Washington State Health Care Authority

Bone Density Regulators – Rank Ligand (RANKL) Inhibitors

Medical policy no. 30.04.48-2 Effective Date: Month, 1, Year

Related medical policies:

Policy Name	Indications
Bone Density Regulators – Sclerostin Inhibitors	Osteoporosis/Bone loss
Bone Density Regulators – Parathyroid Hormone Derivatives	Postmenopausal Osteoporosis Male Osteoporosis Glucocorticoid Induced Osteoporosis
Bone Density Regulators – Calcitonins	Osteoporosis/Bone loss

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Denosumab (Prolia, Xgeva)	**Denosumab (Prolia, Xgeva)** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Postmenopausal Osteoporosis	Denosumab (Prolia) may be covered when all the following documented criteria are met:

	1. Patient is 18 years of age or older; **AND** 2. Diagnosis of osteoporosis; **AND** 3. Patient is a postmenopausal female; **AND** 4. At least **ONE** of the following fracture risk categories is met: a. Presence of fragility fractures of the hip or spine regardless of bone mineral density; **OR** b. T-score ≤ -2.5 in the lumbar spine, femoral neck, total hip; **OR** c. T-score between -1 and -2.5 with a history of recent fragility fracture of proximal humerus, pelvis, or distal forearm; **OR** d. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **AND** 5. Medication will not be used in combination with other bone density regulators (e.g., bisphosphonates, raloxifene, Xgeva); **AND** 6. History of at least **ONE** of the following: a. Treatment with at least one Preferred Apple Health Preferred Drug List (PDL) oral or intravenous bisphosphonate medication has been ineffective unless all are contraindicated or not tolerated [minimum trial of 12 months]; **OR** b. Treatment with at least one Preferred Apple Health Preferred Drug List (PDL) selective estrogen receptor modulator (SERM) medication has been ineffective unless all are contraindicated, or not tolerated [minimum trial of 24 months]. If ALL criteria are met, the request will be authorized for 12 months **Criteria (Reauthorization)** Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Criteria 5 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., patient has not suffered a fragility fracture, bone mineral density continues to improve/remain stable). If ALL criteria are met, the request will be authorized for 12 months
Glucocorticoid-induced osteoporosis denosumab (Prolia)	Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Diagnosis of osteoporosis; **AND**

	3. Patient will be initiating or is continuing systemic glucocorticoid therapy at a daily dosage equivalent to ≥ 7.5 mg of prednisone and is expected to remain on glucocorticoid therapy for at least 6 months; **AND** 4. At least **ONE** of the following fracture risk categories is met: a. Presence of fragility fractures of the hip or spine regardless of bone mineral density; **OR** b. T-score ≤ -2.5 in the lumbar spine, femoral neck, total hip; **OR** c. T-score between -1 and -2.5 with a history of recent fragility fracture of proximal humerus, pelvis, or distal forearm; **OR** d. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **AND** 5. Medication will not be used in combination with other bone density regulators (e.g., bisphosphonates, raloxifene, Xgeva); **AND** 6. Treatment with at least one Preferred Apple Health Preferred Drug List (PDL) oral or intravenous bisphosphonate medication indicated for glucocorticoid induced osteoporosis has been ineffective unless all are contraindicated or not tolerated [minimum trial of 12 months]. If ALL criteria are met, the request will be authorized for **12 months** **Criteria (Reauthorization)** Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Patient has not suffered a fragility fracture while on treatment; **AND** 2. Criteria 5 above continues to be met; **AND** 3. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., patient has not suffered a fragility fracture, bone mineral density continues to improve/remain stable). If ALL criteria are met, the request will be authorized for **12 months**
Treatment of bone loss in men with prostate cancer denosumab (Prolia)	Denosumab (Prolia) may be approved when all the following documented criteria are met: **1.** Patient is 18 years of age or older; **AND** **2.** Patient has a diagnosis of bone loss or osteoporosis indicated by one or more of the following: a. Presence of fragility fractures of the hip or spine regardless of bone mineral density; **OR** b. T-score ≤ -2.5 in the lumbar spine, femoral neck, total hip; **OR** c. T-score between -1 and -2.5 with a history of recent fragility fracture of proximal humerus, pelvis, or distal forearm; **OR**

