Clinical Policy: Denosumab (Xgeva and Biosimilars)

Reference Number: LA.PHAR.58
Effective Date: 04.21
Last Review Date: 07.08.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Denosumab (Xgeva®) and its biosimilars, denosumab-bbdz (Wyost®)®), denosumab-bmwo (Stoboclo®, Osenvelt®), denosumab-bnht (Bomyntra®, Conexxence®), and denosumab-dssb (Ospomyv™, Xbryk™), are receptor activators of nuclear factor kappa-B ligand inhibitor.

FDA Approved Indication(s)

Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, and denosumab-bnht are indicated:

- For the prevention of skeletal-related events in patients with multiple myeloma (MM) and in patients with bone metastases from solid tumors.
- For the 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.
- For the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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It is the policy of Louisiana Healthcare Connections that Bomyntra, Conexxence, Osenvelt, Ospomyv, Stoboclo, Wyost, Xbryk, Xgeva, denosumab-bnht, and denosumab-dssb are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma or Solid Tumor (must meet all)**:**
1. Request is for Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht;
2. Diagnosis of one of the following (a or b):
   a. MM, and member is receiving or initiating therapy (e.g., chemotherapy, transplant) for symptomatic disease;
   b. Bone metastasis secondary to solid tumor (e.g., breast, kidney, lung, prostate, thyroid);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. For indications other than prostate or breast cancer, member meets one of the following (a or b):
   a. Failure of zoledronic acid* (Zometa) or pamidronate* at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendices B and D*);
   **Prior authorization may be required.*
6. Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht are not prescribed concurrently with Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, or denosumab-dssb;
7. Dose does not exceed 120 mg every 4 weeks.

Approval duration: 6 months

B. Giant Cell Tumor of Bone (must meet all)**:**
1. Request is for Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht;
2. Diagnosis of giant cell tumor of bone that is characterized as one of the following (a or b):
   a. Metastatic or unresectable disease;
   b. Localized disease, and Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht are prescribed as a single agent or in combination with radiation therapy;
3. Prescribed by or in consultation with an oncologist;
1. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht are not prescribed concurrently with Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, or denosumab-dssb;
6. Dose does not exceed 120 mg every 4 weeks plus 120 mg on days 8 and 15 of first month of therapy.

Approval duration: 6 months

C. Hypercalcemia of Malignancy (must meet all)**:**
1. Request is for Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht;
2. Diagnosis of hypercalcemia of malignancy:
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. Albumin-corrected calcium > 12.5 mg/dL despite IV bisphosphonate therapy in the last 30 days (*see Appendix B*);
   **Prior authorization may be required.*
6. Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht are not prescribed concurrently with Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, or denosumab-dssb;
7. Dose does not exceed 120 mg every 4 weeks plus 120 mg on days 8 and 15 of first month of therapy.

Approval duration: 6 months

D. Systemic Mastocytosis (off-label) (must meet all)**:**
1. Request is for Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht;
2. Diagnosis of systemic mastocytosis;
3. Member has osteopenia or osteoporosis with bone pain;
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
6. Member meets one of the following (a or b):
   a. Failure of zoledronic acid* (Zometa) or pamidronate* at up to maximally indicated doses unless clinically significant adverse effects are experienced or both are contraindicated *(see Appendices B and D)*;
      **Prior authorization may be required.*
   b. Request is for the treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
7. Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, or denosumab-bnht are not prescribed concurrently with Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, or denosumab-dssb;
8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Xgeva, Conexxence, Wyost, Bomyntra, Ospomyv, Xbryk, Osenvelt, Stoboclo, denosumab-bnht, or denosumab-dssb for a covered cancer-related indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed
   a. Xgeva or Wyost: 120 mg every 4 weeks or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g. diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADT: androgen deprivation therapy
BMD: bone mineral density
CKD-MBD: chronic kidney disease-mineral bone disorder
FDA: Food and Drug Administration
GIO: glucocorticoid-induced osteoporosis
MM: multiple myeloma
PMO: postmenopausal osteoporosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
IV bisphosphonates		
ibandronate (Boniva®)	Treatment: PMO Hypercalcemia of malignancy *(off-label)*	Varies *See prescribing information and compendia for dosing.*
zoledronic acid (Reclast®; Zometa®)	Reclast: Treatment/prevention: PMO, GIO Treatment: male osteoporosis Zometa: MM Bone metastasis from solid tumors Hypercalcemia of malignancy Systemic mastocytosis *(off-label)* Fracture prevention - breast/prostate cancer (*off-label*)	
pamidronate	MM Bone metastasis from breast cancer Hypercalcemia of malignancy Systemic mastocytosis *(off-label)* Fracture prevention – breast/prostate cancer (*off-label*)	
Oral bisphosphonates		
alendronate (Fosamax®)	Treatment: PMO Treatment: GIO, male osteoporosis	Varies *See prescribing information and compendia for dosing.*
Fosamax® Plus D (alendronate / cholecalciferol)	Treatment: PMO, male osteoporosis	
risedronate (Actonel®, Atelvia®)	Actonel: Treatment: PMO, GIO Treatment: male osteoporosis Atelvia: Treatment: PMO	
ibandronate (Boniva®)	Treatment/prevention: PMO	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, and denosumab-bnht: hypocalcemia, known clinically significant hypersensitivity to denosumab products
- Boxed warning(s):
  - Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, and denosumab-bnht: none reported

