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

Effective: January 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	MED	Department to Review	PRECERT /MM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☒ Tufts Health Plan Commercial products – large group plans
☒ Tufts Health Plan Commercial products – small group and individual plans
☒ Tufts Health Freedom Plan products – large group plans
☒ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

All plans except Tufts Health Public Plans: PRECERT:617.972.9409

Tufts Health Public Plans: MM: 888.415.9055

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Prolia (denosumab) is a RANK ligand inhibitor indicated for the:

- **Treatment of Postmenopausal Women with Osteoporosis at High Risk for Fracture**
  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.
- **Treatment to Increase Bone Mass in Men with Osteoporosis**
  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.
- **Treatment of Bone Loss in Men Receiving Androgen Deprivation Therapy for Prostate Cancer**
  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.
- **Treatment of Bone Loss in Women Receiving Adjuvant Aromatase Inhibitor Therapy for Breast Cancer**
  Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

Xgeva (denosumab) is a RANK ligand inhibitor indicated for the:

- **Multiple Myeloma and Bone Metastasis from Solid Tumors**
  Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors.
- **Giant Cell Tumor of Bone**
  Treatment of 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.
- **Hypercalcemia of Malignancy**
  Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

COVERAGE GUIDELINES

Prolia (denosumab)

The plan may authorize coverage of Prolia (denosumab) when the following criteria are met:

Treatment of postmenopausal women with osteoporosis

1. Documentation of one of the following:
    a. T-score of less than or equal to -1.0 and greater than -2.5 and the prescriber determines the Member is at high risk for fracture
    b. T-score less than or equal to -2.5
    c. FRAX score of 10-year risk of major osteoporotic fracture ≥20% or a risk of hip fracture ≥3%
    d. One or more osteoporotic fracture

AND

2. Documentation of the following:
    a. For Commercial Products, Tufts Health Direct, and Tufts Health Together
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥1 of the traditional osteoporosis treatments (e.g., alendronate, calcitonin, ibandronate, raloxifene, risedronate, zoledronic acid), one of which must be a bisphosphonate.
    b. For Tufts Health RITogether
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥2 of the traditional osteoporosis treatments (i.e., alendronate, calcitonin, ibandronate, raloxifene, risedronate, zoledronic acid), one of which must be a bisphosphonate.

Treatment to increase bone mass in men with osteoporosis

1. Documentation of one of the following:
    a. T-score of less than or equal to -1.0 and greater than -2.5 and the prescriber determines the Member is at high risk for fracture
    b. T-score less than or equal to -2.5
    c. FRAX score of 10-year risk of major osteoporotic fracture ≥20% or a risk of hip fracture ≥3%
    d. One or more osteoporotic fracture

AND

2. Documentation of the following:
    a. For Commercial Products, Tufts Health Direct, and Tufts Health Together
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥1 of the traditional osteoporosis treatments (e.g., alendronate, calcitonin, ibandronate, raloxifene, risedronate, zoledronic acid), one of which must be a bisphosphonate.

    b. For Tufts Health RITogether
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥2 of the traditional osteoporosis treatments (i.e., alendronate, calcitonin, ibandronate, raloxifene, risedronate, zoledronic acid), one of which must be a bisphosphonate.

Bone Loss in Breast Cancer and Prostate Cancer

1. Documentation of **one (1)** of the following:
    a. A diagnosis of prostate cancer
    b. A diagnosis of breast cancer
    c. Member is receiving androgen deprivation therapy
    d. Member is receiving aromatase inhibitor therapy

AND

2. Documentation of one of the following:
    a. T-score of less than or equal to -1.0 and greater than -2.5 and the prescriber determines the Member is at high risk for fracture
    b. T-score less than or equal to -2.5
    c. FRAX score of 10-year risk of major osteoporotic fracture ≥20% or a risk of hip fracture ≥3%
    d. One or more osteoporotic fracture

AND

3. Documentation of the following:
    a. For Commercial Products, Tufts Health Direct, and Tufts Health Together:
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥1 bisphosphonate (e.g., alendronate, ibandronate, risedronate, zoledronic acid)
    b. For Tufts Health RITogether:

i. The Member has had an inadequate response to, or is unable to tolerate therapy with ≥2 bisphosphonates (e.g., alendronate, ibandronate, risedronate, zoledronic acid)

Xgeva (denosumab)
The plan may authorize coverage of Xgeva (denosumab) when the following criteria are met:
Multiple Myeloma and Bone Metastasis from Solid Tumors
1. Documentation the Member has bone metastases from multiple myeloma or solid tumors
AND
2. Documentation the Member is receiving Xgeva for prevention of skeletal-related events
AND
3. Documentation the Member has had an inadequate response to or is unable to tolerate therapy with at least one bisphosphonate (e.g., zoleronic acid, pamidronate)

Giant Cell Tumor of Bone
1. Documentation the Member is an adult or skeletally mature adolescent
AND
2. Documentation the Member is being treated for unresectable giant cell tumor of bone or surgical resection of giant cell tumor of bone is likely to result in severe morbidity

Hypercalcemia of Malignancy
1. Documentation the Member has documented diagnosis of hypercalcemia of malignancy
AND
2. Documentation of albumin-corrected calcium greater than 12.5 mg/dL (3.1 mmol/L)
AND
3. Documentation the Member has had an inadequate response to or is unable to tolerate therapy with at least one bisphosphonate (e.g., zoledronic acid, pamidronate)

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 (commissioner) under the provisions of the "Sullivan Law": (M.G.L. c.175, s.47K).

The plan 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: The plan 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, the plan will follow the Centers for Medicare and 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)
4. Wolters Kluwer Lexi-Drugs

"Peer Reviewed Medical Literature"

- American Journal of Medicine
- Annals of Internal Medicine
- Annals of Oncology
- Annals of Surgical Oncology
- Biology of Blood and Marrow Transplantation
- Blood
- Bone Marrow Transplantation
- British Journal of Cancer
- British Journal of Hematology
- British Medical Journal
- Cancer
- Clinical Cancer Research
- Drugs
- European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)
- Gynecologic Oncology
- International Journal of Radiation, Oncology, Biology, and Physics
- The Journal of the American Medical Association
- Journal of Clinical Oncology
- Journal of the National Cancer Institute
- Journal of the National Comprehensive Cancer Network (NCCN)
- Journal of Urology
- Lancet
- Lancet Oncology
- Leukemia
- The New England Journal of Medicine
- Radiation Oncology

When the plan 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

- The plan 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:

Code	Description
J0897	Injection, denosumab, 1 mg

REFERENCES

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12. Langdahl BL, Teglbjærg CS, Ho PR, et al. A 24-month study evaluating the efficacy and safety of denosumab for the treatment of men with low bone mineral density: results from the ADAMO trial. *J Clin Endocrinol Metab*. 2015 Apr;100(4):1335-42.
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26. Xgeva (denosumab) [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2018.

APPROVAL HISTORY

November 9, 2010: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. January 11, 2011: Added Xgeva (denosumab) to Medical Necessity Guidelines. Added limitation for authorization of Prolia (denosumab) or Xgeva (denosumab) for conditions other than those listed above.
2. November 15, 2011: Added pharmacy coverage guidelines for men with nonmetastatic prostate cancer and for women with breast cancer.
3. January 1, 2012: Administrative update: Replaced HCPCS code C9272 with J0897
4. May 8, 2012: For nonmetastatic prostate cancer and for breast cancer, changed the T score requirement from less than or equal to -2.0 to less than -1.0.

5. November 6, 2012: Added pharmacy coverage guidelines for men with osteoporosis
6. July 9, 2013: Added pharmacy coverage guidelines for treatment of adults and skeletally mature adolescents with giant cell tumor of bone. Added Off-label Use Coverage for Other Cancer Diagnoses criteria.
7. July 8, 2014: No changes.
8. January 13, 2015: Added medical necessity guidelines for approval of Xgeva (denosumab) for the diagnosis of hypercalcemia of malignancy.
9. January 1, 2016: Administrative change to rebranded template.
10. February 9, 2016: No changes.
11. February 14, 2017: No changes.
12. April 11, 2017: Administrative update.
13. February 13, 2018: Added multiple myeloma to the coverage criteria for Xgeva for prevention of skeletal-related events based on new indication.
14. February 12, 2019: Effective February 19, 2019, added the Tufts Health RITogether coverage criteria to the Medical Necessity Guideline.
15. May 7, 2019: Effective October 1, 2019, added criteria to require step through a bisphosphonate for all indications and updated T-score requirement to be that of less than -2.5, which is indicative of a high risk of fracture.
16. March 10, 2020: No changes.
17. September 15, 2020: Effective January 1, 2021, for Prolia, changed the criteria for treatment of postmenopausal women with osteoporosis and to increase bone mass in men with osteoporosis from an OR statement to an AND statement. For Prolia, expanded the definition of high risk of fracture for all indications. For Prolia, consolidated criteria for the treatment of bone loss in breast and prostate cancer and accepts documentation member is on androgen deprivation therapy or aromatase inhibitor therapy as documentation of prostate or breast cancer. For Xgeva, For Xgeva, for Multiple Myeloma added the requirement of documentation the Member has had an inadequate response to or is unable to tolerate therapy with at least one bisphosphonate, for Giant Cell Tumor of Bone added the requirement the member is an adult or skeletally mature adolescent, and for hypercalcemia of malignancy added the requirement of documentation of albumin-corrected calcium greater than 12.5 mg/dL (3.1 mmol/L).

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. 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 service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.

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.