Policy:	**Bone Modifiers – Denosumab Products (Xgeva) Utilization Management Medical Policy** • Bomyntra® (denosumab-bnht subcutaneous injection – Fresenius Kabi) • Osenvelt® (denosuamb-bmwo subcutaneous injection – Celltrion) • Wyost® (denosumab-bbdz subcutaneous injection – Sandoz) • Xgeva® (denosumab subcutaneous injection – Amgen)
Date Reviewed:	07/15/2025
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont
Applicable NCDs, LCDs, and/or LCAs	L33394, A52399

SUMMARY OF EVIDENCE

Denosumab products (Xgeva, biosimilars) are receptor activator of nuclear factor kappa-B ligand inhibitors indicated for the following uses:[1-4]

- **Giant cell tumor of bone**, treatment of adults and skeletally mature adolescents with disease that is unresectable or where surgical resection is likely to result in severe morbidity.
- **Hypercalcemia of malignancy**, treatment of, that is refractory to bisphosphonate therapy.
- **Skeletal-related events**, prevention, in patients with multiple myeloma and in those with bone metastases from solid tumors.

Another injectable formulation of denosumab subcutaneous injection is available, Prolia® (biosimilars) but it is not included in this policy.[5]

Guidelines

Several guidelines address denosumab products (Xgeva, biosimilars).

- **Cancer:** Various guidelines from the National Comprehensive Cancer Network (NCCN) [e.g., breast cancer, prostate cancer, lung cancer, multiple myeloma] recommend denosumab products (Xgeva, biosimilars), for the prevention of skeletal related adverse events.[6-9]
- **Hypercalcemia of Malignancy:** Guidelines from the Endocrine Society for the treatment of hypercalcemia of malignancy in adults (2023) have several recommendations.[10] In adults with hypercalcemia of malignancy, treatment with denosumab products (Xgeva, biosimilars) over an intravenous bisphosphonate is recommended.

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of denosumab products (Xgeva, biosimilars). Approval is recommended for those who meet the conditions of coverage in the **Criteria** and **Dosing** for the listed

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indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of denosumab products (Xgeva, biosimilars) are recommended in those who meet one of the following criteria:

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FDA-APPROVED INDICATIONS

1. Bone Metastases from Solid Tumors - Prevention of Skeletal-Related Events. Note: Some examples of cancer in this clinical scenario include breast cancer, prostate cancer, and non-small-cell lung cancer]. ^

Criteria. Approve for 1 year if the patient meets the following criteria (A and B):
- **A)** The patient has bone metastases; [IC-L] AND
- **B)** Patients with prostate cancer must have castration-resistant prostate cancer. [IC-COMP]
  Note: This includes patients who have progressed after treatment with hormonal therapy or after surgical castration (e.g., bilateral orchiectomy). Examples of hormonal therapies for prostate cancer include Lupron Depot (leuprolide for depot suspension), Eligard (leuprolide acetate for injectable suspension), Trelstar (triptorelin pamoate for injectable suspension), or Zoladex (goserelin implant).

Dosing. Approve 120 mg administered as a subcutaneous (SC) injection once every 4 weeks.

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2. Multiple Myeloma (Prevention of Skeletal-Related Events). ^

Criteria. Approve for 1 year.

Dosing in Adults. Approve 120 mg administered as a subcutaneous (SC) injection once every 4 weeks.

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3. Giant Cell Tumor of Bone. ^

Criteria. Approve for 1 year.

Dosing: Approve 120 mg SC once every 4 weeks with loading doses on Day 8 and Day 15 of Month 1.[1,7]

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4. Hypercalcemia of Malignancy. ^

Criteria. Approve for 2 months if the patient meets the following criteria (A and B):
- **A)** The patient has a current malignancy; [IC-L] AND
- **B)** The patient's albumin-corrected calcium (cCa) is ≥ 11.5 mg/dL. [IC-ISGP]

Dosing. Approve 120 mg SC once every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.[1]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of denosumab products (Xgeva, biosimilars) are not recommended in the following situations:

1. Coverage is not recommended for circumstances *not* listed in the *Recommended Authorization Criteria*. Criteria will be updated as new published data are available.

