

## Clinical Criteria

<b>Subject:</b>	Denosumab Agents		
<b>Document #:</b>	ING-CC-0027	<b>Publish Date:</b>	<u>04/01/2019</u> <u>09/23/2019</u>
<b>Status:</b>	Revised	<b>Last Review Date:</b>	<u>08/17/2018</u> <u>08/16/2019</u>

### Table of Contents

<a href="#">Overview</a>	<a href="#">Coding</a>	<a href="#">References</a>
<a href="#">Clinical criteria</a>	<a href="#">Document history</a>	

### Overview

This document addresses the use of denosumab which is approved for the treatment of individuals with osteoporosis, glucocorticoid-induced osteoporosis, treatment induced bone loss, bone metastases, multiple myeloma, giant cell tumor of the bone, hypercalcemia of malignancy and for all other indications as applicable. Denosumab (Prolia, Xgeva) is a subcutaneous, fully human monoclonal antibody that is specifically designed to target the human receptor activator of nuclear factor kappa-B ligand (RANKL).

The Endocrine Society (2019) and The American Association of Clinical Endocrinologists and American College of Endocrinology (AAACE/ACE) (2016) osteoporosis treatment guidelines (2019) recommend bisphosphonate agents (alendronate, risedronate, and zoledronic acid) initial therapy for most individuals at high risk of fracture given their efficacy to reduce hip, nonvertebral, and spine fractures. The Endocrine Society and AAACE/ACE also recommend Prolia (denosumab) as initial (or alternative initial) treatment for those at high risk for fracture. For those at especially high fracture risk, the Endocrine Society recommends anabolic agents Forteo (teriparatide) or Tymlos (abaloparatide); AAACE/ACE recommends Forteo (teriparatide), Prolia (denosumab), or zoledronic acid be considered in this population.

Osteoporosis may be diagnosed by bone mineral density (BMD) testing indicating a T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population. It also may be clinically diagnosed based on a history of a fragility fracture (low trauma fracture).

Higher risk for fracture may be defined as:

1. History of osteoporotic fracture; or
2. Multiple risk factors for fractures, including but not limited to: Prior low-trauma fracture as an adult, advanced age, gender, ethnicity, low bone mineral density, low body weight, family history of osteoporosis, use of glucocorticoids (daily dosage equivalent to 5 mg or greater prednisone for at least 3 months), cigarette smoking, excessive alcohol consumption (3 or more drinks per day), secondary osteoporosis (such as, rheumatoid arthritis), early menopause, height loss or kyphosis, fall risk and low calcium intake; or
3. Failure or intolerance to other osteoporosis therapies.

A failure of other osteoporosis therapies, otherwise known as refractory disease, may be defined as a decline in BMD while on therapy ( $\geq 5\%$ ) or a fragility fracture while on therapy.

### Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

#### Prolia (denosumab)

Requests for Prolia (denosumab) may be approved when the following criteria are met:

- I. Individual is 18 years of age or older;
- AND**
- II. Individual is a male or postmenopausal female with the following:
- AND**

~~III.~~ ~~OR~~  
~~IV-III.~~ A. Individual has a diagnosis of osteoporosis (defined as a T-score -2.5 or less bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture));

Formatted: Indent: Left: 0.5", Hanging: 0.31"

~~IV-III.~~ ~~OR~~  
Individual has glucocorticoid-induced osteoporosis (defined as a T-score -2.5 or less defined as a bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture) and is initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5mg or greater of prednisone and expected to remain on glucocorticoids for a least 6 months;

Formatted: Font: (Default) Arial, 9 pt, Bold

Formatted: Font: (Default) Arial, 9 pt

Formatted: Normal, No bullets or numbering, Tab stops: 0.5", Left

~~V-IV.~~ ~~OR~~

Individual has had at least one osteoporotic (minimal trauma) fracture; ~~OR~~

~~VI-V.~~ Individual has two or more risk factors for osteoporotic fracture; ~~OR~~

~~VII-VI.~~ Individual has failed, is intolerant to or has a medical contraindication to other available osteoporosis therapies (for example, bisphosphonates);

~~OR~~

~~VIII-VII.~~ Individual is a postmenopausal (natural or induced) female receiving adjuvant aromatase inhibitor therapy for treatment of breast cancer;

~~OR~~

~~IX-VIII.~~ Individual is a male receiving androgen deprivation therapy for non-metastatic prostate cancer; ~~AND~~

~~X.~~ Individual has had at least one osteoporotic (minimal trauma) fracture;

~~XI-X.~~ ~~OR~~

Individual has one or more additional risk factors for osteoporotic fracture.

