Denosumab Products: (Xgeva®); Denosumab-bnht (Bomyntra®); Denosumab-bmwo (Osenvelt®); Denosumab-bbdz (Wyost®); Denosumab-dssb (Xbryk™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors
- 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
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

Compendial Uses

- Second line therapy for osteopenia/osteoporosis in patients with systemic mastocytosis
- Thyroid cancer as palliative care for bone metastases

All other indications are considered experimental/investigational and not medically necessary.

COVERAGE CRITERIA

Multiple Myeloma

Authorization of 12 months may be granted for prevention of skeletal-related events in members with multiple myeloma.

Bone Metastases from a Solid Tumor

Authorization of 12 months may be granted for any of the following:

- For prevention of skeletal-related events in members with bone metastases from a solid tumor (e.g., breast cancer, non-small cell lung cancer, thyroid carcinoma, kidney cancer, prostate cancer)
- As palliative care for bone metastases from thyroid carcinoma

Giant Cell Tumor of Bone

Authorization of 12 months may be granted for treatment of giant cell tumor of bone.

Hypercalcemia of Malignancy

Authorization of 2 months may be granted for treatment of hypercalcemia of malignancy that is refractory to intravenous (IV) bisphosphonate therapy OR there is a clinical reason to avoid IV bisphosphonate therapy (see Appendix).

Systemic Mastocytosis

Authorization of 12 months may be granted for second-line therapy for osteopenia or osteoporosis in members with systemic mastocytosis that have not responded to therapy with bisphosphonates or for patients who are not candidates for bisphosphonates because of renal insufficiency.

CONTINUATION OF THERAPY

Hypercalcemia of Malignancy

Authorization of 2 months may be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Giant Cell Tumor of the Bone	Route of Administration: Subcutaneous 120mg on days 1, 8, and 15 of the first month of therapy, followed by 120 mg every 4 weeks
Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Hypercalcemia of Malignancy	Route of Administration: Subcutaneous 120mg on days 1, 8, and 15 of the first month of therapy, followed by 120 mg every 4 weeks
Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Osteopenia or Osteoporosis in patients with Systemic Mastocytosis	Route of Administration: Subcutaneous 60mg every 6 months
Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Palliative Care for Bone Metastases from Thyroid Carcinoma	Route of Administration: Subcutaneous 120mg every 4 weeks

Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Prevention of Skeletal-Related Events in Patients with Bone Metastases from Solid Tumors	Route of Administration: Subcutaneous 120mg every 4 weeks
Xgeva (Denosumab) Bomyntra (Denosumab-bnht) Osenvelt (Denosumab-bmwo) Wyost (Denosumab-bbdz) Xbryk (Denosumab-dssb)	Prevention of Skeletal-Related Events in Patients with Multiple Myeloma	Route of Administration: Subcutaneous 120mg every 4 weeks

APPENDIX

Clinical Reasons to Avoid IV Bisphosphonate Therapy

- Renal insufficiency (creatinine clearance <35 mL/min)
- Acute renal impairment
- History of intolerance to an IV bisphosphonate

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Xgeva [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2020.
2. Bomyntra [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; March 2025.
3. Osenvelt [package insert]. Incheon, South Korea: Celltrion Inc.; February 2025.
4. Wyost [package insert]. Princeton, NJ: Sandoz Inc.; March 2024.
5. Xbryk [package insert]. Incheon, South Korea: Samsung Bioepis.; February 2025.
6. The NCCN Drugs & Biologics Compendium™ © 2025 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed April 8, 2025.
7. Hu M, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. J Clin Endocrinol Metab. 2014; 99(9):3144-3152.
8. Bisphosphonates. Drug Facts and Comparisons. Facts & Comparisons® eAnswers. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed October 3, 2024. https://online.factsandcomparisons.com

BlueCross BlueShield of Tennessee

Policy

Medical Policy Manual **Approved Rev: Do Not Implement until 10/31/25**

EFFECTIVE DATE 10/31/2025

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