PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date August 15, 2024	
	PROLIA PRODUCTS (DENOSUMAB) Jubbonti (denosumab-bbdz)	**Policy #** Prolia Products (denosumab)	
		Review Date 05/28/2024	**Applicable to:** ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the 'Disclaimer' section below for more information.

OVERVIEW

This policy addresses the coverage of Prolia (denosumab) for the treatment of osteoporosis for fracture risk reduction (in males and postmenopausal females).

Denosumab is also indicated for the following indications, which are not addressed in this policy:

- Bone loss (treatment to increase bone mass), in men with non-metastatic prostate cancer at high risk for fracture receiving androgen deprivation therapy;
- Bone loss (treatment to increase bone mass), in women with breast cancer at high risk for fracture receiving adjuvant aromatase inhibitor (AI) therapy;
- Glucocorticoid-induced osteoporosis (treatment), in men and women at high risk of 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;

Denosumab subcutaneous injection is also available under the brand name Xgeva® and is indicated for the prevention of skeletal-related events in patients with multiple myeloma, as well as in patients with bone metastases from solid tumors, giant cell tumor of bone, and hypercalcemia of malignancy. Xgeva and its indications are not address in this policy.

APPLICABLE HCPCS

J0897: Injection, denosumab, 1 mg; 1 mg = 1 billable unit (60 billable units every 6 months)

C9399, J3490, J3590, J9999: Denosumab-bbdz (Jubbonti) (effective 03/05/24)

- Jubbonti (denosumab-bbdz): Biosimilar to Prolia (FDA approved March 2024)

Available as: 60 mg/1 mL single-dose prefilled syringe

Please note: Xgeva and its respective indications are not addressed in this policy. Please refer to Xgeva (denosumab) Clinical Policy.

CLINICAL CRITERIA

POSTMENOPAUSAL OSTEOPOROSIS and MEN with OSTEOPOROSIS AT HIGH RISK OF FRACTURE

A. **INITIAL CRITERIA**

Prolia (denosumab) may be authorized when ALL of the following criteria are met with documentation:

1. Diagnosis of osteoporosis in postmenopausal women who are at a high risk of fracture, OR osteoporosis in men; **AND**

2. Documentation of **ONE** or more of the following:

    a. Hip/femur DXA (femoral neck or total hip) or lumbar spine T-score ≤ -2.5 and/or forearm DXA at the 33% (one-third) radius site (wrist); **OR**

    b. T-score ≤-1 or low bone mass *and* a history of fragility fracture to the hip or spine; **OR**

    c. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥ 20% or hip fracture ≥ 3%.

AND

3. Documentation of **ONE** of the following:

    a. Treatment failure with a *bisphosphonate (oral or IV) defined as **ONE** of the following after at least 12 months of compliant therapy:

        i. Progression of bone loss as documented by bone density measurements (BMD); **or**

        ii. Occurrence of an osteoporotic fracture.

        **Oral bisphosphonate (e.g., alendronate, risedronate, ibandronate); Intravenous bisphosphonate (e.g., ibandronate, zoledronic acid)*

    OR

    b. *Contraindication, hypersensitivity, or intolerance to a bisphosphonate (NOTE: if member has intolerance to oral administration, IV administration will be required)

        **Contraindications to bisphosphonate therapy include: Hypersensitivity to bisphosphonates or any component of the formulations; hypocalcemia (alendronate, ibandronate, risedronate, zoledronic acid [Reclast]); abnormalities of the esophagus that delay esophageal emptying, such as stricture or achalasia (alendronate, etidronate, oral ibandronate, risedronate); increased risk of aspiration (alendronate [effervescent tablet and oral solution]); inability to stand or sit upright for at least 30 minutes (alendronate, risedronate); inability to stand or sit upright for at least 60 minutes (oral ibandronate); clinically overt osteomalacia (etidronate); CrCl less than 35 mL/minute and in those patients with evidence of acute renal impairment due to an increased risk of renal failure (zoledronic acid [Reclast]).(FDA labeling, 2023)*

AND

4. Prescriber attestation or documentation of the following:

    a. Prolia (denosumab) will not be administered concurrent with other medications for osteoporosis [e.g., a bisphosphonate, another form of denosumab (e.g., Xgeva), romosozumab-aggg (Evenity), or parathyroid hormone analog [e.g., abloparatide (Tymlos), teriparatide (Forteo)]; **and**

b. Hypocalcemia was reviewed and corrected prior to initiation of treatment if applicable; **and**

c. Member is taking calcium (1000 mg) and vitamin D (400-1200 international units) supplements in conjunction with Prolia as recommended in product labeling.

