

**Denosumab:**  
**Prolia®; Jubbonti®; Xgeva®; Wyost®**  
**(Subcutaneous)**

Document Number: MODA-0098

Last Review Date: 04/04/2024

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, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 01/2017, 05/2017, 08/2017, 11/2017, 02/2018, 05/2018, 06/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023, 10/2023, 04/2024

**I. Length of Authorization**

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

**II. Dosing Limits**

**A. Quantity Limit (max daily dose) [NDC Unit]:**

- Prolia & Jubbonti: 60 mg/1 mL single-dose prefilled syringe: 1 syringe every 6 months
- Xgeva & Wyost: 120 mg/1.7 mL single-dose vial:
  - Load: 4 vials for one 29-day cycle
  - Maintenance: 1 vial monthly

**B. Max Units (per dose and over time) [HCPCS Unit]:**

<b>Prolia</b>	<u>All indications:</u> <ul style="list-style-type: none"> <li>• 60 billable units every 6 months</li> </ul>
<b>Jubbonti</b>	<u>All indications:</u> <ul style="list-style-type: none"> <li>• 60 mg every 6 months</li> </ul>
<b>Xgeva</b>	<u>Giant Cell Tumor of Bone &amp; Hypercalcemia of Malignancy</u> <ul style="list-style-type: none"> <li>- <u>Loading Dose:</u> <ul style="list-style-type: none"> <li>• 120 billable units on days 1, 8, 15, and 29</li> </ul> </li> <li>- <u>Maintenance:</u> <ul style="list-style-type: none"> <li>• 120 billable units every 4 weeks</li> </ul> </li> </ul> <u>Bone metastases from solid tumors, Multiple Myeloma, &amp; Systemic Mastocytosis:</u> <ul style="list-style-type: none"> <li>• 120 billable units every 4 weeks</li> </ul>

<b>Wyost</b>	<u><i>Giant Cell Tumor of Bone &amp; Hypercalcemia of Malignancy</i></u>
	<ul style="list-style-type: none"> <li>- <u>Loading Dose:</u> <ul style="list-style-type: none"> <li>• 120 mg on days 1, 8, 15, and 29</li> </ul> </li> <li>- <u>Maintenance:</u> <ul style="list-style-type: none"> <li>• 120 mg every 4 weeks</li> </ul> </li> </ul>
	<u><i>Bone metastases from solid tumors, Multiple Myeloma, &amp; Systemic Mastocytosis:</i></u> <ul style="list-style-type: none"> <li>• 120 mg every 4 weeks</li> </ul>

### III. Initial Approval Criteria

Site of care specialty infusion program requirements are met (refer to [Moda Site of Care Policy](#)).

#### **Prolia & Jubbonti**

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

#### **Universal Criteria** <sup>1,2,31,35</sup>

- Patient must be supplementing with 1,000 mg of calcium and at least 400 IU of vitamin D daily; **AND**
- Patient must not have hypocalcemia; **AND**
- Patients with advanced kidney disease (i.e., eGFR < 30 mL/min/1.73 m<sup>2</sup> and including dialysis-dependent patients) will be monitored for the presence of chronic kidney disease-mineral and bone disorder (CKD-MBD) with intact parathyroid hormone (iPTH), serum calcium, 25(OH) vitamin D, and 1,25 (OH)<sub>2</sub> vitamin D prior to decisions regarding denosumab treatment; **AND**
- Pregnancy is ruled out prior to administration in biologic females of child-bearing potential; **AND**
- Will not be used in combination with other denosumab products, bisphosphonates, romosozumab, or parathyroid hormone analogs/related peptides; **AND**

#### **Osteoporosis in Men and Women** † <sup>1,2,28,29,31,33,35</sup>

- Biological female patient must be post-menopausal; **AND**
- Patient must be at a high risk for fracture<sup>\*\*</sup>; **AND**
- Patient has a documented diagnosis of osteoporosis indicated by one or more of the following:
  - T-score by DXA of ≤ -2.5 measured at the lumbar spine, femoral neck, total hip, or forearm at the 33% (one-third) radius site; **OR**
  - History of fragility fracture to the hip or spine, regardless of T-score; **OR**

- T-score by DXA between -1.0 and -2.5 measured at the lumbar spine, femoral neck, total hip, or forearm at the 33% (one-third) radius site; **AND**
  - History of fracture of proximal humerus, pelvis, or distal forearm; **OR**
  - FRAX 10-year probability for major fracture  $\geq 20\%$  or hip fracture  $\geq 3\%$ ; **AND**
- Patient has one of the following:
  - Documented treatment failure or ineffective response<sup>±</sup> 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

