Denosumab (Prolia®)	Place of Service Office Administration Home Infusion Outpatient Facility Administration Infusion Center Administration HCPCS: J0897 per 1mg

Conditions listed in policy (*see criteria for details*)

- Osteoporosis
- To increase bone mineral density in breast cancer, secondary to hormone ablation therapy
- To increase bone mineral density in prostate cancer, secondary to androgen deprivation therapy

AHFS therapeutic class: bone resorption inhibitor

Mechanism of action: Denosumab is a monoclonal antibody that inhibits RANK ligand activity and prevents osteoclast formation, leading to decreased bone resorption and increased bone mass

(1) Special Instructions and Pertinent Information

Covered under the Medical Benefit, please submit clinical information for prior authorization review via fax.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for Prolia® (denosumab) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Osteoporosis

1. One of the following:
    a. Provider attestation of one or more non-traumatic fractures, OR
    b. T-scores less than -2.5 S.D, OR
    c. T-score is between -1.0 and -2.5 and patient is at high risk for fracture

    [e.g. multiple risk factors or 10-year hip fracture probability >/= 3% or a 10-year major osteoporosis-related fracture probability >/= 20% based on USA-adapted WHO absolute fracture risk model (FRAX risk assessment)]

AND

2. One of the following:
    a. Intolerance to prior oral and IV bisphosphonate therapy that would cause discontinuation, or contraindication to oral and IV bisphosphonates, OR
    b. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate, OR
    c. Patient is initiating or continuing long-term glucocorticoid treatment (≥3 months), OR
    d. Patient is at very high risk of fracture by meeting at least one of the following:
        i. Fracture while taking a bisphosphonate, or
        ii. Provider attestation that patient has experienced a recent fracture (within the past 12 months) or history of multiple fractures, or

iii. Provider attestation that patient experienced a fracture while on long-term glucocorticoid therapy, or
iv. T-score less than −3.0, or
v. Provider attestation that patient is at high risk for falls, or
vi. 10-year hip fracture probability of > 4.5% based on FRAX score, or
vii. 10-year major osteoporosis-related fracture probability > 30% based on FRAX score

Covered Dose
Up to 60 mg SC administered once every 6 months

Coverage Period
Indefinite

ICD-10:
M81.0-M81.9

Increase BMD in patients with hormone-responsive breast cancer undergoing hormone ablation therapy

1. Patient is currently taking an aromatase inhibitor, tamoxifen, or GNRH agonist, **AND**
2. Meets one of the following:
    a. Patient is unable to take an oral bisphosphonate and has intolerance or contraindication to an IV bisphosphonate, OR
    b. Patient experienced a non-traumatic fracture while on a bisphosphonate, OR
    c. Patient has had intolerable gastric side effects to a monthly oral bisphosphonate regimen that would cause him/her to discontinue therapy, OR
    d. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate

Covered Dose
Up to 60 mg SC administered once every 6 months

Coverage Period
Cover yearly

ICD-10:
C50.X11, C50.X12, C50.X19
(X = numbers 0-6, 8, 9)

C50.X21, C50.X22, C50.X29
(X=numbers 1-6, 8, 9)

Z85.3

Increase BMD in patients with prostate cancer undergoing androgen deprivation therapy

1. Patient is currently taking androgen deprivation therapy [e.g. gonadotropin-releasing hormone GnRH agonists such as leuprolide (Lupron)] or has had surgical castration, **AND**
2. Meets one of the following:
    a. Patient is unable to take an oral bisphosphonate and has intolerance or contraindication to an IV bisphosphonate, OR
    b. Patient experienced a non-traumatic fracture while on a bisphosphonate, OR
    c. Patient has had intolerable gastric side effects to a monthly oral bisphosphonate regimen that would cause him/her to discontinue therapy, OR
    d. Inadequate response, as evidenced by documented worsening BMD, following at least two years of therapy with a bisphosphonate