B. **REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA**

Prolia (denosumab) may be authorized for continuation of therapy when initial criteria have been met **AND** there is documentation of beneficial response from previous course of treatment:

1. Clinical benefit to treatment as evidenced by:

   a. A stable BMD or an increasing BMD after a minimum trial of one year of therapy; **or**

   b. Member has not experienced a fragility fracture while on Prolia (denosumab) treatment.

AND

2. Absence of unacceptable toxicity from the drug (e.g., severe symptomatic hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, dermatological adverse reactions, severe infection, severe hypersensitivity/anaphylaxis, musculoskeletal pain, etc.).

AND

3. Confirmation that member is still receiving the recommended calcium and vitamin D supplementation.

STEP THERAPY

Step therapy criteria do not apply for members who are currently being treated with the requested medications. Step therapy is only applied for members that are new to therapy (have not received the requested drug in the last 365 days.

A. PREFERRED DRUGS: Zoledronic acid (first preferred) and ibandronate (second preferred)-- NO STEP THERAPY REQUIRED

B. Prolia (denosumab), may be authorized when the clinical criteria above are met **AND** member meets **ONE** of the following with documentation:

1. History of use of zoledronic acid or ibandronate resulting in minimal clinical response to therapy (defined as a decrease in BMD or a fracture while on therapy);

OR

2. *Contraindication, intolerance, or adverse event(s) to zoledronic acid or ibandronate;

   *Contraindications to zoledronic acid therapy: Hypersensitivity to zoledronic acid or any component of the formulation; hypocalcemia (*Reclast* only); CrCl <35 mL/minute and in those with evidence of acute renal impairment (*Reclast* only).

   *Contraindications to ibandronate: Hypocalcemia; known hypersensitivity to ibandronate or any component of the formulation

OR

3. Member has previously received Prolia (denosumab) within the past 365 days and therefore not subject to step therapy requirements.

DOSAGE AND AUTHORIZATION TIMEFRAMES

1. Recommended Dose: 60 mg once every 6 months

2. Maximum Quantity: ONE injection every 6 months (60 billable units every 6 months); TWO injections per year.

3. Authorization Period: Re-authorization is required every 12 months based on criteria in the 'Continuation of Therapy' section.

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Bone-Modifying Agent; Monoclonal Antibody

ROUTE OF ADMINISTRATION: Subcutaneous

FDA-APPROVED INDICATIONS: Osteoporosis/bone loss (Prolia [denosumab])
1. Osteoporosis, fracture risk reduction (males and postmenopausal females)
2. Osteoporosis, glucocorticoid-induced (males and females)
3. Androgen deprivation therapy-induced bone loss in males with prostate cancer, treatment *(not addressed in policy)*
4. Aromatase inhibitor-induced bone loss in females with breast cancer, treatment *(not addressed in this policy)*

COMPENDIAL APPROVED (OFF-LABELED) USES: NONE

CONTRAINDICATIONS: Hypersensitivity (systemic) to denosumab or any component of the formulation; preexisting hypocalcemia; pregnancy.

OTHER CONSIDERATIONS:

Clinical Considerations: Correct hypocalcemia and vitamin D deficiency (e.g., to a 25-hydroxyvitamin D level ≥20 ng/mL [≥50 nmol/L]), when appropriate, before initiation, and ensure adequate calcium and vitamin D intake during therapy.

CLINICAL SUMMARY / APPENDIX

FDA-labeled dose of Prolia (denosumab): 60 mg administered as a single subcutaneous (SC) injection once every 6 months. All patients should receive calcium 1000 mg daily and at least 400 IU of vitamin D daily.

