

Prolia®/Xgeva® (denosumab)

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I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:

<u>Prolia</u>	60 billable units every 6 months
<u>Xgeva</u>	<i>Giant Cell Tumor of Bone; Hypercalcemia of malignancy</i>
	<u>Loading Dose:</u> 120 billable units on days 1, 8, 15, and 29
	<u>Maintenance:</u> 120 billable units every 4 weeks
	<i>Bone metastases from solid tumors:</i> 120 billable units every 4 weeks

III. Initial Approval Criteria

Prolia

- Patient must be supplementing with 1,000 mg of calcium and at least 400 IU of vitamin D daily; **AND**
- Patients must be \geq 18 years old; **AND**
- Patient must not have hypocalcemia; **AND**
- Patient must be at a high risk for fracture****; AND**

Coverage is provided in the following conditions:

Osteoporosis in Men and Women †

- Women only: Patient must be post-menopausal; **AND**

- Patient has a documented diagnosis of osteoporosis indicated by one or more of the following:
 - Hip DXA (femoral neck or total hip) or lumbar spine T-score ≤ -2.5 and/or forearm DXA 33% (one-third) radius; **OR**
 - T-score ≤ -1 or low bone mass and a history of fragility fracture to the hip or spine; **OR**
 - T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture $\geq 20\%$ or hip fracture $\geq 3\%$; **AND**
- Documented treatment failure or ineffective response \pm to a minimum (12) month trial on previous therapy with bisphosphonates (oral or IV) such as alendronate, risedronate, ibandronate, or zoledronic acid; **OR**
- Patient has a documented contraindication* or intolerance to BOTH oral bisphosphonates AND intravenous (IV) bisphosphonates such as alendronate, risedronate, ibandronate, or zoledronic acid

Osteoporosis treatment and prevention in prostate cancer patients †

- Documented Hip DXA (femoral neck or total hip) or lumbar spine T-score ≤ -1 (or patient meets the diagnostic criteria for osteoporosis above); **AND**
- Patient must be receiving androgen deprivation therapy for nonmetastatic prostate cancer

Osteoporosis treatment and prevention in breast cancer patients †

- Patient must be receiving adjuvant aromatase inhibitor therapy for breast cancer

<p>\pmIneffective response is defined as one or more of the following:</p> <ul style="list-style-type: none"> – Decrease in T-score in comparison with baseline T-score from DXA scan – Patient has a new fracture while on bisphosphonate therapy
<p>**High risk for fractures include, but are not limited to, one or more of the following:</p> <ul style="list-style-type: none"> – History of an osteoporotic fracture as an adult – Parental history of hip fracture – Low BMI – Rheumatoid arthritis – Alcohol intake (3 or more drinks per day) – Current smoking – History of oral glucocorticoids ≥ 5 mg/d of prednisone for >3 months (ever)
<p>*Examples of contraindications to oral bisphosphonate therapy include the following:</p> <ul style="list-style-type: none"> – Documented inability to sit or stand upright for at least 30 minutes – Documented pre-existing gastrointestinal disorder such as inability to swallow, Barrett's esophagus, esophageal stricture, dysmotility, or achalasia

Xgeva

- Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia; **AND**

Coverage is provided in the following conditions:

Prevention of skeletal-related events in patients with bone metastases from solid tumors †

- Patients must be ≥ 18 years old

Giant Cell Tumor of the Bone †

- Patient must be an adult or ≥ 13 years old and skeletally mature; **AND**
- Disease is unresectable or surgical resection is likely to result in severe morbidity; **OR**
- For metastatic disease ‡: **AND**
 - As a single agent; **OR**
- For localized disease ‡: **AND**
 - As a single agent; **OR**
 - In combination with interferon alpha or radiation therapy

Hypercalcemia of malignancy †

- Patients must be ≥ 18 years old; **AND**
- Patient must have a diagnosis of cancer (malignancy); **AND**
- Patient must have a diagnosis of refractory hypercalcemia of malignancy defined as an albumin-corrected calcium of >12.5 mg/dL (3.1 mmol/L) despite treatment with a minimum seven (7) day trial on previous therapy with intravenous (IV) bisphosphonates such as ibandronate (Boniva) or zoledronic acid (Reclast); **OR**
- Patient has a documented contraindication or intolerance to intravenous (IV) bisphosphonates such as ibandronate (Boniva) or zoledronic acid (Reclast)

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria

Coverage can be renewed based on the following criteria:

- Patient continues to meet the criteria indicated in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe symptomatic hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, dermatological adverse reactions, severe infection, etc.; **AND**

Prolia

- Disease response as indicated by one or more of the following:
 - Absence of fractures
 - Increase in bone mineral density compared to pretreatment baseline

Xgeva

- Disease response as indicated by the following:
 - Bone metastases: absence/delay in skeletal-related events (e.g., pathologic fracture, radiation therapy to bone, surgery to bone, or spinal cord compression)

- Giant Cell Tumor of the Bone: tumor response with disease stabilization or decrease in size or spread of tumor
- Hypercalcemia of Malignancy: corrected serum calcium \leq 11.5 mg/dL

V. Dosage/Administration

Prolia

Indication	Dose
All indications	60 mg subcutaneously by a health care provider every 6 months

Xgeva

Indication	Dose
Bone metastases from solid tumors	120 mg subcutaneously by a health care provider every 4 weeks
Giant Cell Tumor of Bone	120 mg subcutaneously by a health care provider every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.
Hypercalcemia of malignancy	120 mg subcutaneously by a health care provider every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.