**Glucocorticoid-Induced Osteoporosis † ‡ 1,2,21,37**

- Patient will be initiating or is continuing systemic glucocorticoid therapy at a daily dosage equivalent to  $\geq 2.5$  mg of prednisone and is expected to remain on glucocorticoid therapy for at least 3 months; **AND**
- Patient must be at an increased risk for fracture **¥; AND**
  - Documented treatment failure or ineffective response<sup>±</sup> 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 † ‡ 1,2,5,22,38**

- Patient must be receiving androgen deprivation therapy; **AND**
- Patient must be at a high risk for fracture\*\*

**Osteoporosis treatment and prevention in breast cancer patients † ‡ 1,2,5,23,39**

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

<b>±Ineffective response is defined as one or more of the following:</b> <sup>31,33,35</sup>
<ul style="list-style-type: none"> <li>– Decrease in T-score in comparison with baseline T-score from DXA scan</li> <li>– Patient has a new fracture while on bisphosphonate therapy</li> </ul>
<b>**High risk for fractures include, but are not limited to, one or more of the following:</b> <sup>31,35</sup>
<ul style="list-style-type: none"> <li>– History of an osteoporotic fracture as an adult</li> <li>– Parental history of hip fracture</li> <li>– Low BMI</li> <li>– Rheumatoid arthritis</li> <li>– Alcohol intake (3 or more drinks per day)</li> <li>– Current smoking</li> <li>– History of oral glucocorticoids <math>\geq 5</math> mg/d of prednisone (or equivalent) for &gt;3 months (ever)</li> </ul>

**\*Examples of contraindications to oral bisphosphonate therapy include the following:** <sup>32</sup>

- Documented inability to sit or stand upright for at least 30 minutes
- Documented pre-existing esophageal disorders such as achalasia, esophageal stricture, esophageal varices, or Barrett’s esophagus
- Surgical anastomoses are present in the GI tract after certain types of bariatric surgery (e.g., Roux-en-Y gastric bypass)
- Documented pre-existing hypocalcemia
- Documented pre-existing renal insufficiency defined as creatinine clearance < 30-35 mL/min

**\*Examples of contraindications to injectable bisphosphonate therapy include the following:** <sup>32</sup>

- Documented pre-existing hypocalcemia
- Documented pre-existing renal insufficiency defined as creatinine clearance < 30-35 mL/min

**‡ Increased risk for glucocorticoid-induced osteoporosis fracture include, but are not limited to, one or more of the following:** <sup>1,2,37</sup>

- Prior osteoporotic fracture
- High-dose glucocorticoid use (i.e., prednisone [or equivalent]  $\geq 30$  mg/d  $> 30$  d or  $\geq 5$  g/year)
- FRAX glucocorticoid adjusted  $\diamond$  10-year risk of major osteoporotic fracture  $\geq 20\%$  or hip  $> 3\%$
- T-score by DXA of  $\leq -2.5$  measured at the lumbar spine, femoral neck, total hip, or forearm at the 33% (one-third) radius site

$\diamond$  Note: If glucocorticoid dose is  $> 7.5$  mg/day, multiply the FRAX 10-year risk of major osteoporotic fracture by 1.15 and the hip fracture risk by 1.2 (e.g., if hip fracture risk is 2.0% multiply by 1.2 = 2.4% risk)

**Xgeva & Wyost**

**Coverage is provided in the following conditions:**

**Universal Criteria** <sup>3,4,34,35,38,39</sup>

- Patient will receive calcium and vitamin D as necessary to treat or prevent hypocalcemia (*Note: excludes when use is for hypercalcemia of malignancy*); **AND**
- Patient must not have hypocalcemia; **AND**
- Will not be used in combination with other denosumab products, bisphosphonates, romosozumab, or parathyroid hormone analogs/related peptides; **AND**

**Prevention of skeletal-related events in patients with multiple myeloma OR bone metastases from solid tumors** † <sup>3-5,16-18,25,27,38,39</sup>

- Patient is at least 18 years of age; **AND**
  - Patient must try and have an inadequate response, contraindication\*, or intolerance to at least a three (3) month trial of zoledronic acid; **OR**
  - Patient has metastatic breast cancer, metastatic castration-resistant prostate cancer, or metastatic lung cancer (both SCLC and NSCLC)

