treatment and denosumab as an alternative initial treatment in postmenopausal women at high risk for fractures

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS. Available by subscription at http://www.lexi.com
5. DrugDex. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
6. Cosman F, de Beur SJ, LeBoff MS et al. Clinician's guide to prevention and treatment of osteoporosis. Osteoporosis Int 2014;25(10):2359-81.
7. Camacho PM, Petak SM, Blinkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2020 UPDATE. Endocr Pract. 2020;26(Suppl 1):1-46
8. National Comprehensive Cancer Network. Breast Cancer (Version 4.2024). Available at: www.nccn.org.
9. National Comprehensive Cancer Network. Prostate Cancer (Version 4.2024). Available at: www.nccn.org.
10. Prolia (denosumab) [Prescribing information]. Thousand Oaks, CA: Amgen Inc.; 3/2024.
11. Qaseem A, Forciea MA, McLean RM, Denberg TD, Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians. Ann Intern Med. 2017;166(11):818-839. doi:10.7326/M15-1361
12. Shoback D, Rosen CJ, Black DM, et al. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society guideline update. J Clin Endocrinol Metab 2020; 105:587-594.
13. ACOG Committee on Clinical Practice Guidelines–Gynecology. Management of Postmenopausal Osteoporosis: ACOG Clinical Practice Guideline No. 2. Obstet Gynecol. 2022 Apr 1;139(4):698-717. doi: 10.1097/AOG.0000000000004730. Erratum in: Obstet Gynecol. 2022 Jul 01;140(1):138.

Review History

Date of Last Annual Review: 4Q2024
Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee

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