

Medicare Advantage Medical Benefit Drug Policy



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Effective Date: 10/07/2021

Denosumab (Prolia®/Xgeva®)

FDA approval: Prolia: 6/1/2010; Xgeva: 11/18/2010

HCPCS: J0897

Benefit: Medical

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. For the prevention of skeletal-related events in patients with multiple myeloma or with bone metastases from solid tumors (Xgeva only) when the below criteria are met:
 - i. Documentation that at least one IV bisphosphonate has been ineffective, not tolerated or contraindicated
OR
 - ii. National Comprehensive Cancer Network (NCCN) supported category 1 preferred agent for prevention of skeletal related events in patients with bone metastases for the specific oncological diagnosis
AND
 - iii. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily
OR
 - b. For the treatment of adults and skeletally mature adolescents with giant cell tumor of bone (Xgeva only) when these criteria have been met:
 - i. Documentation of confirmed giant cell tumor of bone and radiologic evidence of measurable disease (via CT scan or MRI)
 - ii. Bone is unresectable or surgical resection is likely to result in severe morbidity
 - iii. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily
OR
 - c. For the treatment of hypercalcemia of malignancy (HCM) refractory to bisphosphonate therapy (Xgeva only)
 - i. Diagnosis of hypercalcemia secondary to a malignancy (including hematologic malignancies)
 - ii. Albumin corrected serum calcium (CSC) $\geq 12\text{mg/dL}$ (3.0mmol/L)
 - iii. Documentation that at least one IV bisphosphonate has been ineffective, not tolerated or contraindicated

OR

- d. For the treatment of osteoporosis (Prolia only) when all of the criteria below are met:
 - i. BMD T-score at or below -2.5 at the lumbar spine or total hip
 - ii. At least one bisphosphonate (if patient has intolerance to oral administration, IV administration will be required) is not effective after at least a 24-month treatment period based on objective documentation except if:
 - 1. Bisphosphonates (oral and intravenous formulations) are contraindicated
 - iii. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily
 - iv. Will NOT be used in combination with any anabolic bone modifying agent
- OR
- di. To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer OR women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for nonmetastatic breast cancer when all of the criteria below are met (Prolia only):
 - i. When the 10-year probability of hip fracture is $\geq 3\%$ or the 10-year probability of a major osteoporosis-related fracture is $\geq 20\%$.
 - ii. At least one bisphosphonate (if patient has intolerance to oral administration, IV administration will be required) is not effective after at least a 24-month treatment period based on objective documentation except if:
 - 1. Bisphosphonates (oral and intravenous formulations) are contraindicated
 - iii. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily
 - dii. Trial and failure of the preferred products as specified in the BCBSNE MA Part B drugs prior authorization list

B. Quantity Limitations, Authorization Period and Renewal Criteria

- a. For all FDA approved indications for Prolia, quantity limit of 60 mg administered once every 6 months
- b. For the prevention of skeletal-related events in patients with multiple myeloma or with bone metastases from solid tumors (Xgeva), quantity limit of 120 mg administered once every 4 weeks
- c. For the treatment of giant cell tumor of bone (Xgeva), quantity limit of three 120mg doses for the first month, followed by 120mg every 4 weeks
- d. For the treatment of hypercalcemia of malignancy (Xgeva), quantity limit of three 120mg doses for the first month, followed by 120mg every 4 weeks
- e. Renewal Criteria:
 - i. Xgeva (multiple myeloma or bone metastases from solid tumors and breast cancer): If more than 1 fracture in the last 6 months alternative therapy is recommended.
 - ii. Xgeva (giant cell tumor of the bone): Goals of therapy have been met.
 - iii. Xgeva (hypercalcemia of malignancy): decrease in albumin CSC levels from baseline.
 - iv. Prolia: Documentation of improved or stable T-scores while on Prolia.

