**Original Effective Date: 07/01/2012**
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**Last P&T Approval/Version: 07/30/2025**
**Next Review Due By: 07/2026**
**Policy Number: C8848-A**

# Prolia (denosumab) and Biosimilars

## PRODUCTS AFFECTED

Prolia (denosumab), Jubbonti (denosumab-bbdz), Stoboclo (denosumab-bmwo), Conexxence (denosumab-bnht)
*Xgeva (denosumab) - SEE XGEVA (DENOSUMAB) MHI C8849-A

## COVERAGE POLICY

*Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.*

***Documentation Requirements:***
*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.*

**DIAGNOSIS:**
Osteoporosis at high risk for fracture, Glucocorticoid-induced osteoporosis, Men at high risk for fracture and receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer, Women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

**REQUIRED MEDICAL INFORMATION:**
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

Drug and Biologic Coverage Criteria

A. ALL INDICATIONS:

1. (a) IF THIS IS A PHARMACY BENEFIT REQUEST FOR A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Documentation of medication(s) tried, dates of trial(s) and reason for treatment failure(s) is required
   AND
   (b) If request is for reference product with a biosimilar available for initial or continuation of therapy requests: Documentation of a trial and failure, serious side effects or contraindication to a majority (not more than 3) biosimilar product(s) is required (unless otherwise specified per applicable state regulations and/or there is data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs).
   [DOCUMENTATION REQUIRED: Document when the preferred biologic product or biosimilar was tried and the length of the trial period. Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache).]
   OR
2. FOR INITIAL OR CONTINUATION OF THERAPY REQUESTS OF A PHYSICIAN ADMINISTERED MEDICATION: BIOSIMILAR DRUGS are preferred when requested as a physician administered drug per applicable state regulations and/or there is a lack of data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs. A reference medication is approved under the following conditions:
   a) Treatment with at least two associated biosimilar drug(s) has been ineffective, resulted in serious side effects, or is contraindicated (i.e., an allergic reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR an adverse reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure while taking the preferred biologic product or biosimilar documented by patient diary or medical charted notes)

   [DOCUMENTATION REQUIRED: Document when the preferred biologic product or biosimilar was tried and the length of the trial period. Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache).]
   AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to denosumab include: hypocalcemia, pregnancy, known hypersensitivity to denosumab.]

B. POSTMENOPAUSAL OSTEOPOROSIS AND MEN WITH OSTEOPOROSIS AT HIGH RISK OF FRACTURE:

1. Documented diagnosis of postmenopausal osteoporosis in women who are at a high risk of fracture, OR osteoporosis in men
   AND
2. (a) The member has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist)
   OR
   (b) The member has had an osteoporotic fracture or a fragility fracture of the spine, hip, proximal humerus, pelvis, or distal forearm
   OR
   (c) The member has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip and/or 33% [one-third] radius

[wrist]) and the prescriber determines the member is at high risk for fracture
AND

3. Documentation of trial and failure (12-month total trial), contraindication, or serious side effects to bisphosphonate therapy (oral and/or IV). Document drug, date, and duration of trial.
   NOTE: Treatment failure is defined by progression of bone loss as documented by bone density measurements (BMD) after at least 12 months of therapy OR Occurrence of an osteoporotic fracture after having been compliant on at least 12 months of therapy on an oral bisphosphonate

C. GLUCOCORTICOID-INDUCED OSTEOPOROSIS:

1. Documented diagnosis of glucocorticoid-induced osteoporosis
   AND
2. Documentation of history of prednisone or its equivalent at a dose of > 2.5 mg/day for > 3 months
   AND
3. (a) The member has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist)
   OR
   (b) The member has had an osteoporotic fracture or a fragility fracture of the spine, hip, proximal humerus, pelvis, or distal forearm
   OR
   (c) Fracture Risk Assessment Tool (FRAX) (GC-adjusted) 10-year risk of major osteoporotic fracture score of 20% or greater OR FRAX (GC-adjusted) 10-year risk of hip fracture score of 3% or greater indicating member is at high risk for fracture
   AND
4. Documentation of trial and failure, serious side effects, or clinical contraindication to one oral generic and one intravenous generic bisphosphonate therapy
   NOTE: An exception to the requirement of one oral generic and one intravenous generic bisphosphonate can be made if the member has already had a trial of brand oral and intravenous bisphosphonate.