SOURCES OF INFORMATION

1. Xgeva® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; June 2020.
2. Wyost® subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; March 2024.
3. Prolia® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2024.

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4. Jubbonti® subcutaneous injection [prescribing information]. Princeton, NJ: Sandoz; October 2024.
5. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – December 4, 2024). © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 14, 2025.
6. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – March 5, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 14, 2025.
7. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 1.2025 – September 17, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 14, 2025.
8. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 14, 2025.
9. Ghada El-Hajj Fuleihan, Clines GA, Hu MI, et al. Treatment of hypercalcemia of malignancy in adults: an Endocrine Society Clinical Practice guideline. *J Clin Endocrinol Metab*. 2023;108(3):507-528.
10. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article: Billing and Coding: Denosumab (Prolia ™, Xgeva ™) - Related to LCD L33394 (A52399) (Original effective date 10/1/15; revision effective date 12/21/2023). Accessed on July 15, 2025.
11. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L33394) [original date 10/01/2015; revision effective date 07/13/2025]. Accessed on July 15, 2025.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Policy created	New Medicare Advantage Medical Policy	07/11/18
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52399 and Bone Modifiers - Xgeva Utilization Review Policy.	08/28/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52399, and Bone Modifiers - Xgeva Utilization Review Policy.	11/22/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Determination L33394, Local Coverage Article A52399, and Bone Modifiers - Xgeva Utilization Review Policy.	02/26/2020
Policy revision	*Added the following to the Policy Statement "Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles." *Updated references	08/10/2020

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	* Removed criteria for all indications requiring hypocalcemia be corrected prior to initiation with Prolia and requiring that patient take concomitant calcium and vitamin D supplementation *Added criteria that Patients with prostate cancer have received at least one hormonal therapy for Bone Metastases from Solid Tumors	
Policy revision	The following changes were made: **1. Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events:** The examples of breast cancer, prostate cancer, and non-small-cell lung cancer were moved as examples of cancers from the cited indication to a Note. Regarding the criterion that patients with prostate cancer must have received at least one hormonal therapy, the examples of hormonal therapies for prostate cancer were moved from the criteria to a Note. **Hypercalcemia of Malignancy:** Regarding the criteria that the patient has tried intravenous bisphosphonate therapy, the qualifier of "at least one" bisphosphonate therapy was added and examples were moved from the criteria to a Note.	03/08/2021
Policy revision	**Bone Metastases From Solid Tumors – Prevention of Skeletal-Related Events:** Criteria changed from "patient with prostate cancer must have received at least one hormonal therapy" to "patient with prostate cancer must have castration-resistant prostate cancer." In the Note, it was added that this includes patients who have progressed after treatment with hormonal therapy or after surgical castration (e.g., bilateral orchiectomy). The examples of hormonal therapies for prostate cancer remain in the Note.	11/14/2022
Policy revision	**Hypercalcemia of Malignancy:** Requirements were deleted that the patient has tried at least one intravenous bisphosphonate therapy or that the patient has an estimated calculated creatinine clearance < 30 mL/min.	04/14/2023
Policy review	No criteria changes. Reviewed based on commercial policy annual review	04/03/2024
Policy revision	No criteria changes. Formatting and notation updates.	02/26/2025
Policy revision	Wyost was added to the policy with the same criteria as Xgeva. The Policy name was changed from "Bone Modifiers – Xgeva" to "Bone Modifiers – Denosumab Products (Xgeva)". Throughout the policy, wording was changed from Xgeva to denosumab products (Xgeva, biosimilar).	05/28/2025
Policy revision	Osenvelt was added to the policy with the same criteria as Xgeva. Throughout the policy, wording was changed to note that there are multiple biosimilars to Xgeva. Bomyntra was added to the policy with the same criteria as the other denosumab (Xgeva, biosimilars) products.	07/15/2025

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