Covered Dose
Up to 60 mg SC administered once every 6 months

Coverage Period
Cover yearly

ICD-10:
C61

---

(3) The following condition(s) DO NOT require Prior Authorization/Preservice
All requests for Prolia® (denosumab) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically for the following condition(s)
Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- Combination therapy with other agents for osteoporosis

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information
How supplied:
Single-use prefilled syringe containing 60 mg in a 1 mL solution
Single-use vial containing 60 mg in a 1 mL solution

Table 1. Oral Bisphosphonates

Brand/generic	Daily	Weekly	MONTHLY
Fosamax/alendronate	5-10mg	35mg-70mg	
Boniva/ ibandronate			**150mg**
Actonel/ risedronate	5mg	35mg	**75mg x2 or 150mg x 1**

Atelvia/ risedronate		35mg delayed release	

CLINICAL Pharmacology accessed 1/2015

Table 2. Comparison of PIs for Osteoporosis Treatment

	Oral bisphosphonates	IV bisphosphonates	Prolia
Contraindications			
Abnormalities of the esophagus such as **stricture or achalasia**	X		
Inability to stand/sit upright for at least 30 minutes	X		
Hypocalcemia	X	X	X
CrCl < 35 mL/min	"Not recommended"	Contraindicated	No dose adj for renal impairment
Pregnancy	Category C	Category D: "Can cause fetal harm"	Contraindicated
Warnings and Precautions			
Upper Gastrointestinal Adverse Reactions	X		
Severe Bone, Joint, Muscle Pain	X In post-marketing experience, time to onset of symptoms varied from one day to several months after starting the drug. Most patients had relief of symptoms after stopping. A subset had recurrence of symptoms when re-challenged with the same drug or another bisphosphonate.		X In post-marketing experience, the time to onset of symptoms varied from one day to several months after starting Prolia.
Osteonecrosis of the Jaw	X	X	X
Serious infections including skin infections			X
Dermatologic reactions			X
Suppression of bone turnover			X
More Common Adverse Events			
Gastrointestinal:			
Abdominal pain	X		
Acid regurgitation	X		
Constipation	X		
Diarrhea	X	X	
Nausea	X	X	
Vomiting		X	
Dyspepsia	X		
Musculoskeletal:			
Musculoskeletal pain	X		X
Back pain			X

Myalgia		X	
Arthralgia		X	X
Pain in extremity		X	X
Other:			
Nasopharyngitis			X
Cystitis			X
Pyrexia		X	
Flu-like illness		X	
Headache		X	
Eye inflammation		X	
Pancreatitis			X
Hypercholesterolemia			X

Table 3. Clinical Risk Factors for Osteoporosis-Related Fractures in POSTMENOPAUSAL WOMEN

Risk Factor
Prior low-trauma fracture as an adult
Advanced age (>/= 65yrs)
Low body weight [<57.6 kg(127lb)]
Family history of osteoporosis or fractures
Use of corticosteroids
Cigarette smoking
Excessive alcohol consumption (≥ 3 drinks per day)
Secondary osteoporosis (e.g. rheumatoid arthritis)
Early menopause

https://www.aace.com/files/postmenopausal-guidelines.pdf

FRAX tool: FRAX is a tool developed by the World Health Organization (WHO) to predict a patient's risk of having an osteoporosis-related fracture in the next 10 years. Generally it is used for people not already being treated for osteoporosis. The calculation tool can be found at this link: http://www.shef.ac.uk/FRAX/

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- 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.
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- National Comprehensive Cancer Network. Breast Cancer (Version 4.2022). Available at: www.nccn.org.
- National Comprehensive Cancer Network. Prostate Cancer (Version 4.2022). Available at: www.nccn.org.
- Prolia (denosumab) [Prescribing information]. Thousand Oaks, CA: Amgen Inc.; 1/2023.
- 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
- 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.

(7) Policy Update

Date of last review: 4Q2023

Date of next review: 4Q2024

Changes from previous policy version:

- No clinical change to policy following routine annual review.

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee