Approved Revision: Do Not Implement until 8/31/21

Denosumab (Prolia®, Xgeva®)

NDC CODE(S) 55513-0710-XX - Prolia 60 MG/ML Solution Prefilled Syringe (AMGEN)
55513-0730-XX - Xgeva 120 MG/1.7ML Solution (AMGEN)

DESCRIPTION

Denosumab is a monoclonal antibody that is specific for the receptor activator of nuclear factor kappa-B ligand (RANKL). RANKL is a soluble protein essential for the formation, function and survival of osteoclasts, those cells responsible for bone resorption.

In osteoporosis and other conditions, the balance of bone remodeling is disturbed: Osteoclasts break down more bone than osteoblasts are able to form. This leads to decreased bone mass and bone strength. When RANKL binds to denosumab it is inhibited from binding with and activating RANK, receptor activator of nuclear factor kappa-B. RANK, located on the surface of osteoclasts and their precursors, must be activated to form new osteoclasts and for those present to survive and function to break down bone. By interrupting that action, denosumab diminishes bone resorption.

POLICY

- Denosumab for the treatment/prevention of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Osteoporosis
  - Giant cell tumor of bone
  - Hypercalcemia of malignancy
  - Prevention of skeletal related events (Bone Metastases from solid tumors; Multiple Myeloma)
  - Systemic Mastocytosis
- Denosumab for the prevention of skeletal-related events (e.g., to increase bone mass) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Denosumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

Prolia

Universal Criteria

- Patient must be supplementing with 1,000 mg of calcium and at least 400 IU of vitamin D daily; **AND**
- Patient must not have hypocalcemia; **AND**
- Patient is at least 18 years of age; **AND**
- Patient must be at a high risk for fracture**; **AND**
- Pregnancy ruled out prior to starting therapy in women of child-bearing potential; **AND**

Osteoporosis in Men and Women

- Women only: Patient must be post-menopausal; **AND**
- Patient has a documented diagnosis of osteoporosis indicated by one or more of the following:

- Hip/femur DXA (femoral neck or total hip) or lumbar spine T-score ≤-2.5 and/or forearm DXA 33% (one-third) of the radius; **OR**
- T-score ≤ -1 or low bone mass and a history of fragility fracture to the hip or spine; **OR**
- T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥20% or hip fracture ≥3%; **AND**

- Documented treatment failure or ineffective response± to a minimum (12) month trial on previous therapy with bisphosphonates (oral or IV) such as alendronate, risedronate, ibandronate, or zoledronic acid; **OR**
- Patient has a documented contraindication* or intolerance to BOTH oral bisphosphonates AND intravenous (IV) bisphosphonates such as alendronate, risedronate, ibandronate, or zoledronic acid

Glucocorticoid-Induced Osteoporosis

- 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**
  - Documented treatment failure or ineffective response± to a minimum (12) month trial on previous therapy with bisphosphonates (oral or IV) such as alendronate, risedronate, ibandronate, or zoledronic acid; **OR**
- Patient has a documented contraindication* or intolerance to BOTH oral bisphosphonates AND intravenous (IV) bisphosphonates such as alendronate, risedronate, ibandronate, or zoledronic acid

Osteoporosis treatment and prevention in prostate cancer patients

- Documented Hip DXA (femoral neck or total hip) or lumbar spine T-score ≤-1 (or patient meets the diagnostic criteria for osteoporosis above); **AND**
- Patient must be receiving androgen deprivation therapy for non-metastatic prostate cancer

Osteoporosis treatment and prevention in breast cancer patients

- Patient must be receiving adjuvant aromatase inhibitor therapy for breast cancer

±Ineffective response is defined as one or more of the following:
– Decrease in T-score in comparison with baseline T-score from DXA scan – Patient has a new fracture while on bisphosphonate therapy
****High risk for fractures include, but are not limited to, one or more of the following:**
– History of an osteoporotic fracture as an adult – Parental history of hip fracture – Low BMI – Rheumatoid arthritis – Alcohol intake (3 or more drinks per day) – Current smoking – History of oral glucocorticoids ≥5 mg/d of prednisone (or equivalent) for >3 months (ever)
***Examples of contraindications to oral bisphosphonate therapy include the following:**
– Documented inability to sit or stand upright for at least 30 minutes – Documented pre-existing gastrointestinal disorder such as inability to swallow, Barrett's esophagus, esophageal stricture, dysmotility, or achalasia

