

## Prolia®/Xgeva® (denosumab)

Document Number: IC-0098

Last Review Date: 05/31/2016

Date of Origin: 11/28/2011

Dates Reviewed: 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 5/2015, 8/2015, 11/2015, 02/2016, 05/2016

### I. Length of Authorization

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

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

– N/A

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

##### Prolia

*Osteoporosis treatment and prevention in cancer patients; Osteoporosis in Men and Women*

**Male:** 60 billable units every 6 months

**Female:** 60 billable units every 6 months

##### Xgeva

*Giant Cell Tumor of Bone; Hypercalcemia of malignancy*

##### Loading Dose:

**Male:** 120 billable units days 1, 8, 15, and 29

**Female:** 120 billable units days 1, 8, 15, and 29

##### Maintenance:

**Male:** 120 billable units every 4 weeks

**Female:** 120 billable units every 4 weeks

*Bone metastases from solid tumors:*

**Male:** 120 billable units every 4 weeks

**Female:** 120 billable units every 4 weeks

### III. Initial Approval Criteria

All patients receiving denosumab therapy must meet the following criteria:

- Patient must be supplementing with 1,000 mg calcium and at least 400iu of Vitamin D daily; **AND**

#### Prolia

Coverage is provided in the following conditions:

#### **Osteoporosis in Men and Women †**

- Patients must be  $\geq 18$  years old; **AND**
- Women only: Patient must be post-menopausal; **AND**
- Documented Hip DXA (femoral neck or total hip) or lumbar spine T-score  $\leq -2.5$ ; **AND**
- Patient must be at a high risk for fracture ‡; **AND**
- Patient does not have hypocalcemia; **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 (Fosamax), risedronate (Actonel), ibandronate (Boniva) or zoledronic acid (Reclast); **OR**
- Patient has a documented contraindication\* or intolerance to BOTH to oral bisphosphonates **AND** intravenous (IV) bisphosphonates such as alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva) or zoledronic acid (Reclast)

#### **Osteoporosis treatment and prevention in cancer patients †**

- Patients must be  $\geq 18$  years old; **AND**
- Documented Hip DXA (femoral neck or total hip) or lumbar spine T-score  $\leq -1$ ; **AND**
- Patient must be at a high risk for fracture‡; **AND**
- Patient does not have hypocalcemia; **AND**
- Patient must be receiving androgen deprivation therapy for prostate cancer; **OR**
- Patient must be receiving adjuvant aromatase inhibitor therapy for breast cancer

**$\pm$ Ineffective response is defined as one of the following:**

- Decrease in T-score in comparison with baseline T-score from DXA scan
- Patient has a new fracture while on bisphosphonate therapy

**‡High risk for fractures is defined as one of the following:**

- History of an osteoporotic fracture as an adult
- Parental history of hip fracture

- Low BMI
- Rheumatoid arthritis
- Alcohol abuse (3 or more drinks per day)
- Current tobacco smoking
- History of oral glucocorticoids >5 mg/d of prednisone for >3 months

**\*Examples of contraindication to oral bisphosphonate therapy include the following:**

- 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**

Coverage is provided in the following conditions:

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

- Patients must be  $\geq 18$  years old;

#### **Giant Cell Cancer of the Bone †**

- Patients must be  $\geq 13$  years old; **AND**
- For metastatic disease; **AND**
  - As a single agent; **OR**
- For localized disease; **AND**
  - As a single agent; **OR**
  - In combination with: interferon alpha, peginterferon, or radiation therapy

#### **Hypercalcemia of malignancy †**

- Patients must be  $\geq 18$  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)

## **IV. Renewal Criteria**

Coverage can be renewed based on the following criteria:

- Patient continues to meet the criteria indicated in section III; **AND**
- Disease response with improvement in patient’s symptoms; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe symptomatic hypocalcemia.

## V. Dosage/Administration

### Prolia

Indication	Dose
All indications	60 mg every 6 months

### Xgeva

Indication	Dose
Bone metastases from solid tumors	120 mg every 4 weeks
Giant Cell Tumor of Bone	120 mg subcutaneously once every 4 weeks; give 2 additional 120 mg doses on day 8 and 15 of the first month of therapy only.
Hypercalcemia of malignancy	120 mg subcutaneously on days 1, 8, and 15 initially, then 120 mg every 4 weeks beginning on day 29.

## VI. Billing Code/Availability Information

### Jcode:

- J0897 – Prolia (Amgen) 60 mg injection: 1 billable unit = 1 mg
- J0897 – Xgeva (Amgen) 120 mg injection: 1 billable unit = 1 mg

### NDC:

- N/A

## VII. References

1. Prolia [package insert]. Thousand Oaks, CA; Amgen, Inc.; February 2015. Accessed April 2016.
2. Xgeva [package insert]. Thousand Oaks, CA; Amgen, Inc.; March 2016. Accessed April 2016.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Denosumab. National Comprehensive Cancer Network, 2016. 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 April 2016.