Appendix D: IV/PO Bisphosphonates: Examples of Contraindications and Adverse Effects

Bisphosphonates	Oral Formulations	IV Formulations
Contraindications		
Hypocalcemia	X	X
Increased risk of aspiration	X	-
Hypersensitivity to product component	X	X
Inability to stand/sit upright for at least 30 minutes	X	-
Creatinine clearance < 35 mL/min or evidence of acute renal impairment	-	X
Esophagus abnormalities which delay emptying such as stricture or achalasia	X	-
Clinically significant warnings or adverse side effects		
Pregnancy	X	X
Eye inflammation	X	X
Acute renal failure	X	X
Osteonecrosis of the jaw	X	X
Atypical femoral shaft fracture	X	X
Drug interactions (product-specific)	X	X
Severe or incapacitating musculoskeletal pain	X	X

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Denosumab (Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, denosumab-bnht, denosumab-dssb)	Treatment: PMO, GIO, male osteoporosis	60 mg SC once every 6 months	60 mg/dose
	Oncology: fracture prevention - Men at high risk for fracture receiving ADT for nonmetastatic prostate cancer - Women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer		
Denosumab (Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, denosumab-bnht)	MM Solid tumor - bone metastasis	120 mg SC once every 4 weeks	20 mg/dose
	Giant cell tumor of bone Hypercalcemia of malignancy	120 mg SC every 4 weeks plus 120 mg on Days 8 and 15 of first month of therapy	120 mg/dose

VI. Product Availability

Drug Name	Availability
Denosumab (Prolia, Conexxence, Jubbonti, Ospomyv, Stoboclo, denosumab-bnht, denosumab-dssb)	Injection (single-use prefilled syringe): 60 mg/mL
Denosumab (Xgeva, Bomyntra, Osenvelt, Wyost, Xbryk, denosumab-bnht)	• Injection (single-use vial): 120 mg/1.7 mL (70 mg/mL) • *Bomyntra and denosumab-bnht only* – Injection (single-dose prefilled syringe): 120 mg/1.7 mL (70 mg/mL)

VII. References

1. Prolia Prescribing Information. Thousand Oaks, CA: Amgen Inc.; March 2024. Available at: http://www.prolia.com. Accessed November 4, 2024.
2. Jubbonti Prescribing Information. Princeton, NJ: Sandoz Inc.: October 2024. Available at: http://www.jubbonti.com. Accessed November 4, 2024.
3. Xgeva Prescribing Information. Thousand Oaks, CA: Amgen Inc.; June 2020. Available at: http://www.xgeva.com. Accessed November 4, 2024.
4. Wyost Prescribing Information. Princeton, NJ: Sandoz Inc.: March 2024. Available at: http:www.wyost.com. Accessed November 4, 2024.
5. Ospomyv Prescribing Information. Incheon, Republic of Korea: Samsung Bioepis Co., Ltd.: February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761392Orig1s000lbl.pdf. Accessed March 4, 2025.
6. Xbryk Prescribing Information. Incheon, Republic of Korea: Samsung Bioepis Co., Ltd.: February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761392Orig1s000lbl.pdf. Accessed March 4, 2025.
7. Denosumab-dssb Prescribing Information. Incheon, Republic of Korea: Samsung Bioepis Co., Ltd.: February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761392Orig1s000lbl.pdf. Accessed March 4, 2025.
8. Stoboclo Prescribing Information. Jersy City, NJ: Celltrion USA, Inc.; February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761404s000lbl.pdf. Accessed March 6, 2025.
9. Osenvelt Prescribing Information. Jersy City, NJ: Celltrion USA, Inc.; February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761404s000lbl.pdf. Accessed March 6, 2025.
10. Bomyntra Prescribing Information. Lake Zurich, IL: Fresenius Kabi USA, LLC; March 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761398Orig1s000lbl.pdf. Accessed April 14, 2025.
11. Conexxence Prescribing Information. Lake Zurich, IL: Fresenius Kabi USA, LLC; March 2025. Available at:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761398Orig1s000lbl.pdf. Accessed April 14, 2025.
12. Denosumab-bnht Prescribing Information. Lake Zurich, IL: Fresenius Kabi USA, LLC; March 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761398Orig1s000lbl.pdf. Accessed April 14, 2025.
13. Clinical Pharmacology [database online]. Tampa, FL: Elsevier. 2023. URL: www.clinicalkeys.com/pharmacology.