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. FDA approved indication/Diagnosis

**Please refer to most recent prescribing information.*

B. Background Information

- a. Denosumab is a fully human monoclonal antibody against the receptor activator of nuclear factor- κ B ligand (RANKL)
- b. RANKL is a cytokine that is essential for the formation, function, and survival of osteoclasts
- c. By binding RANKL, denosumab prevents the interaction of RANKL with its receptor on osteoclasts and osteoclasts precursors and reversibly inhibits osteoclast-mediated bone resorption
- d. As a monoclonal antibody, denosumab has potential safety risks/significant safety concerns that must be balanced against its potential benefits
- e. For osteoporosis, treatment should be considered if the 10-year risk is 3% or more for hip fracture or 20% or more for “major” osteoporosis-related fracture based on the US-adapted WHO algorithm
- f. 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
- g. Prevention of Osteoporosis Due to Hormone Suppression:
 - i. In breast and prostate cancer patients on hormone suppression therapy, hormone suppression increases bone turnover and decreases bone mineral density (BMD)
 - ii. Oral bisphosphonates are the best value for the prevention of osteoporosis in patients on hormone suppression therapy
 - iii. For prevention of osteoporosis in patients with prostate cancer during androgen deprivation therapy (ADT), there is evidence that denosumab, pamidronate, zoledronic acid, and alendronate increase BMD during ADT
 - iv. NCCN prostate cancer guidelines recommend zoledronic acid once annually or alendronate 70 mg weekly when risk of fracture warrants treatment
 - v. Bisphosphonate treatment for the 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
- h. Cancer-Related Bone Metastases:
 - i. Zoledronic acid provides the best value for prevention of skeletal complications, decreasing the incidence and rate of skeletal events, and delaying skeletal events in women with breast cancer with bone metastases
 - ii. Denosumab and zoledronic acid appear to be at least similar in delaying the time to first skeletal related event in patients with metastasis from solid tumor cancers
- i. Hypercalcemia of Malignancy:
 - i. HCM is a serious complication that is indicative of poor malignancy prognosis
 - ii. It results from cancer driven increases in bone resorption, and if untreated, can lead to renal

failure, progressive mental impairment, coma, and death

- iii. Denosumab acts by inhibiting the osteoclast mediated bone resorption, which results in decrease in bone destruction and calcium release, thus lowering calcium levels in HCM patients

C. Efficacy

**Please refer to most recent prescribing information.*

D. Medication Safety Considerations

**Please refer to most recent prescribing information.*

E. Dosing and administration

**Please refer to most recent prescribing information.*

F. How supplied

**Please refer to most recent prescribing information.*

References:

1. Prolia (denosumab) [prescribing information]. Amgen, Inc. May 2021.
2. Xgeva (denosumab) [prescribing information]. Amgen, Inc. June 2020.
3. NCCN Guidelines Version 1.2022. Prostate Cancer.
4. CHU Brugmann. Prevention and treatment of side-effects of systemic treatment: bone loss. *Annals of Oncology*. 2010) 21 (suppl 7): vii180-vii185.
5. FDA Approves Xgeva (denosumab) for Hypercalcemia of Malignancy Refractory to Bisphosphonate Therapy. <http://www.drugs.com/newdrugs/fda-approves-xgeva-denosumab-hypercalcemia-malignancy-refractory-bisphosphonate-therapy-4117.html>. Accessed Jan 16, 2015.
6. Saag KG, Wagman RB, Geusens P, Adachi JD, et al. Denosumab versus risedronate in glucocorticoid-induced osteoporosis: a 4randomized4, 4andomized, double-blind, active-controlled, double-dummy, non-inferiority study. *Lancet Diabetes Endocrinol*. 2018 Jun; 6(6):445-454.
7. Rajee N, Terpos E, Willenbacher W, Shimizu K, et al. Denosumab versus zoledronic acid in bone disease treatment of newly diagnosed multiple myeloma: an international, double-blind, double-dummy, 4andomized, controlled, phase 3 study. *Lancet Oncol*. 2018 Mar;19(3):370-381.

Policy/UM Medical Management System Update History		
#	Date	Change Description
1.1	Effective Date: 10/07/2021	Annual Review of Medical Policy
1.0	Effective Date: 10/08/2020	Medical policy established.

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*