VI. Billing Code/Availability Information

Jcode:

- J0897 – Injection, denosumab, 1 mg; 1 mg = 1 billable unit

NDC:

- Prolia 60 mg/1 mL single-use prefilled syringe: 55513-0710-XX
- Xgeva 120 mg/1.7 mL single-use vial: 55513-0730-XX

VII. References

1. Prolia [package insert]. Thousand Oaks, CA; Amgen, Inc.; May 2017. Accessed June 2017.
2. Xgeva [package insert]. Thousand Oaks, CA; Amgen, Inc.; May 2017. Accessed June 2017.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Denosumab. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc.” To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2017.

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12. Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians. *Ann Intern Med.* 2017 May 9. doi: 10.7326/M15-1361.
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14. First Coast Service Options, Inc. Local Coverage Determination (LCD): Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications (L33270). Centers for Medicare & Medicaid Services, Inc. Updated on 10/18/2016 with effective date 10/14/2016. Accessed June 2017.
15. National Government Services, Inc. Local Coverage Article: Denosumab (Prolia™, Xgeva™) - Related to LCD L33394 (A52399). Centers for Medicare & Medicaid Services, Inc. Updated on 03/17/2017 with effective date 03/23/2017. Accessed June 2017.
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Appendix 1 – Covered Diagnosis Codes

Prolia

ICD-10	ICD-10 Description
C50.011- C50.929	Malignant neoplasms of breast
C61	Malignant neoplasm of prostate
M80.00XA- M80.08XS	Age-related osteoporosis with current pathological fracture
M80.80XA- M80.88XS	Other osteoporosis with current pathological fracture
M81.0	Age-related osteoporosis without current pathological fracture
M81.6	Localized osteoporosis [Lequesne]
M81.8	Other osteoporosis without current pathological fracture
M85.80	Other specified disorders of bone density and structure, unspecified site
M85.851	Other specified disorders of bone density and structure, right thigh
M85.852	Other specified disorders of bone density and structure, left thigh
M85.859	Other specified disorders of bone density and structure, unspecified thigh
M85.88	Other specified disorders of bone density and structure, other site
M85.89	Other specified disorders of bone density and structure, multiple sites

Dual coding requirement

- Osteoporosis treatment and prevention in breast cancer patients on aromatase inhibitors:
 - One code from the M80.00XA - M80.88XS, M81.X, or M85.X series plus one code from the C50.X
- Treatment of bone loss in men with prostate cancer receiving androgen deprivation therapy:
 - One code from the M80.00XA - M80.88XS, M81.X, or M85.X series plus C61

Xgeva

ICD-10	ICD-10 Description
C00-C14	Malignant neoplasms of lip, oral cavity and pharynx
C15-C26	Malignant neoplasms of digestive organs
C30-C39	Malignant neoplasms of respiratory and intrathoracic organs
C40-C41	Malignant neoplasms of bone and articular cartilage
C43-C44	Melanoma and other malignant neoplasms of skin
C45-C49	Malignant neoplasms of mesothelial and soft tissue
C50.011- C50.929	Malignant neoplasms of breast
C51-C58	Malignant neoplasms of female genital organs
C60-C63	Malignant neoplasms of male genital organs

ICD-10	ICD-10 Description
C64-C68	Malignant neoplasms of urinary tract
C69-C72	Malignant neoplasms of eye, brain and other parts of central nervous system
C73-C75	Malignant neoplasms of thyroid and other endocrine glands
C7A.00- C7A.8	Malignant neuroendocrine tumors
C7B.00- C7B.8	Secondary neuroendocrine tumors
C76-C80	Malignant neoplasms of ill-defined, other secondary and unspecified sites
C81	Hodgkin lymphoma
C82	Follicular lymphoma
C83	Non-follicular lymphoma
C84	Mature T/NK-cell lymphomas
C85	Other specified and unspecified types of non-Hodgkin lymphoma
C86	Other specified types of T/NK-cell lymphoma
C88	Malignant immunoproliferative diseases and certain other B-cell lymphomas
C96	Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue
D00-D09	In situ neoplasms
D10-D36	Benign neoplasms, except benign neuroendocrine tumors
D3A.00- D3A.8	Benign neuroendocrine tumors
D37-D44	Neoplasm of uncertain behavior of oral cavity and digestive organs - Neoplasm of uncertain behavior of endocrine glands
D48	Neoplasm of uncertain behavior of other and unspecified sites
D49.0- D49.9	Neoplasms of unspecified behavior
E83.52	Hypercalcemia
Z85	Personal history of malignant neoplasm

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Prolia and Xgeva

Jurisdiction(s): 6, K	NCD/LCD Document (s): A52399
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A52399&bc=gAAAAAAAAAAAAAA==	
Jurisdiction(s): N	NCD/LCD Document (s): L33270
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L33270&bc=gAAAAAAAAAAAAAA==	
Jurisdiction(s): 15	NCD/LCD Document (s): A52424
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A52424&bc=gAAAAAAAAAAAAAA==	

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Cahaba Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC