EFFECTIVE DATE: 11|01|2016
POLICY LAST UPDATED: 10|18|2016

OVERVIEW

Prolia (denosumab) is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture and to increase bone mass in men with osteoporosis. It is also indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer and to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer. Xgeva (denosumab) is indicated for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors and giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

MEDICAL CRITERIA

BlueCHiP for Medicare

Denosumab (Prolia®) is indicated for the treatment of individuals with the following:

• Postmenopausal women with osteoporosis at high risk for fracture,
defined as a history of osteoporotic fracture, or multiple risk factors for fractures;
• Postmenopausal women with osteoporosis who have failed or are intolerant to other available osteoporosis therapy.
• Patients with significant renal failure where treatment with biphosphonate is not indicated, CrCl less than 35 ml/min.
• To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia® also reduced the incidence of vertebral fractures.
• To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.
• To increase bone mass in men with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Denosumab (Xgeva®) is indicated for the treatment of individuals with the following:

• Bone metastases from solid tumors.
• Adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. (Effective June 12, 2013 based on FDA approval)
• Hypercalcemia of malignancy refractory to bisphosphonate therapy. (Effective December 5, 2014 based on (FDA) approval)

- Denosumab (Prolia™) is contraindicated in patients with hypocalcemia.
- Denosumab (Xgeva™) is not approved for patients with multiple myeloma or other cancer of the blood.

Commercial Products

Prolia (denosumab) for treatment of osteoporosis and to increase bone mass:

Prolia (denosomab) is considered medically necessary for treatment of osteoporosis and to increase bone mass for the following:

- Women with postmenopausal osteoporosis; or
- Men with osteoporosis; or
- Women with breast cancer who are receiving adjuvant aromatase inhibitor therapy; or

- Men with nonmetastatic prostate cancer who are receiving androgen deprivation therapy;

In addition to meeting one of the above indications, the patient must meet all of the criteria below:

1. Does not have uncorrected hypocalcemia; and
2. Vitamin D status has been evaluated and corrected; and
3. Will receive adequate intake of supplemental calcium and vitamin D; and
4. Has tried an oral bisphosphonate or an intravenous bisphosphonate; and
5. Had an inadequate response to at least one bisphosphonate:
    a. Received osteoporosis-related fracture while on the bisphosphonate for at least one year; or
    b. Had significant decline in bone mineral density while on the bisphosphonate for at least one year; and
    b. Was compliant with bisphosphonate therapy and received adequate calcium and vitamin D supplementation; or
6. Was unable to tolerate at least two different bisphosphonates; or if the patient has not tried any bisphosphate therapy, they must meet one of the following criteria:
    a. Has a diagnosis of esophageal stricture, achalasia, or other severe esophageal dysmotility disorder; or
    b. Is unable to stand or sit upright for 60 minutes; or
    c. Has a history of severe malabsorption making the use of oral bisphosphonates ineffective; or
    d. Has renal impairment (creatinine clearance <35 nK/min).

Xgeva (denosumab) for bone metastases from solid tumors:
Xgeva (denosumab) is considered medically necessary for the prevention of skeletal related events for the following:

1. Patient does not have multiple myeloma AND
2. Patient has documented bone metastases from a solid tumor cancer OR giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity AND
3. Patient does not have pre-existing hypocalcemia OR
4. Patient will have hypocalcemia corrected prior to starting Xgeva AND
5. Patient will receive calcium and vitamin D as needed to prevent hypocalcemia.

PRIOR AUTHORIZATION
Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial products.

POLICY STATEMENT
BlueCHiP for Medicare and Commercial Products
Denosumab (Prolia and Xgeva) is considered medically necessary when the medical criteria for each indication above are met.

Denosumab (Prolia and Xgeva) is considered not medically necessary for other treatments not mentioned above due to insufficient evidence in the published, peer reviewed, scientific literature to support its use.

COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for the applicable section regarding prescription drugs dispensed and administered by a licensed health care provider (other than a pharmacist) coverage/benefits.

Specialty Pharmacy
For contracts with specialty drug coverage, please refer to the member agreement for benefits and preauthorization guidelines.

BACKGROUND

Denosumab is a fully human monoclonal antibody that specifically binds to and inhibits the receptor activator of NF-kappaB ligand (RANK Ligand), the primary mediator of bone resorption. RANK Ligand is the protein responsible for activating osteoclasts, the cells that break down bone. An increased amount of the protein has been linked as the primary cause of a broad range of bone loss conditions including osteoporosis, treatment-induced bone loss, bone erosions, and bone metastases.

In June 2010 the U.S. Food and Drug Administration (FDA) approved denosumab (Prolia) for the treatment of postmenopausal women with osteoporosis at high risk for fracture. In November 2010 the FDA approved the same drug, denosumab (Xgeva) in a higher dose for the prevention of skeletal-related events in patients with bone metastases from solid tumors. In September 2011 the FDA also approved denosumab for the treatment of bone loss in patients with non-metastatic prostate or breast cancer. In September 2012 denosumab (Prolia) was approved by the FDA as a treatment of bone loss in men with osteoporosis at high-risk for fracture. They were given distinct trade names in order to differentiate between their unique dosing schedules and indications for use. The two are the same drug, but they have different clinical indications for use and dosing.

Indicated Treatment
Osteoporosis and as a treatment to increase bone mass:
Denosumab (Prolia) is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture and to increase bone mass in men with osteoporosis. It is also indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer and to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer. The recommended dose of denosumab is 60 mg administered as a single subcutaneous injection once every 6 months. Pre-existing hypocalcemia must be corrected prior to initiating therapy with denosumab. Hypocalcemia is a serious risk in patients with severe renal impairment (creatinine clearance < 30 mL/min), or receiving dialysis. Calcium levels must be maintained with adequate calcium and vitamin D supplementation. Denosumab is supplied in a single-use prefilled syringe with a safety guard or in a single-use vial as 60 mg/1 mL in a single-use prefilled syringe in 1 vial per carton or a 60 mg/1 mL in a single-use vial in 1 per carton.

Bone metastases from solid tumors:
Denosumab (Xgeva) is indicated for the prevention of skeletal-related events in patients with bone metastases from solid tumors. Denosumab is not indicated for the prevention of skeletal-related events in patients with multiple myeloma. The recommended dose of denosumab is 120 mg administered as a subcutaneous injection every 4 weeks. Calcium and vitamin D are necessary to treat or prevent hypocalcemia. Denosumab is supplied in a single-use 120 mL vial.

CODING

BlueCHiP for Medicare and Commercial Products
The following HCPCS code is medically necessary when the medical criteria are met:
J0897

RELATED POLICIES

None

PUBLISHED

Provider Update, January 2017
Provider Update, December 2015
Provider Update, July 2013

Provider Update, August 2012
Provider Update, December 2011
Provider Update, February 2011

REFERENCES

1. Amgen. Prolia (denosumab) injection product information. Thousand Oaks, CA: Amgen Inc. Sept 2012. Revised Feb 2015
2. Amgen. Xgeva (denosumab) injection product information. Thousand Oaks, CA: Amgen Inc. Revised June 2015
3. CMS.gov Centers for Medicare and Medicaid Services Local Coverage Article: Denosumab (Prolia ™, Xgeva ™) - Related to LCD L33394 (A52399)

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