Osteoporosis is a skeletal disorder characterized by decreased bone mass. The most common diagnostic test is the DEXA scan (dual energy X-ray absorptiometry) to measure BMD (bone mineral density). Results are typically reported as a T-score, which compares the BMD of the subject to a standard BMD of a healthy young adult. T-Scores are reported as standard deviations (SD) World Health Organization criteria:

- Normal - T-Score within 1 SD of normal
- Osteopenia- T-Score of -1 to -2.5 SD below normal
- Osteoporosis- T-Score of -2.5 or less SD below normal
- Severe Osteoporosis- T-Score of -2.5 or less SD below normal with fragility fractures

Fracture Risk Assessment Tool (FRAX®) tool: The FRAX® tool (www.shef.ac.uk/FRAX) was developed by the World Health Organization (WHO) to evaluate fracture risk of patients. It integrates clinical risk factors with BMD at the femoral neck. The FRAX® tool provides the 10-year probability of fracture. The output is a 10-year probability of hip fracture and a 10-year probability of major osteoporotic fracture (forearm, shoulder, or clinical vertebral fracture).

The US National Osteoporosis Foundation recommends treatment of osteopenic patients whose FRAX score for hip fracture is 3% or greater, or whose risk for other bone fracture is greater than 20%.

Professional Society Guidelines

The National Osteoporosis Foundation (NOF) states that the diagnosis of osteoporosis can be established by either measurement of BMD or by the occurrence of adulthood hip or vertebral fracture in the absence of major trauma (such as a motor vehicle accident or multiple story fall). For evaluation, BMD measurement should be taken by central dual-energy X-ray absorptiometry at the lumbar spine and femoral neck (hip). A BMD taken at the one-third (33%) radius site can be used for diagnosing osteoporosis when the hip and lumbar spine cannot be measured or are unusable or uninterpretable. In postmenopausal women and men age 50 and older, WHO diagnostic T-score criteria is applied to the BMD measurement. For those patients that are not postmenopausal women and not men age 50 and older, WHO BMD classification should not be applied, and the diagnosis of osteoporosis should not be made on densitometric criteria alone.

The American College of Endocrinology (AACE/ACE) (2020) osteoporosis treatment guidelines stratify initial treatment based on risk status.

- For individuals at high risk or no prior fractures, initial therapy options include bisphosphonates (alendronate, risedronate, or zoledronic acid) or denosumab.
- The 2020 AACE Guidelines created a 'very high' risk category for post-menopausal women with osteoporosis. The following patients are considered a very high fracture risk:
    - Patients with a recent fracture (within the past 12 months), fractures while on approved osteoporosis therapy multiple fractures, or fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids),
    - Patients with a very low T-score (less than -3.0),
    - Patients with a high risk for falls or history of injurious falls, and very high fracture probability by FRAX (e.g., major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm.

Patients who have been diagnosed with osteoporosis but do not meet the above definition of very high fracture risk are to be considered to be at high risk (AACE, 2020).

The AACE recommends alendronate, denosumab, risedronate, and zoledronate as appropriate initial therapy for most osteoporotic patients with high fracture risk. Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for patients unable to use oral therapy and as initial therapy for patients at very high fracture risk (AACE, 2020).

The Endocrine Society osteoporosis guideline update (2020) recommends initial therapy with bisphosphonates (alendronate, risedronate, zoledronic acid, or ibandronate) or alternatively denosumab for those at high risk.

According to UpToDate (2023), "There are currently no head-to-head trials comparing the anti-fracture efficacy of denosumab with other available osteoporosis therapies (e.g., oral and intravenous bisphosphonates, teriparatide). The reduction in vertebral fracture noted with denosumab is similar to the reductions reported for subcutaneous teriparatide and intravenous zoledronic acid and greater than that reported for oral alendronate. However, these data are based upon clinical trials in different patient populations, not head-to-head comparison trials." (Rosen 2023)

Monitoring Parameters: For osteoporosis, it is recommended that serial BMD should be evaluated at baseline and every 1 to 3 years (usually at ~2 years following initiation of therapy, then more or less frequently depending on patient-specific factors and stability of BMD) (AACE/ACE [Camacho 2020]; ES [Eastell 2019]; NOF [Cosman 2014]); may consider monitoring biochemical markers of bone turnover (eg, fasting serum CTX or urinary NTX) at baseline, 3 months, and 6 months, to assess treatment response (ES [Eastell 2019]).

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Government Agency

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IMPORTANT REMINDER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section below to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

POLICY HISTORY

Version	Approval Date	Summary of Changes
1	9/27/2023	New Policy
1.1	5/28/2024	Added Jubbonti (denosumab-bbdz): Biosimilar to Prolia (FDA approved March 2024). Updated name of policy from Prolia (denosumab) to Prolia Products (denosumab) to include biosimilar product.