	d. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **AND** 3. Patient is currently receiving androgen deprivation therapy (ADT) (e.g., leuprolide, degarelix, relugolix) for non-metastatic prostate cancer; **AND** 4. Medication will not be used in combination with denosumab (Xgeva) If ALL criteria are met, the request will be authorized for **12 months**
	Criteria (Reauthorization) Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Criteria 3 and 4 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., patient has not suffered a fragility fracture, bone mineral density continues to improve/remain stable). If ALL criteria are met, the request will be authorized for **12 months**
Treatment of bone loss in women with breast cancer denosumab (Prolia)	Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Patient has a diagnosis of bone loss or osteoporosis indicated by one or more of the following: a. Presence of fragility fractures of the hip or spine regardless of bone mineral density; **OR** b. T-score ≤ -2.5 in the lumbar spine, femoral neck, total hip; **OR** c. T-score between -1 and -2.5 with a history of recent fragility fracture of proximal humerus, pelvis, or distal forearm; **OR** d. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **AN** 3. Patient is receiving adjuvant aromatase inhibitor therapy (e.g., anastrozole, exemestane, letrozole) for breast cancer; **AND** 4. Medication will not be used in combination with denosumab (Xgeva) If ALL criteria are met, the request will be authorized for **12 months**
	Criteria (Reauthorization) Denosumab (Prolia) may be approved when all the following documented criteria are met: 1. Criteria 3 and 4 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., patient has not suffered a fragility fracture, bone mineral density continues to improve/remain stable).

	If ALL criteria are met, the request will be authorized for **12 months**
Multiple Myeloma and bone metastasis from solid tumors denosumab (Xgeva)	Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Patient has one of the following: a. Diagnosis of multiple myeloma with skeletal-related events (i.e., radiation to bone, pathologic fracture, surgery to bone, and spinal cord compression) ; **OR** b. Bone metastases from solid tumors (i.e., metastatic breast cancer, metastatic castration-resistant prostate cancer, or metastatic lung cancer) **AND** 3. History of failure, contraindication, or intolerance to zoledronic acid**; AND** 4. Medication will not be used in combination with denosumab (Prolia) If ALL criteria are met, the request will be authorized for **12 months**
	Criteria (Reauthorization) Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Criteria 4 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., patient has not suffered a fracture, bone mineral density continues to improve/remain stable). If ALL criteria are met, the request will be authorized for **12 months**
Giant cell tumor of bone denosumab (Xgeva)	Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Patient is 12 years of age or older AND skeletally mature; **AND** 2. Diagnosis of giant cell tumor of the bone; **AND** a. Disease is unresectable or surgical resection is likely to result in severe morbidity; **OR** b. Disease is recurrent or metastatic 3. Medication will not be used in combination with denosumab (Prolia). If ALL criteria are met, the request will be authorized for **12 months**
	Criteria (Reauthorization) Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Criteria 3 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., decrease in tumor size or spread of tumor).

	If ALL criteria are met, the request will be authorized for **12 months**
Hypercalcemia of malignancy denosumab (Xgeva)	Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Diagnosis of hypercalcemia of malignancy; **AND** 3. Baseline corrected serum calcium > 12.5 mg/dL 3. Treatment with at least one Preferred Apple Health Preferred Drug List (PDL) oral or intravenous bisphosphonate medication indicated for glucocorticoid induced osteoporosis has been ineffective unless all are contraindicated or not tolerated [minimum trial of 12 months]. 4. Medication will not be used in combination with denosumab (Prolia). If ALL criteria are met, the request will be authorized for **12 months**
	Criteria (Reauthorization)
	Denosumab (Xgeva) may be approved when all the following documented criteria are met: 1. Criteria 4 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., decrease in corrected serum calcium). If ALL criteria are met, the request will be authorized for **12 months**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
denosumab (Prolia)	Treatment of postmenopausal women with osteoporosis at high risk for fracture; Treatment to increase bone mass in men with osteoporosis at high risk for fracture; Treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture; Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer; Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer	60 mg every 6 months	• 60 mg/1 mL in a single-dose prefilled syringe: 1 syringe (60 mg or 60 billable units) every 6 months

denosumab (Xgeva)	Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors; Treatment of adults and skeletally mature adolescents with giant cell tumor of the bone that is unresectable or where surgical resection is likely to result in severe morbidity; Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy	Multiple Myeloma: 120 mg every 4 weeks Giant cell tumor of bone: 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy Hypercalcemia of malignancy: 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy	• 120 mg/1.7 mL in a single-dose vial: ○ Load: 4 vials per 28 days (480 mg or billable units) ○ Maintenance: 1 vial every month (120 mg or billable units)

Coding:

HCPCS Code	Description
J0897	Injection, denosumab, 1 mg

Background:

Osteoporosis is characterized by decreased bone mass and increased fracture risk, most commonly at the spine, hip, and wrist. The definition of osteoporosis with high risk of fracture is defined for men and women as BMD T-score of spine, femoral neck, and/or total hip <-2.5 without fracture, having history of hip or vertebral fracture regardless of BMD, T-score ≤ -1 and a history of recent fracture of proximal humerus, pelvis, or distal forearm, T-score between -1.0 and -2.5 in the spine, femoral neck, or total hip with a -20% 10-year FRAX risk of any fracture or -3% risk of hip fracture, and receiving long-term glucocorticoid doses greater than or equal to prednisone 7.5mg per day. The treatment of osteoporosis consists of lifestyle management (e.g., adequate calcium and vitamin D, exercise, smoking cessation, fall prevention measures, and avoidance of heavy alcohol use) and pharmacologic therapy. Patients with the highest risk of fracture are expected to derive the greatest benefit from medication therapy. The 2020 AACE/ACE treatment guideline recommendations are as follows:

1. Initial treatment for high fracture risk: alendronate, denosumab, risedronate, or zoledronic acid
2. Treatment for very-high fracture risk or patients who cannot tolerate or adhere to oral bisphosphonates: zoledronic acid, abaloparatide, denosumab, romosozumab, teriparatide

Additionally, the 2020 Endocrine Society guidelines recommend bisphosphonates as initial treatment for high-risk patients, while denosumab may be considered as an alternative initial treatment. For patients with a very high risk of fracture, teriparatide and abaloparatide are recommended. It is recommended that antiresorptive therapies follow treatment with parathyroid hormones.

References

1. Prolia [package insert]. Thousand Oaks, CA; Amgen, Inc.; January 2023.
2. Xgeva [package insert]. Thousand Oaks, CA; Amegen, Inc.; June 2020.

3. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/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.
4. Shoback D, Rosen CJ, Black DM, Cheung AM, Murad MH, Eastell R. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society guideline update. J Clin Endocrinol Metab. 2020;105(3):dgaa048.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Pending Approval (draft/unpublished version) - Removed denosumab (Prolia) from broader Bone Density Regulators policy and aged denosumab (Xgeva) to the RankL policy - Broke out policy criteria by indication - Added safety monitoring criteria to each section (e.g., pregnancy, hypocalcemia, supplementation) - Updated verbiage around prior treatment with bisphosphonates - Added language in around requirement to be high risk of fracture - Added criteria for denosumab (Xgeva) for respective indications

Washington State Health Care Authority

Rank Ligand (RANKL) Inhibitors

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation demonstrating disease stability or a positive clinical response)?
   ☐ Yes ☐ No

2. Indicate patient's diagnosis:
   - ☐ Glucocorticoid-induced osteoporosis
   - ☐ Postmenopausal osteoporosis
   - ☐ Bone loss in men with prostate cancer
   - ☐ Bone loss in women with breast cancer
   - ☐ Bone metastasis from solid tumors
   - ☐ Multiple myeloma with skeletal-related events
   - ☐ Giant cell tumor of bone
   - ☐ Hypercalcemia of malignancy

3. Will the medication be used in combination with other bone density regulators? ☐ Yes ☐ No
   If yes, specify:
   ☐ bisphosphonates ☐ raloxifene
   ☐ Prolia (denosumab) ☐ Xgeva (denosumab)

4. Indicate if patient has any of the following:
   - ☐ Presence of fragility fractures of the hip or spine regardless of bone mineral density
   - ☐ T-score ≤ -2.5 in the lumbar spine, femoral neck, total hip
   - ☐ T-score between -1 and -2.5 with a history of recent fragility fracture of proximal humerus, pelvis, or distal forearm
   - ☐ T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%

5. Has the patient been treated with at least one Apple Health Preferred Drug (oral or intravenous) unless ineffective, contraindicated or not tolerated? Please select all that apply:
   - ☐ Bisphosphonate (minimum trial of 12 months) , specify: _____
   - ☐ Selective estrogen receptor modulator (SERM) (minimum trial of 24 months) , specify: _____
   - ☐ Other, specify: _____
   - ☐ Contraindicated, provide contraindication: _____

For the diagnosis of Glucocorticoid Induced Osteoporosis:

6. Will patient be initiating or continuing systemic glucocorticoid therapy at a daily dosage equivalent to ≥ 7.5 mg of prednisone? ☐ Yes ☐ No
   If yes, is patient expected to remain on glucocorticoid therapy for at least 6 months? ☐ Yes ☐ No

For bone loss in men and prostate cancer:

7. Is patient currently receiving androgen deprivation therapy (ADT) (e.g., leuprolide, degarelix, relugolix) for non-metastatic prostate cancer? ☐ Yes ☐ No

For bone loss in women with breast cancer:

8. Will patient be receiving adjuvant aromatase inhibitor therapy (e.g., anastrozole, exemestane, letrozole) for breast cancer? ☐ Yes ☐ No

For Multiple Myeloma:

9. Does patient have a history of failure, contraindication, or intolerance to zoledronic acid? ☐ Yes ☐ No
   If contraindicated, provide contraindication: _____

For giant cell tumor of bone:

10. Indicate the following for patient. Check all that apply.
    ☐ Disease is unresectable or surgical resection is likely to result in severe morbidity?
    ☐ Disease recurrent or metastatic

For hypercalcemia of malignancy

11. Does patient have a baseline corrected serum calcium > 12.5 mg/dL? ☐ Yes ☐ No

CHART NOTES ARE REQUIRED WITH THIS REQUEST

Prescriber signature	Prescriber specialty	Date