**Giant Cell Tumor of the Bone** †  $\Phi$  <sup>3-5,7,25,26</sup>

- Patient must be an adult or at least 12 years of age and skeletally mature; **AND**
  - Disease is unresectable or surgical resection is likely to result in severe morbidity; **OR**

- Disease is localized, recurrent, or metastatic ‡; **AND**
  - Used as a single agent; **OR**
  - Used in combination with serial embolization and/or radiation therapy

**Hypercalcemia of malignancy † Φ<sup>3-5,11</sup>**

- Patient is at least 18 years of age; **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 or zoledronic acid; **OR**
  - Patient has a documented contraindication\* or intolerance to intravenous (IV) bisphosphonates such as ibandronate or zoledronic acid

**Systemic Mastocytosis ‡<sup>5,30</sup>**

- Patient has osteopenia or osteoporosis and coexisting bone pain; **AND**
  - Used as second line therapy if patient is not responding to bisphosphonate therapy; **OR**
  - Patient is not a candidate for bisphosphonate therapy due to renal insufficiency

**\*Examples of contraindications to injectable bisphosphonate therapy include the following:<sup>32</sup>**

- |   |
|---|
| <ul style="list-style-type: none"> <li>- Documented pre-existing hypocalcemia</li> <li>- Documented pre-existing renal insufficiency defined as creatinine clearance &lt; 30-35 mL/min</li> </ul> |
|---|

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

**IV. Renewal Criteria<sup>1-4</sup>**

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe symptomatic hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, dermatological adverse reactions, severe infection, severe hypersensitivity/anaphylaxis, musculoskeletal pain, etc.; **AND**

**Prolia & Jubbonti<sup>1,2,5,28,29,33,37-39</sup>**

- Beneficial disease response as indicated by one or more of the following:
  - Absence of fractures
  - Increase in bone mineral density compared to pretreatment baseline; **AND**

### Osteoporosis in Men and Women:

- After 5 years of treatment, patient will have a repeat DXA performed; **AND**
- Patients with low-to moderate risk disease will have therapy changed to an oral or IV bisphosphonate unless there is a contraindication or intolerance to both dosage forms

### Glucocorticoid-Induced Osteoporosis:

- After 2 years of treatment, patient will have a repeat DXA performed; **AND**
- Patients with low-to moderate risk disease will have therapy changed to an oral or IV bisphosphonate unless there is a contraindication or intolerance to both dosage forms

### Xgeva & Wyost <sup>3-5,26,38,39</sup>

- Beneficial disease response as indicated by the following:
  - Multiple Myeloma OR Bone metastases from solid tumors: 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: stabilization of disease or decrease in size of tumor or spread of tumor
  - Hypercalcemia of Malignancy: corrected serum calcium  $\leq 11.5$  mg/dL (2.9 mmol/L)
  - Systemic Mastocytosis: improvement or resolution of bone pain as compared to pretreatment baseline

## V. Dosage/Administration <sup>1-4</sup>

### Prolia & Jubbonti

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

### Xgeva & Wyost

Indication	Dose
Bone metastases from solid tumors, Multiple Myeloma, & Systemic Mastocytosis	120 mg administered subcutaneously by a health care provider every 4 weeks
Giant Cell Tumor of Bone & Hypercalcemia of Malignancy	120 mg administered 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

### HCPCS Code(s):

## **Prolia & Xgeva**

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

## **Jubbonti & Wyost**

- J3590 – Unclassified biologics

### NDC(s):

- Prolia 60 mg/1 mL single-dose prefilled syringe: 55513-0710-xx
- Jubbonti 60 mg/1 mL single-dose prefilled syringe: 61314-0240-xx
- Xgeva 120 mg/1.7 mL single-dose vial: 55513-0730-xx
- Wyost 120 mg/1.7 mL single-dose vial: 61314-0228-xx

## **VII. References**

1. Prolia [package insert]. Thousand Oaks, CA; Amgen, Inc.; March 2024. Accessed March 2024.
2. Jubbonti [package insert]. Princeton, NJ; Sandoz, Inc.; March 2024. Accessed March 2024.
3. Xgeva [package insert]. Thousand Oaks, CA; Amgen, Inc.; June 2020. Accessed March 2024.
4. Wyost [package insert]. Princeton, NJ; Sandoz, Inc.; March 2024. Accessed March 2024.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Denosumab. National Comprehensive Cancer Network, 2024. 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 March 2024.
6. 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.
7. Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumor of bone: an open-label, phase 2 study. *Lancet Oncol.* 2010 Mar;11(3):275-80.
8. 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.
9. 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.
10. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014.

