Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines

Medical Benefit Drugs

# Xgeva (denosumab) and Biosimilars

*Effective: October 1, 2026*

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|---|---|
| **Guideline Type** | ☒ Prior Authorization<br>☐ Non-Formulary<br>☐ Step-Therapy<br>☐ Administrative |

**Applies to:**

**Commercial Products**

☐ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988

☒ Tufts Health Plan Commercial products; Fax 617-673-0988

**Public Plans Products**

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988

☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939

☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939

☐ Tufts Health One Care* – A Medicare-Medicaid Plan (a dual eligible product); Fax 617-673-0956

*The MNG applies to Tufts Health One Care members unless a less restrictive LCD or NCD exists.

**Senior Products**

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956

☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956

☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

**Note:** While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

## Overview

**Food and Drug Administration Approved Indications**

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

- **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

**Aukelso (denosumab-kyqq), Bilprevda (denosumab-nxxp), Bomyntra (denosumab-bnht)**, **Jubereq (denosumab-desu)**, **Osenvelt (denosumab-bmwo), Wyost (denosumab-bbdz), Xbryk (denosumab-dssb), and Xtrenbo (denosumab-qbde)** are biosimilars to Xgeva.

***Note****: Providers and Members enrolled with Harvard Pilgrim Health Care may reference the HPHC/OncoHealth guideline located at https://oncohealth.us/medicalpolicies/harvardpilgrim/.*

## Clinical Guideline Coverage Criteria

The plan may authorize coverage of Xgevaand biosimilar when the following criteria are met:

**Multiple Myeloma and Bone Metastasis from Solid Tumors**

1. Documented diagnosis of bone metastases from multiple myeloma or solid tumors

**AND**

2. Patient is 18 year of age or older

**AND**

3. Documentation that the Member has had an inadequate response to or is unable to tolerate therapy with at least one bisphosphonate (e.g., zoledronic acid, pamidronate)

**Giant Cell Tumor of Bone**

1. Documented diagnosis of Giant cell tumor of the bone

**AND**

2. Documentation of **one (1)** of the following:
    a. Patient is at least 18 years of age
    b. Patient is a skeletally mature adolescent

**AND**

3. Documentation that 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. Documented diagnosis of hypercalcemia of malignancy

**AND**

2. Patient is 18 years of age or older

**AND**

3. Documentation of albumin-corrected calcium greater than 12.5 mg/dL (3.1 mmol/L)

**AND**

4. Documentation that 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"**

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

None

## Codes

The following code(s) require prior authorization:

**Table 1: Codes**

| Codes | Description |
|---|---|
| J0897 | Injection, denosumab, 1 mg |
| Q5136 | Injection, denosumab-bbdz (jubbonti/wyost), biosimilar, 1 mg |
| Q5157 | Injection, denosumab-bmwo (stoboclo/osenvelt), biosimilar, 1 mg |
| Q5158 | Injection, denosumab-bnht (bomyntra/conexxence), biosimilar, 1 mg |
| Q5161 | Injection, denosumab-kyqq (aukelso/bosaya), biosimilar, 1 mg |
| Q5162 | Injection, denosumab-nxxp (bildyos/bilprevda), biosimilar, 1 mg |

## References:


1. Branstetter DG, Nelson SD, Manivel JC, et al. Denosumab induces tumor reduction and bone formation in patients with giant-cell tumor of bone. Clin Cancer Res. 2012 Aug 15; 18(16):4415- 24.
2. Diel IJ, Body JJ, Stopeck AT, Vadhan-Raj S, Spencer A, et al. The role of denosumab in the prevention of hypercalcaemia of malignancy in cancer patients with metastatic bone disease. Eur J Cancer. 2015 Jul;51(11):1467-75.
3. Ellis GK, Bone HG, Chlebowski R, Paul D, Spadafora S, et al. Randomized trial of denosumab in patients receiving adjuvant aromatase inhibitors for nonmetastatic breast cancer. J Clin Oncol 2008; 26:4875-4882.
4. Hu MI, Glezerman I, Leboulleux S, et al. Denosumab for patients with persistent or relapsed hypercalcemia of malignancy despite recent bisphosphonate treatment. J Natl Cancer Inst. 2013 Sep 18;105(18):1417-20.