Formatted: Font: (Default) Arial, 9 pt, Bold

Formatted: Normal, Indent: Left: 0.25", No bullets or numbering

Formatted: Font: (Default) Arial, 9 pt

#### Xgeva (denosumab)

Requests for Xgeva (denosumab) may be approved when the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Individual is using for the prevention of skeletal-related events with one of the following conditions:
  - A. Multiple myeloma; **OR**
  - B. Solid tumor bone metastases (excluding prostate cancer unless castration resistant/recurrent);

**OR**

- III. Individual is 18 years of age or older; **AND**
- IV. Individual is using for the treatment of hypercalcemia of malignancy (defined as an albumin-corrected serum calcium level greater than 12.5 mg/dL (3.1 mmol/L)) and is refractory to recent (within last 30 days) treatment with intravenous bisphosphonate therapy (such as pamidronate or zoledronic acid);

**OR**

- V. Individual is using for the treatment of localized or metastatic giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity; **AND**
  - A. Individual is 18 years of age or older; **OR**
  - B. Individual is a skeletally mature adolescent (defined by at least one mature long bone [for example; closed epiphyseal growth plate of the humerus]).

Request for denosumab agents (Prolia, Xgeva) may not be approved when the above criteria are not met and for all other indications.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

#### HCPCS

**J0897** Injection, denosumab, 1 mg [Prolia, Xgeva]

#### ICD-10 Diagnosis

**C00.0-C39.9** Malignant neoplasms

<b>C40.00-C41.9</b>	Malignant neoplasm of bone and articular cartilage
<b>C43.0-C60.9</b>	Malignant neoplasms
<b>C61</b>	Malignant neoplasm of prostate
<b>C62.00-C75.9</b>	Malignant neoplasms
<b>C76.0-C76.8</b>	Malignant neoplasm of other and ill-defined sites
<b>C79.51</b>	Secondary malignant neoplasm of bone
<b>C90.00-C90.32</b>	Multiple myeloma and malignant plasma cell neoplasms
<b>D48.0</b>	Neoplasm of uncertain behavior of bone and articular cartilage [specified as GCTB]
<b>E83.52</b>	Hypercalcemia
<b>M81.0-M81.8</b>	Osteoporosis without current pathological fracture
<b>M85.80-M85.9</b>	Other specified disorders of bone density and structure [osteopenia]
<b>N95.1</b>	Menopausal and female climacteric states
<b>Z08</b>	Encounter for follow-up examination after completed treatment for malignant neoplasm
<b>Z51.11-Z51.12</b>	Encounter for antineoplastic chemotherapy and immunotherapy
<b>Z79.51-Z79.52</b>	Long term (current) use of steroids
<b>Z79.811</b>	Long term (current) use of aromatase inhibitors
<b>Z79.899</b>	Other long term (current) drug therapy [prophylactic drug therapy]
<b>Z85.00-Z85.45</b>	Personal history of malignant neoplasms
<b>Z85.46</b>	Personal history of malignant neoplasm of prostate
<b>Z85.47-Z85.59</b>	Personal history of malignant neoplasms
<b>Z85.810-Z85.9</b>	Personal history of malignant neoplasms
<b>Z87.310</b>	Personal history of (healed) osteoporosis fracture
<b>M80.00XA- M80.88XS</b>	Osteoporosis with current pathological fracture

## Document History

Revised: 08/16/2019

Document History:

- 08/16/2019 – Annual Review: Clarify Prolia PA definition of osteoporosis for consistency with other agents in the class. Wording and formatting changes for clarity. Coding Reviewed: No changes.
- 11/08/2018 – Code review: no changes. Added X80.00XA-M80.88XS.
- 08/17/2018 – Annual Review: Initial review of CG-DRUG-73. Update Prolia PA to delete specific examples of fracture risk factors for consistency with other agents in the class review and as they are available in the overview section. Wording and formatting changes for clarity.

## References

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2016. *Endocrine Practice*. 2016;22(4):1-42.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. URL: <http://www.clinicalpharmacology.com>. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: June 18, 2018.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Drug Facts and Comparisons. Facts and Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 2018. Updated periodically.
6. Eastell R, Rose CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 5, May 2019, Pages 1595–1622, <https://doi.org/10.1210/ic.2019-00221>.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

© CPT Only – American Medical Association