D. CANCER INDUCED BONE LOSS:

1. Diagnosis of hormone receptor positive breast cancer OR non-metastatic prostate cancer
   AND
2. Documentation member is currently or has received androgen deprivation therapy for nonmetastatic prostate cancer OR member is at high risk for bone fractures after receiving adjuvant aromatase inhibitor therapy for breast cancer
   AND
3. Documentation member has tried and failed ONE of the following: zoledronic acid 4 mg, pamidronate, OR oral bisphosphonate

**CONTINUATION OF THERAPY:**

A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. a) Documentation of stable bone mineral density (BMD) or an increasing BMD after a minimum trial of one year of therapy OR demonstrate improvement by providing reference to the sequential progression or stability of the BMD. T-score test results may date back as far as five years, depending on level of BMD progression retesting may be done from every one to five years.
   OR
   b) Documentation member is currently or has received androgen deprivation therapy for nonmetastatic prostate cancer OR member is at high risk for bone fractures after receiving adjuvant aromatase inhibitor therapy for breast cancer

AND

3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., severe hypocalcemia in patients on dialysis, etc.)

**DURATION OF APPROVAL:**
Initial authorization: 12 months, Continuation of therapy: 12 months

**PRESCRIBER REQUIREMENTS:**
None

**AGE RESTRICTIONS:**
18 years of age and older

**QUANTITY:**
One injection (60MG) every 6 months

**PLACE OF ADMINISTRATION:**
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.

## DRUG INFORMATION

**ROUTE OF ADMINISTRATION:**
Subcutaneous

**DRUG CLASS:**
RANK Ligand (RANKL) Inhibitors

**FDA-APPROVED USES:**
Indicated for treatment:

- Of postmenopausal women with osteoporosis at high risk for fracture
- To increase bone mass in men with osteoporosis at high risk for fracture
- Of glucocorticoid-induced osteoporosis in men and women at high risk for fracture
- To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

**COMPENDIAL APPROVED OFF-LABELED USES:**
None

## APPENDIX

**APPENDIX:**
A biosimilar is a highly similar version of a brand name biological drug that meets strict controls for structural, pharmaceutical, and clinical consistency. A biosimilar manufacturer must demonstrate that there are no meaningful clinical differences (i.e., safety and efficacy) between the biosimilar and the reference product. Clinical performance is demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.[1]
As costs for biological specialty drugs continue to rise, the growing biosimilar market will benefit providers and patients by broadening biological treatment options and expanding access to these medications at lower costs. Molina Healthcare, Inc. continues to be committed to continually reevaluating preferred strategies and applying innovative cost-controls to ensure patients receive safe, effective, and quality

healthcare. This commitment includes potentially creating a preference for biosimilars when value can be added without compromising patient satisfaction and safety.

1. Food and Drug Administration. Biosimilar and Interchangeable Products. Retrieved from https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products. Accessed October 8, 2019.

**Appendix 1:**

Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Renal insufficiency (creatinine clearance < 30 to 35 ml/min)

**Appendix 2:**

WHO Fracture Risk Assessment Tool 10-year probability of major osteoporotic fracture; calculation tool available at: http://www.shef.ac.uk/FRAX/tool.jsp

## BACKGROUND AND OTHER CONSIDERATIONS

**BACKGROUND:**

Denosumab is a human monoclonal antibody. It acts by reducing the production of osteoclasts and therefore by reducing the turnover and destruction of bone. It does this by binding to the RANKL molecule and rendering it unable to bind to the RANK receptor.

Denosumab (Prolia) is FDA-approved for treatment of osteoporosis in postmenopausal women at high risk for fracture. Injected subcutaneously once every 6 months, denosumab has been shown to increase BMD and reduce the incidence of new vertebral and hip and other non-vertebral fractures in postmenopausal women (SR Cummings et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. 2009). It has been shown to increase BMD more than alendronate, but no studies directly comparing the efficacy of denosumab and bisphosphonates for prevention of fractures are available.

The optimal duration of treatment with denosumab is not known. Data are available supporting its continued efficacy for 10 years (HG Bone et al. 2017).

Denosumab's effects on BMD and bone turnover are reversible with discontinuation of the drug. Discontinuation of the drug after 24 months of treatment resulted in increased bone turnover markers within 3 months and a decline in BMD to pretreatment values within 2 years (HG Bone etal. 2017). Vertebral fractures have been reported 8-16 months after stopping denosumab (AD Anastasilakis etal. 2017).

Drug holidays are not recommended. If denosumab is stopped, administering another drug, typically bisphosphonate, is recommended to prevent a rapid decline in BMD. Switching from denosumab to teriparatide has resulted in progressive or transient bone loss (BZ Leder et al. 2015).

Denosumab is not considered initial therapy for most members with osteoporosis. Initial therapy for most members includes lifestyle measures and oral bisphosphonates (Rosen, HN 2017).

Due to the lack of long-term safety data and the availability of other agents, denosumab is not recommended for osteoporosis prevention (Rosen, HN 2017).

Bisphosphonate treatment for prevention of bone loss, regardless of cause, is the standard of care due to the body of evidence supporting efficacy and track record of safety.

