Effective Date: 05/3/2018

Denosumab (Prolia®/Xgeva®)

FDA approval: June 1, 2010
HCPCS: J0897
Benefit: Medical

Policy/Criteria:

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

1. Denosumab may be considered medically necessary when the criteria below are met:

   A. For the prevention of skeletal-related events in patients with bone metastases from breast cancer (Xgeva only) when the below criteria are met:
      I. Documentation that IV pamidronate or zoledronic acid has been ineffective, not tolerated or contraindicated
      II. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily

   OR

   B. For the prevention of skeletal-related events in patients with bone metastases from solid tumors besides breast cancer (Xgeva only) when the below criteria are met:
      I. Documentation that at least one IV bisphosphonate has been ineffective, not tolerated or contraindicated
      II. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily

   OR

   C. 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

   D. 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) ≥ 12mg/dL (3.0mmol/L)
      III. Documentation that at least one IV bisphosphonate has been ineffective, not tolerated or contraindicated
E. 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 considered as an option) 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 OR
       2. Not tolerated due to clinical side effects, such as esophageal irritation despite taking it as recommended
   III. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily

F. 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 ≥ 3% or the 10 year probability of a major osteoporosis-related fracture is ≥ 20%.
   II. At least one bisphosphonate (if patient has intolerance to oral administration, IV administration will be considered as an option) is not effective after at least a 24 month treatment period unless:
       1. Bisphosphonates (oral and intravenous formulations) are contraindicated OR
       2. Not tolerated due to clinical side effects, such as esophageal irritation despite taking it as recommended
   III. Patient will supplement with calcium 1000 mg daily and at least 400 IU vitamin D daily

Approval Lengths, Quantity Limits 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 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 (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.

Denosumab is considered investigational in conditions including, but not limited to:

A. Patients with contraindications to denosumab
B. Prevention of osteoporosis
C. For the prevention of skeletal-related events in patients with bone metastases from multiple myeloma
D. Rheumatoid arthritis

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E. Systemic Lupus Erythematosus
F. Hypercalcemia secondary to diseases other than malignancies

***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
   Prolia
   - Bone loss in men with prostate cancer
   - Bone loss in women with breast cancer
   - Osteoporosis in men
   - Osteoporosis in postmenopausal women

   Xgeva
   - Bone metastases from solid tumors
   - Giant cell tumor of the bone
   - Hypercalcemia of malignancy

   Limitation of use: Denosumab is not indicated for prevention of skeletal-related events in patients with multiple myeloma

   *Please refer to most recent prescribing information.

B. Background Information
   Denosumab is a fully human monoclonal antibody against the receptor activator of nuclear factor-kB ligand (RANKL). RANKL is a cytokine that is essential for the formation, function, and survival of osteoclasts. By binding RANKL, denosumab prevents the interaction of RANKL with its receptor on osteoclasts and osteoclasts precursors and reversibly inhibits osteoclast-mediated bone resorption. As a monoclonal antibody, denosumab has potential safety risks/significant safety concerns that must be balanced against its potential benefits. Due to its mechanism of action, denosumab presents a novel approach to fracture prevention.

   Cross References
   | Drug Review | None |

C. Efficacy

   *Please refer to most recent prescribing information.

D. Medication Safety Considerations

   Black Box Warning: No

   *Please refer to most recent prescribing information.

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E. Dosing and administration
   a. For the treatment of osteoporosis in postmenopausal women: 60 mg subcutaneously every 6 months
   b. For the prevention of skeletal-related events in patients with bone metastases from solid tumors: 120 mg subcutaneously every 4 weeks
   c. For the treatment of HCM: 120 mg subcutaneously every 4 weeks

   *Please refer to most recent prescribing information.

F. How supplied
   a. Single-use prefilled syringe containing 60 mg in a 1 mL solution
   b. Single-use vial containing 60 mg in a 1 mL solution

References:

2. Xgeva™ (denosumab) [prescribing information]. Amgen, Inc. August 2016.

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<tr>
<th>#</th>
<th>Date</th>
<th>Change Description</th>
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<tbody>
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<td>1.0</td>
<td>Effective Date: 11/08/2012</td>
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<td>1.1</td>
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<td>1.2</td>
<td>Effective Date: 8/14/2014</td>
<td>Criteria update to treatment of osteoporosis and including continuation of therapy</td>
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<td>1.3</td>
<td>Effective Date: 05/07/2015</td>
<td>Policy update added new indication: hypercalcemia of malignancy (HCM)</td>
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<td>1.4</td>
<td>Effective Date: 11/10/2016</td>
<td>Annual Review; No changes to criteria, document template updated.</td>
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<td>1.5</td>
<td>Effective Date: 5/4/2017</td>
<td>Changes: Annual Review/Medicare Disclaimer added</td>
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<td>1.6</td>
<td>Effective Date: 5/3/2018</td>
<td>Annual Review of Medical Policy</td>
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* 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