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Xgeva

Universal Criteria

- Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia; **AND**

Prevention of skeletal-related events in patients with multiple myeloma OR bone metastases from solid tumors

- Patient is at least 18 years of age; **AND**
  - Patient must try and have an inadequate response, contraindication, or intolerance to at least a three (3) month trial of Zoledronic Acid; **OR**
  - Patient has metastatic breast cancer, metastatic castration-resistant prostate cancer, or metastatic lung cancer (both SCLC and NSCLC)

Giant Cell Tumor of the Bone

- Patient must be an adult or at least 13 years of age and skeletally mature; **AND**
  - Disease is unresectable or surgical resection is likely to result in severe morbidity; **OR**
  - Disease is localized, recurrent, or metastatic; **AND**
    - Used as a single agent; **OR**
    - Used in combination with interferon alpha, serial embolization, or radiation therapy

Hypercalcemia of malignancy

- Patient is at least 18 years of age; **AND**
- Patient must have a diagnosis of cancer (malignancy); **AND**
  - Patient must have a diagnosis of refractory hypercalcemia of malignancy defined as an albumin-corrected calcium of >12.5 mg/dL (3.1 mmol/L) despite treatment with a minimum seven (7) day trial on previous therapy with intravenous (IV) bisphosphonates such as ibandronate or zoledronic acid; **OR**
  - Patient has a documented contraindication or intolerance to intravenous (IV) bisphosphonates such as ibandronate or zoledronic acid

Systemic Mastocytosis

- Patient has osteopenia or osteoporosis and coexisting bone pain; **AND**
- Used as second line therapy; **AND**
  - Patient is not responding to bisphosphonate therapy; **OR**
  - Patient is not a candidate for bisphosphonate therapy due to renal insufficiency

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe symptomatic hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, dermatological adverse reactions, severe infection, severe hypersensitivity/anaphylaxis, musculoskeletal pain, etc.; **AND**

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- Disease response as indicated by one or more of the following:
  - Absence of fractures
  - Increase in bone mineral density compared to pretreatment baseline; **AND**
- **Osteoporosis in Men and Women ONLY:**
  - After 5 years of treatment, patient will have a repeat DXA performed; **AND**
    - Patients with low-to moderate risk disease will have therapy changed to an oral or IV bisphosphonate unless there is a contraindication or intolerance to both dosage forms

Xgeva

- Disease response as indicated by the following:
  - Multiple Myeloma OR Bone metastases from solid tumors: absence/delay in skeletal-related events (e.g., pathologic fracture, radiation therapy to bone, surgery to bone, or spinal cord compression)
  - Giant Cell Tumor of the Bone: stabilization of disease or decrease in size of tumor or spread of tumor
  - Hypercalcemia of Malignancy: corrected serum calcium ≤ 11.5 mg/dL (2.9 mmol/L)
  - Systemic Mastocytosis: improvement or resolution of bone pain as compared to pretreatment baseline

DOSAGE/ADMINISTRATION

Prolia

INDICATION	DOSE
All indications	60 mg subcutaneously by a health care provider every 6 months

Xgeva

INDICATION	DOSE
Bone metastases from solid tumors, Multiple Myeloma, & Systemic Mastocytosis	120 mg subcutaneously by a health care provider every 4 weeks
Giant Cell Tumor of Bone	120 mg subcutaneously by a health care provider every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy
Hypercalcemia of Malignancy	120 mg subcutaneously by a health care provider every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.

LENGTH OF AUTHORIZATION

Coverage will be provided for 12 months and may be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Prolia	All indications: • 60 billable units every 6 months

Xgeva	*Giant Cell Tumor of Bone & Hypercalcemia of Malignancy*
	• Loading Dose:
	  ○ 120 billable units on days 1, 8, 15, and 29
	• Maintenance:
	  ○ 120 billable units every 4 weeks

	Bone metastases from solid tumors, Multiple Myeloma, & Systemic Mastocytosis: • 120 billable units every 4 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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EFFECTIVE DATE 8/31/2021

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