Pharmacy Medical Necessity Guidelines:
Prolia® and Xgeva® (denosumab)

Effective: October 1, 2014

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<th>Pharmacy (RX) or Medical (MED) Benefit</th>
<th>RX</th>
<th>Department to Review</th>
<th>RxUM</th>
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<td>Type of Review – Clinical Review Fax: 617-673-0988</td>
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OVERVIEW

FDA-APPROVED INDICATIONS

**Prolia** (denosumab) is indicated
- For the treatment of postmenopausal women 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. In postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures.
- For treatment 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.
- As a treatment 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.
- As a treatment 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 in patients with bone metastases from solid tumors. Xgeva (denosumab) is not indicated for the prevention of skeletal-related events in patients with multiple myeloma.
- For the treatment of adults and skeletally mature adolescents with giant cell tumor of bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity.

Denosumab is a monoclonal antibody that binds to receptor activator of nuclear factor kappa-B ligand (RANKL), a transmembrane protein that is vital for osteoclast formation, function, and survival. Denosumab prevents the normal binding of RANKL to its receptor, RANK. This impairs normal osteoclast function of bone resorption, which causes increased bone mass and strength in the trabecular and cortical bone.

PHARMACY COVERAGE GUIDELINES

**For Xgeva** (denosumab)
Tufts Health Plan – Network Health may authorize coverage of Xgeva (denosumab) when the following criteria are met:

1. The Member has bone metastases from solid tumors and is receiving Xgeva (denosumab) for prevention of skeletal-related events OR
2. The Member is being treated for unresectable giant cell tumor of bone (GCTB) or surgical resection of GCTB is likely to result in severe morbidity.

**For Prolia** (denosumab)
Tufts Health Plan – Network Health may authorize coverage of Prolia (denosumab) when the following criteria are met:

**For the treatment of postmenopausal women with osteoporosis**
1. The Member is at high risk of fracture defined as
   a. a history of osteoporotic fracture OR
   b. multiple risk factors for fracture and a T score less than or equal to -2.0 as evidenced via bone density scan OR
2. The Member has had an inadequate response to, or is unable to tolerate therapy with, at least one of the traditional osteoporosis treatments [e.g., alendronate (Fosamax®), calcitonin (Miacalcin®), ibandronate (Boniva®), raloxifene (Evista®), risedronate (Actonel®), zoledronic acid (Reclast®)].

**For treatment to increase bone mass in men with osteoporosis**

1. The member is at high risk of fracture defined as
   a. a history of osteoporotic fracture OR
   b. multiple risk factors for fracture and a T score less than or equal to -2.0 as evidenced via bone density scan, OR
2. The Member has had an inadequate response to, or is unable to tolerate therapy with, at least one of the traditional osteoporosis treatments [e.g., alendronate (Fosamax®), calcitonin (Miacalcin®), ibandronate (Boniva®), risedronate (Actonel®), zoledronic acid (Reclast®)].

**For men with nonmetastatic prostate cancer**

1. The member has a diagnosis of nonmetastatic prostate cancer AND
2. The member is at high risk of fracture defined as
   a. a history of osteoporotic fracture OR
   b. multiple risk factors for fracture and a T score at the lumbar spine, total hip, or femoral neck of less than -1.0 as evidenced via bone density scan AND
3. The Member is receiving androgen deprivation therapy.

**For women with breast cancer**

1. The member has a diagnosis of breast cancer AND
2. The member is at high risk of fracture defined as
   a. a history of osteoporotic fracture OR
   b. multiple risk factors for fracture and a T score at the lumbar spine, total hip, or femoral neck of less than -1.0 as evidenced via bone density scan AND
3. The Member is receiving adjuvant aromatase inhibitor therapy.

**Off-label Use Coverage for Other Cancer Diagnoses**

Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia, or in the medical literature, or by the Massachusetts commissioner of Insurance under the provisions of the “Sullivan Law”: (M.G.L. c.175, s.47K).

Tufts Health Plan – Network Health may authorize coverage for use for other cancer diagnoses provided effective treatment with such drug is recognized as a “Medically Accepted Indication” according to the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium as indicated by a Category 1 or 2A for quality of evidence and level of consensus.

**Note:** Tufts Health Plan – Network Health requires prescribers to submit clinical documentation supporting the drug’s effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s).

In cases where the requested off-label use for the diagnosis is not recognized by the NCCN Drugs and Biologics Compendium, Tufts Health Plan will follow the Centers for Medicare & Medicaid Services (CMS) guidance, unless otherwise directed by the commissioner, and accept clinical documentation referenced in one of the other “Standard Reference Compendia” noted below or supported by clinical research that appears in a regular edition of a "Peer-Reviewed Medical Literature" noted below.

*"Standard Reference Compendia"

1. American Hospital Formulary Service – Drug Information (AHFS-DI)
2. Thomson Micromedex DrugDex
3. Clinical Pharmacology (Gold Standard)

*"Peer-Reviewed Medical Literature"*
When Tufts Health Plan – Network Health evaluates the evidence in published, peer-reviewed medical literature, consideration will be given to the following:

1. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence
2. Whether the administered chemotherapy regimen is adequately represented in the published evidence
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients
4. Whether the study is appropriate to address the clinical question:
   a. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover);
   b. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,
   c. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

LIMITATIONS

1. Tufts Health Plan – Network Health will not authorize the use of Prolia (denosumab) or Xgeva (denosumab) for conditions other than those listed above without appropriate documentation.

CODES

The following HCPCS/CPT code(s) are:

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<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>J0897</td>
<td>Injection, denosumab, 1 mg</td>
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REFERENCES

Pharmacy Medical Necessity Guidelines: Prolia® and Xgeva® (denosumab)


APPROVAL HISTORY
- October 21, 2010: Reviewed by the Pharmacy and Therapeutics Committee
- July 8, 2014: Reviewed by the Pharmacy and Therapeutics Committee

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION
Pharmacy Medical Necessity Guidelines have been developed for determining coverage for Tufts Health Plan – Network Health benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with the applicable Member Handbook and in coordination with the member’s physician(s). Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the Tufts Health Plan – Network Health service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Tufts Health Plan – Network Health reviews Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

Pharmacy Medical Necessity Guidelines apply to all fully insured Tufts Health Plan – Network Health offerings unless otherwise noted in this policy or the applicable Member Handbook. Check the applicable product formulary in the Pharmacy section of our website to determine if the drug requires you to get prior authorization.

For Tufts Health Unify (Medicare-Medicaid One Care for people ages 21 – 64), please refer to Tufts Health Unify Prior Authorization Medical Necessity Guidelines.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines, when applicable, and adherence to plan policies and procedures and claims editing logic.