11. 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.
12. 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. *Endocr Pract.* 2016 Sep 2; 22(Suppl 4):1-42.
13. Gnant M, Pfeiler G, Dubsy PC, et al. Adjuvant denosumab in breast cancer (ABCSG-18): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet.* 2015 Aug 1;386(9992):433-43.
14. 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.
15. Jeremiah MP, Unwin BK, Greenawald MH, et al. Diagnosis and Management of Osteoporosis. *Am Fam Physician.* 2015 Aug 15;92(4):261-8.
16. Henry DH, Costa L, Goldwasser F, et al. Randomized, Double-Blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma. *Journal of Clinical Oncology* 2011 29:9, 1125-1132. 2011 Mar 20.
17. Stopeck AT, Lipton A, Body JJ, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. *J Clin Oncol.* 2010 Dec 10;28(35):5132-9.
18. Fizazi K, Carducci M, Smith M, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *Lancet.* 2011 Mar 5;377(9768):813-22.
19. Cummings SR, San Martin J, McClung MR, et al. Denosumab for Prevention of Fractures in Postmenopausal Women With Osteoporosis. *N Engl J Med,* 361 (8), 756-65; 2009 Aug 20. PMID: 19671655. DOI: 10.1056/NEJMoa0809493.
20. Orwoll E, Teglbjaerg CS, Langdahl BL, et al. A Randomized, Placebo-Controlled Study of the Effects of Denosumab for the Treatment of Men With Low Bone Mineral Density. *J Clin Endocrinol Metab,* 97 (9), 3161-9; Sept 2012. PMID: 22723310. DOI: 10.1210/jc.2012-1569.
21. Saag KG, Wagman RB, Geusens P, et al. Denosumab Versus Risedronate in Glucocorticoid-Induced Osteoporosis: A Multicentre, Randomised, Double-Blind, Active-Controlled, Double-Dummy, Non-Inferiority Study. *Lancet Diabetes Endocrinol,* 6 (6), 445-454; Jun 2018. PMID: 29631782. DOI: 10.1016/S2213-8587(18)30075-5.
22. Smith MR, Egerdie B, Hernandez Toriz N, et al. Denosumab in Men Receiving Androgen-Deprivation Therapy for Prostate Cancer. *N Engl J Med.* 2009 Aug 20; 361(8): 745-755.



23. Ellis GK, Bone HG, Chlebowski R, et al. Randomized Trial of Denosumab in Patients Receiving Adjuvant Aromatase Inhibitors for Nonmetastatic Breast Cancer. *J Clin Oncol*, 26 (30), 4875-82; 2008 Oct 20. PMID: 18725648. DOI: 10.1200/JCO.2008.16.3832.
24. Raje N, Terpos E, Willenbacher W, et al. Denosumab Versus Zoledronic Acid in Bone Disease Treatment of Newly Diagnosed Multiple Myeloma: An International, Double-Blind, Double-Dummy, Randomised, Controlled, Phase 3 Study. *Lancet Oncol*, 19 (3), 370-381; Mar 2018. PMID: 29429912. DOI: 10.1016/S1470-2045(18)30072-X.
25. Chawla S, Henshaw R, Seeger L, et al. Safety and Efficacy of Denosumab for Adults and Skeletally Mature Adolescents With Giant Cell Tumour of Bone: Interim Analysis of an Open-Label, Parallel-Group, Phase 2 Study. *Lancet Oncol*, 14 (9), 901-8; Aug 2013. PMID: 23867211. DOI: 10.1016/S1470-2045(13)70277-8.
26. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Bone Cancer. Version 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
27. Scagliotti GV, Hirsh V, Siena S, et al. Overall Survival Improvement in Patients With Lung Cancer and Bone Metastases Treated With Denosumab Versus Zoledronic Acid: Subgroup Analysis From a Randomized Phase 3 Study. *J Thorac Oncol*, 7 (12), 1823-1829; Dec 2012. PMID: 23154554. DOI: 10.1097/JTO.0b013e31826aec2b.
28. Eastell R, Rosen 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/jc.2019-00221>. Published: 25 March 2019.
29. Shoback D, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Guideline Update. *J Clin Endocrinol Metab*. 2020 Mar 1;105(3):dgaa048. Doi: 10.1210/clinem/dgaa048.
30. Orsolini G, Gavioli I, Tripi G, et al. Denosumab for the Treatment of Mastocytosis-Related Osteoporosis: A Case Series. *Calcif Tissue Int*. 2017 Jun;100(6):595-598. doi: 10.1007/s00223-017-0241-z.
31. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. *Menopause*. 2021 Sep 1;28(9):973-997. Doi: 10.1097/GME.0000000000001831.
32. Rosen HN. (2023). Bisphosphonate therapy for the treatment of osteoporosis. In Rosen CJ, Schumacher KE (Eds.), *UptoDate*. Last updated: May 03, 2023. Accessed March 7, 2024. Available from <https://www.uptodate.com/contents/bisphosphonate-therapy-for-the-treatment-of-osteoporosis?sectionName=Contraindications%20to%20bisphosphonates&search=postmeno>

