Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines
Medical Benefit Drug
Prolia (denosumab) and Biosimilar

Effective: October 1, 2026

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ 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

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

- Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Treatment to increase bone mass in men with osteoporosis at high risk for fracture
- Treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

Bildyos (denosumab-nxxp), Bosaya (denosumab-kyqq), Conexxence (denosumab-bnht), Enoby (denosumab – qbde), Jubbonti (denosumab-bbdz), Ospomyv (denosumab-dssb), Osvyrti (denosumab-desu) and **Stoboclo (denosumab-bmwo)** are biosimilars to Prolia.

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

Clinical Guideline Coverage Criteria

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

Treatment of postmenopausal women with osteoporosis, to increase bone mass in men with osteoporosis, and treatment of glucocorticoid-induced osteoporosis in patients at high risk of fracture

1. Documented diagnosis of **one (1)** of the following:
    a. Postmenopausal osteoporosis
    b. Osteoporosis
    c. Glucocorticoid-induced osteoporosis

AND

2. Documentation of **one (1)** 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 and Tufts Health Direct
        i. The Member has had an inadequate response to or is unable to tolerate therapy with at least 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 at least 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 (1)** 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 and Tufts Health Direct:
        i. The Member has had an inadequate response to, or is unable to tolerate therapy with at least 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 at least 2 bisphosphonates (e.g., alendronate, ibandronate, risedronate, zoledronic acid)

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

None

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS 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

References:

1. Bone HG, Chapurlat R, Brandi ML, et al. The effect of three or six years of denosumab exposure in women with postmenopausal osteoporosis: results from the FREEDOM extension. *J Clin Endocrinol Metab*. 2013 Nov;98(11):4483-92.
2. Boonen S, Adachi JD, Cummings SR, et al. Treatment with denosumab reduces the incidence of new vertebral and hip fractures in postmenopausal women at high risk. *J Clin Endocrinol Metab* 2011; 96:1727-36.
3. Brown JP, Prince RL, Deal C et al. Comparison of the effect of denosumab and alendronate on bone mineral density and biochemical markers of bone turnover in postmenopausal women with low bone mass: a randomized, blinded, phase 3 trial. *J Bone Miner Res*. 2009 Jan; 24(1):153-61.
4. Cummings SR, San Martin, J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009 Aug 20; 361(8): 756-65.
5. 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.
6. Dore RK, Cohen SB, Lane NE, et al. Effects of denosumab on bone mineral density and bone turnover in patients with rheumatoid arthritis receiving concurrent glucocorticoids or bisphosphonates. Ann Rheum Dis 2010;69:872-5.
7. 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.
8. Hu MI, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. *J Clin Endocrinol Metab*. 2014 Sep;99(9):3144-52.
9. Kendler DL, Roux C, Benhamou CL, et al. Effects of denosumab on bone mineral density and bone turnover in postmenopausal women transitioning from alendronate therapy. J Bone Miner Res 2010; 25:72-81.
10. 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.
11. Leder BZ, Tsai JN, Uihlein AV, et al. Two years of Denosumab and teriparatide administration in postmenopausal women with osteoporosis (The DATA Extension Study): a randomized controlled trial. *J Clin Endocrinol Metab*. 2014 May;99(5):1694-700.
12. Lewiecki EM. Denosumab- an emerging treatment for postmenopausal osteoporosis. *Expert Opinion Biol Ther*. 2010 Mar; 10(3): 467-76.
13. Lewiecki EM, Miller PD, McClung MR, et al. Two-year treatment with denosumab (AMG 162) in a randomized phase 2 study of postmenopausal women with low BMD. J Bone Miner Res 2007; 22:1832-41.
14. McClung MR, Lewiecki EM, Cohen SB, et al. Denosumab in postmenopausal women with low bone mineral density. N Eng J Med 2006; 354:821-31.
15. National Osteoporosis Foundation. Prevalence Report. Available at: nof.org/print/219. Accessed October 4, 2012.
16. NIH Osteoporosis and Related Bone Diseases National Resource Center, Osteoporosis in Men. Available at: niams.nih.gov/Health_Info/Bone/Osteoporosis/men.asp. Accessed October 4, 2012.
17. North American Menopause Society. Management of osteoporosis in postmenopausal women: 2010 Position statement of the North American Menopause Society. Menopause. 2010 Jan-Feb; 17(1): 25-54.
18. Prolia (denusomab) [package insert]. Thousand Oaks, CA: Amgen Inc.; May 2025.
19. Roux C, Hofbauer LC, Ho PR, et al. Denosumab compared with risedronate in postmenopausal women suboptimally adherent to alendronate therapy: efficacy and safety results from a randomized open-label study. *Bone*. 2014 Jan;58:48-54.
20. Sweet MG, Sweet JM, Jeremiah MP, Galazka SS. Diagnosis and treatment of osteoporosis. *Am Fam Physician*. 2009; 79(3):193-200.
21. Jubbonti (denosumab-bbdz) [prescribing information]. Princeton, NJ: Sandoz Inc; October 2024.
22. Stoboclo (denosumab-bmwo) [prescribing information]. Jersey City, NJ: Celltrion USA, Inc; February 2025
23. Conexxence (denosumab-bnht) [prescribing information]. Lake Zurich, IL: Fresenius Kabi USA LLC; March 2025.

24. Bildyos (denosumab-nxxp) [package insert]. Jersey City, NJ: Organon & Co.; August 2025.
25. Bosaya (denosumab-kyqq) [package insert]. Cambridge, MA: Biocon Biologics Inc.; September 2025.
26. Enoby (denosumab) [prescribing information]. Cherry Hill, NJ: Hikma Pharmaceuticals USA Inc; September 2025.
27. Ospomyv (denosumab-dssb) [prescribing information]. Yeonsu-gu. Incheon, South Korea: Samsung Bioepis Co Ltd; October 2025.
28. Osvyrti (denosumab-desu) [prescribing information]. Raleigh, NC: Accord BioPharma Inc; October 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: Removed the Limitation The plan will not authorize the use of Prolia for conditions other than those listed above without appropriate documentation. Added coverage criteria for glucocorticoid-induced osteoporosis. Added diagnosis requirements and combined coverage criteria, for Treatment of postmenopausal women with osteoporosis, to increase bone mass in men with osteoporosis, and treatment of glucocorticoid-induced osteoporosis in patients at high risk of fracture (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 Conexxene, Jubbonti and Stoboclo to Medical Necessity Guideline with coverage criteria in line with Prolia. Updated Medical Necessity Guideline title to “Prolia (denosumab) and Biosimilar”. Added HCPCS codes Q5136, Q5157 and Q5158. Effective 10/1/25.
- December 9, 2025: Added Bildyos (denosumab-nxxp) and Bosaya (denosumab-kyqq) to the Medical Necessity Guideline (eff 1/1/26).
- September 2026 E-Vote: Added biosimilar Enoby, Ospomyv, and Osvyrti to Medical Necessity Guideline with coverage criteria in line with Prolia. Administrative update to remove CareLink from the Medical Necessity Guideline template. Template updated from “Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans” to “Tufts Health Together- MassHealth Accountable Care Partnership Plans”.

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.