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 member populations, not head-to-head comparison trials. There are few studies evaluating the benefits and risks of denosumab in men with osteoporosis that is unrelated to androgen deprivation therapy. According to new clinical guidelines from the American College of Physicians (ACP), women with osteoporosis should be treated with one of the three main bisphosphonates or the biologic denosumab for a duration of 5

years, during which time monitoring of bone-mineral density (BMD) is not necessary (ACP 2017). The ACP also advises physicians to prescribe generics over brand- name drugs whenever possible and to discuss medication adherence with their members, especially for bisphosphonates.
Serious risks associated with denosumab include hypocalcemia, osteonecrosis of the jaw (ONJ), atypical femur fractures, and serious infections.
Denosumab suppresses bone remodeling and therefore may contribute to adverse outcomes, such as ONJ.

**FDA Safety Alert for Severe Hypocalcemia in Patients on Dialysis Receiving Prolia**
FDA review of interim results from an ongoing safety study of Prolia suggests an increased risk of hypocalcemia, in patients with advanced kidney disease. Preliminary results from a separate internal FDA study further investigating hypocalcemia in dialysis patients treated with Prolia show a substantial risk with serious outcomes, including hospitalization and death. Health care professionals should consider the risks of hypocalcemia with the use of Prolia in patients on dialysis. When Prolia is used in these patients, adequate calcium and vitamin D supplementation and frequent blood calcium monitoring, possibly more often than is already being conducted, may help decrease the likelihood or severity of these risks. Advise patients on dialysis to immediately seek help if they experience symptoms of hypocalcemia.

Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of Jubbonti, Stoboclo, And Conexxence has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in their Full Prescribing Information.

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**
All other uses of denosumab are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to denosumab include: hypocalcemia, pregnancy, and known hypersensitivity to denosumab. Do not take with Xgeva. Hypocalcemia must be corrected prior to initiating denosumab.

**Exclusions/Discontinuation:**
Do not use concurrently with bisphosphonates, Xgeva (denosumab), parathyroid hormone analog (e.g., Forteo, Tymlos), or anabolic agent (e.g., Evenity).

**OTHER SPECIAL CONSIDERATIONS:**
Denosumab has a Black Box Warning for severe hypocalcemia in patients with advanced kidney disease. Patients with advanced chronic kidney disease are at greater risk of severe hypocalcemia following denosumab administration. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported. The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia. Prior to initiating denosumab in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with denosumab in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD.

Denosumab should be administered by a healthcare professional.

Patients should be counseled to concurrently take calcium (1000 mg) and vitamin D (400-1200 international units) supplements in conjunction with denosumab.

## CODING/BILLING INFORMATION

***CODING DISCLAIMER.*** *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective*

*at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

| HCPCS CODE | DESCRIPTION |
|---|---|
| J0897 | Injection, denosumab, 1 mg |
| Q5136 | Injection, denosumab-bbdz (jubbonti/wyost), biosimilar, 1 mg |

**AVAILABLE DOSAGE FORMS**:
Prolia SOSY 60MG/ML single-dose prefilled syringe
Jubbonti SOSY 60MG/ML single-dose prefilled syringe

## REFERENCES


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2. Jubbonti (denosumab-bbdz) injection, for subcutaneous use [prescribing information]. Princeton, NJ: Sandoz Inc.; October 2024.
3. Stoboclo (denosumab-bmwo) injection, for subcutaneous use [prescribing information]. Jersey City, NJ: Celltrion USA, Inc.; February 2025.
4. Conexxence (denosumab-bnht) injection, for subcutaneous use [prescribing information]. Lake Zurich, IL: Fresenius Kabi USA, LLC; March 2025.
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Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: A living clinical guideline from the American College of Physicians. Annals of Internal Medicine, 176(2), 224–238. doi:10.7326/m22-1034

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| SUMMARY OF REVIEW/REVISIONS | DATE |
|---|---|
| REVISION- Notable revisions:<br>Products Affected<br>Required Medical Information<br>Continuation of Therapy<br>Appendix<br>Background<br>Contraindications/Exclusions/Discontinuation<br>Other Special Considerations<br>Available Dosage Forms<br>References | Q3 2025 |
| REVISION- Notable revisions:<br>Required Medical Information<br>FDA-Approved Uses<br>Other Special Considerations<br>References | Q3 2024 |
| REVISION- Notable revisions:<br>Products Affected<br>Required Medical Information<br>Continuation of Therapy<br>Quantity<br>Place of Administration<br>Background<br>Contraindications/Exclusions/Discontinuation<br>References | Q3 2023 |

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|---|---|
| REVISION- Notable revisions:<br>Required Medical Information<br>Continuation of Therapy<br>Appendix<br>Background<br>Contraindications/Exclusions/Discontinuation<br>Other Special Considerations<br>References | P&T QUARTER/YEAR |
| Q2 2022 Established tracking in new format | Historical changes on file |