4. Branstetter DG, Nelson SD, Manivel JC, et al. Denosumab induces tumor reduction and bone formation in patients with giant-cell tumor of bone. Clin Cancer Res. 2012 Aug 15;18(16):4415-24.
5. Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. Lancet Oncol. 2010 Mar;11(3):275-80.
6. WHO Scientific Group on the Prevention and Management of Osteoporosis. Prevention and management of osteoporosis: report of a WHO scientific group. (WHO technical report series; 921). Geneva, Switzerland: WHO; 2000.
7. Kanis JA on behalf of the World Health Organization Scientific Group (2007). Assessment of osteoporosis at the primary health care level. Technical Report. World Health Organization Collaborating Center for Metabolic Bone Diseases. University of Sheffield, UK; 2007.
8. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014.
9. 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. doi: 10.1210/jc.2014-1001. Epub 2014 Jun 10.
10. 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 03/11/2016 with effective date 03/10/2016. Accessed April 2016.
11. National Government Services, Inc. Local Coverage Article: Denosumab (Prolia™, Xgeva™) - Related to LCD L33394 (A52399). Centers for Medicare & Medicaid Services, Inc. Updated on 01/29/2016 with effective date 10/1/2015. Accessed April 2016.

## Appendix 1 – Covered Diagnosis Codes

### Prolia

ICD-10	ICD-10 Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast

ICD-10	ICD-10 Description
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast

ICD-10	ICD-10 Description
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C61	Malignant neoplasm of prostate
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 M81.X or M85.X series plus one code from the C50.X series
- Treatment of bone loss in men with prostate cancer receiving androgen deprivation therapy:  
One code from the 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

ICD-10	ICD-10 Description
C50-C50	Malignant neoplasms of breast
C51-C58	Malignant neoplasms of female genital organs
C60-C63	Malignant neoplasms of male genital organs
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-C7A	Malignant neuroendocrine tumors
C7B-C7B	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-D3A	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-D49	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

<b>Jurisdiction(s):</b> K	<b>NCD/LCD Document (s):</b> A52399
<a href="https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52399&amp;ver=15&amp;SearchType=Advanced&amp;CoverageSelection=Both&amp;NCSelection=NCD&amp;ArticleType=Ed&amp;PolicyType=Final&amp;s=All&amp;KeyWord=J0897&amp;KeyWordLookUp=Doc&amp;KeyWordSearchType=Exact&amp;kq=true&amp;bc=IAAABAAAAAAAAA%3d%3d&amp;">https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52399&amp;ver=15&amp;SearchType=Advanced&amp;CoverageSelection=Both&amp;NCSelection=NCD&amp;ArticleType=Ed&amp;PolicyType=Final&amp;s=All&amp;KeyWord=J0897&amp;KeyWordLookUp=Doc&amp;KeyWordSearchType=Exact&amp;kq=true&amp;bc=IAAABAAAAAAAAA%3d%3d&amp;</a>	

### Prolia and Xgeva

<b>Jurisdiction(s):</b> 9 (N)	<b>NCD/LCD Document (s):</b> L33270
<a href="https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=33270&amp;ver=11&amp;SearchType=Advanced&amp;CoverageSelection=Both&amp;NCSelection=NCD&amp;ArticleType=Ed&amp;PolicyType=Final&amp;s=All&amp;KeyWord=J0897&amp;KeyWordLookUp=Doc&amp;KeyWordSearchType=Exact&amp;kq=true&amp;bc=IAAABAAAAAAAAA%3d%3d&amp;">https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=33270&amp;ver=11&amp;SearchType=Advanced&amp;CoverageSelection=Both&amp;NCSelection=NCD&amp;ArticleType=Ed&amp;PolicyType=Final&amp;s=All&amp;KeyWord=J0897&amp;KeyWordLookUp=Doc&amp;KeyWordSearchType=Exact&amp;kq=true&amp;bc=IAAABAAAAAAAAA%3d%3d&amp;</a>	

### Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
E	CA, HI, NV, AS, GU, CNMI	Noridian Administrative Services (NAS)
F	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Administrative Services (NAS)
5	KS, NE, IA, MO	Wisconsin Physicians Service (WPS)
6	MN, WI, IL	National Government Services (NGS)
H	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions
8	MI, IN	Wisconsin Physicians Service (WPS)
9 (N)	FL, PR, VI	First Coast Service Options
10 (J)	TN, GA, AL	Cahaba Government Benefit Administrators
11 (M)	NC, SC, VA, WV	Palmetto GBA
12 (L)	DE, MD, PA, NJ, DC	Novitas Solutions

#### PROLIA®/XGEVA® (denosumab) Prior Auth Criteria

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K	NY, CT, MA, RI, VT, ME, NH	National Government Services (NGS)
15	KY, OH	CGS Administrators, LLC