5. Smith MR, Egerdie B, Toriz NH, et al. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Eng J Med 2009;361-745-55.
6. Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumor of bone: an open-label, phase 2 study. Lancet Oncol. 2010 Mar; 11(3):275-80.
7. von Moos R, Body JJ, Egerdie B, et al. Pain and health-related quality of life in patients with advanced solid tumors and bone metastases: integrated results from three randomized, double- blind studies of denosumab and zoledronic acid. Support Care Cancer. 2013 Dec;21(12):3497- 507.
8. Xgeva (denosumab) [package insert]. Thousand Oaks, CA: Amgen Inc.; May 2025.
9. Wyost (denosumab-bbdz) [prescribing information]. Princeton, NJ: Sandoz Inc; March 2024.
10. Osenvelt (denosumab-bmwo) [prescribing information]. Jersey City, NJ: Celltrion USA, Inc; February 2025.
11. Bomyntra (denosumab-bnht) [prescribing information]. Lake Zurich, IL: Fresenius Kabi USA LLC; March 2025.
12. Bilprevda (denosumab-nxxp) [package insert]. Jersey City, NJ: Organon & Co.; August 2025.
13. Aukelso (denosumab-kyqq) [package insert]. Cambridge, MA: Biocon Biologics Inc.; September 2025.
14. Jubereq (denosumab-desu) [prescribing information]. Raleigh, NC: Accord BioPharma Inc; October 2025.
15. Xbryk (denosumab-dssb) [prescribing information]. Yeonsu-gu. Incheon, South Korea: Samsung Bioepis Co Ltd; February 2025.
16. Xtrenbo (denosumab) [prescribing information]. Cherry Hill, NJ: Hikma Pharmaceuticals USA Inc; September 2025.

## Approval And Revision History

May 17, 2023: Reviewed by the Medical Policy Approval Committee (MPAC)

June 13, 2023: Reviewed by Pharmacy and Therapeutics Committee (P&T)

Subsequent endorsement date(s) and changes made:

- Originally approved September 13, 2022 by P&T and September 21, 2022 by MPAC committees effective January 1, 2023
- Administrative update: April 2023 added Medical Benefit Drugs to title, updated MATogether and RITogether fax numbers to 617-673-0939
- May 17, 2023: Annual review, no change, effective July 1, 2023
- August 2023: Administrative update to rebrand Tufts Health Unify to Tufts Health One Care for 2024
- July 9, 2024: Updated age requirements for Giant Cell Tumor of the Bone. Removed the Limitation “The Plan will not authorize the use of Xgeva for conditions other than those listed above without appropriate documentation.” Minor wording updates (eff 10/1/24).
- June 2025 Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template.
- September 9, 2025: Added biosimilar Bomyntra, Osenvelt, and Wyost to Medical Necessity Guideline with coverage criteria in line with Xgeva. Updated medical necessity guideline title to “Xgeva (denosumab) and Biosimilar”. Added HCPCS codes Q5136, Q5157 and Q5158. Effective 10/1/25.
- December 9, 2025: Added Aukelso (denosumab-kyqq) and Bilprevda (denosumab-nxxp) to the Medical Necessity Guideline (eff 1/1/26).
- April 2026: Updated J codes for Aukelso/Bosaya (Q5161) and Bildyos/Bilprevda (Q5162) effective 4/1/26. Removed Carelink from template.
- September 2026 E-Vote: Added biosimilar Jubereq, Xbryk, and Xtrenbo to Medical Necessity Guideline with coverage criteria in line with Xgeva. Template updated from “Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans” to “Tufts Health Together- MassHealth Accountable Care Partnership Plans”. (eff 10/1/26)

## Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member’s benefit document, and in coordination with the Member’s physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven 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 our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update 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 Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

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