Osteoporosis Diagnosis, Fracture Risk, and Treatment

14. Shoback D, Rosen CJ, Black DM, et al. Pharmacological management of osteoporosis in postmenopausal women: an endocrine society guideline update. J Clin Endocrinol Metab; March 2020, 105(3): 587-594.
15. Eastell R, Rosen CJ, Black DM, et al. Pharmacological management of osteoporosis in postmenopausal women: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab; 2019, 104: 1595–1622.
16. Camacho PM, Petak SM, Brinkley N et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2020 update. Endocr Pract. 2020;26(1):1-46..
17. LeBoggs MS, Greenspan SL, Insongna KL, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2022 Oct;33(10):2049-2102. doi:10.1007/s00198-021-05900-y. Erratum in: *Osteoporos Int.* 2022 Jul 28.
18. Siris ES, Adler R, Bilezikian J, et al. The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. Osteoporos Int (2014) 25:1439–1443. DOI 10.1007/s00198-014-2655-z.
19. Hodsman AB, Bauder DC, Dempster DW, et al. Parathyroid hormone and teriparatide for the treatment of osteoporosis: a review of the evidence and suggested guidelines for its use. Endocr Rev. 2005 Aug;26(5):688-703. Epub 2005 Mar 15.
20. Qaseem A, Hicks LA, Etxeandia-Ikobaltzeta I, et al. Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline From the American College of Physicians (Version 1, Update Alert). Ann Intern Med. 2024 Jun; 177(6): eL230113.

Male Osteoporosis

21. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society clinical practice guidelines. J Clin Endocrinol Metab 2012;97(6):1802-1822.

Glucocorticoid-Induced Osteoporosis

22. Humphrey MB, Russell L, Danila MI, et al. 2022 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. *Arthritis Rheumatol.* 2023 Oct 16. doi:10.1002/art.42646. Epub ahead of print. PMID:37845798.

Oncology

23. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 4, 2024.
24. National Comprehensive Cancer Network. Multiple Myeloma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed November 4, 2024.

25. National Comprehensive Cancer Network. Bone Cancer Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed November 4, 2024.
26. National Comprehensive Cancer Network. Breast Cancer Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 4, 2024.
27. National Comprehensive Cancer Network. Prostate Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 4, 2024.
28. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 11.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 4, 2024.
29. National Comprehensive Cancer Network. Kidney Cancer Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 4, 2024.
30. National Comprehensive Cancer Network. Systemic Mastocytosis Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed November 4, 2024.
31. National Comprehensive Cancer Network. Thyroid Carcinoma Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 4, 2024.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0897	Injection, denosumab, 1 mg
Q5136	Injection, denosumab-bbdz (jubbonti/wyost), biosimilar, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	01.21	04.21
Removed Prolia criteria. LDH Prolia criteria utilized for Physician Administered Medication Prior Authorizations. For multiple myeloma or solid tumor and systemic mastocytosis: allowed bypassing of redirection of step therapy in Stage IV or metastatic cancer settings.	04.22	07.01.22
Template changes applied to other diagnoses/indications and continued therapy section. References reviewed and updated. Added blurb this policy is for medical benefit only. Minor grammatical and formatting edits. Updated maximum dosage for MM.	06.27.23	01.03.24

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Annual review; no material changes to policy content; appendices updated for clarity, references reviewed and updated.	05.07.24	08.20.24
Added new biosimilar Wyost to policy; Added HCPCS code [Q5136]. Removal of Appendix E, as LDH Pharmacy has previously clarified that the cancer provisions referenced do not apply to the Medicaid line of business. References reviewed and updated.	10.04.24	1.27.25
Added new biosimilars to criteria.	07.08.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

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