[pausal%20osteoporosis&topicRef=2064&anchor=H3422893804&source=see\\_link#H3422893804](#)

33. Camacho PM, Petak SM, Binkley 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 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL.
34. Jackson RD, LaCroix AZ, Gass M, Women’s Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med.* 2006; 354(7):669–683.
35. LeBoff MS, Greenspan SL, Insogna KL, et al. The clinician’s guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2022 Oct;33(10):2049-2102. Doi: 10.1007/s00198-021-05900-y. Epub 2022 Apr 28.
36. Qaseem A, Hicks LA, Etzeandia-Ikobaltzeta I, et al; Clinical Guidelines Committee of the American College of Physicians. Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline From the American College of Physicians. *Ann Intern Med.* [Epub 3 January 2023]. doi:10.7326/M22-1034.
37. Humphrey, M.B., Russell, L., Danila, M.I., et al. (2023), 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Rheumatol*, 75: 2088-2102. <https://doi.org/10.1002/art.42646>
38. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Prostate Cancer. Version 3.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
39. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Breast Cancer. Version 2.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
40. National Government Services, Inc. Local Coverage Article: Billing and Coding: Denosumab (Prolia™, Xgeva™) (A52399). Centers for Medicare & Medicaid Services, Inc. Updated on 12/15/2023 with effective date 12/21/2023. Accessed March 2024.

## Appendix 1 – Covered Diagnosis Codes

### Prolia & Jubbonti

ICD-10	ICD-10 Description
C50.011- C50.929	Malignant neoplasms of breast
C61	Malignant neoplasm of prostate
D05.10	Intraductal carcinoma in situ of unspecified breast
D05.11	Intraductal carcinoma in situ of right breast
D05.12	Intraductal carcinoma in situ of left breast
D05.80	Other specified type of carcinoma in situ of unspecified breast
D05.81	Other specified type of carcinoma in situ of right breast
D05.82	Other specified type of carcinoma in situ of left breast
D05.90	Unspecified type of carcinoma in situ of unspecified breast
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
M80.00XA- M80.08XS	Age-related osteoporosis with current pathological fracture
M80.8B2A- M80.8B2S	Osteoporosis with current pathological fracture
M80.8B9A- M80.8B9S	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
T38.0X5A	Adverse effect of glucocorticoids and synthetic analogues, initial encounter
T38.0X5S	Adverse effect of glucocorticoids and synthetic analogues, sequela
Z79.810	Long term (current) use of selective estrogen receptor modulators (SERMs)
Z85.3	Personal history of malignant neoplasm of breast

### **Xgeva & Wyost**

ICD-10	ICD-10 Description
C00-C14	Malignant neoplasms of lip, oral cavity and pharynx

ICD-10	ICD-10 Description
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
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
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having reached remission
C90.11	Plasma cell leukemia in remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having reached remission
C90.21	Extramedullary plasmacytoma in remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission

ICD-10	ICD-10 Description
C90.31	Solitary plasmacytoma in remission
C90.32	Solitary plasmacytoma in relapse
C94.30	Mast cell leukemia not having achieved remission
C94.31	Mast cell leukemia, in remission
C94.32	Mast cell leukemia, in relapse
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
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
D47.02	Systemic mastocytosis
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage
D49.0- D49.9	Neoplasms of unspecified behavior
E83.52	Hypercalcemia
Z85	Personal history of malignant neoplasm
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.3	Personal history of malignant neoplasm of breast
Z85.528	Personal history of other malignant neoplasm of kidney

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

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

**Prolia and Xgeva**

<b>Medicare Part B Covered Diagnosis Codes</b>		
<b>Jurisdiction</b>	<b>NCD/LCA/LCD Document (s)</b>	<b>Contractor</b>
6, K	A52399	National Government Services, Inc

<b>Medicare Part B Administrative Contractor (MAC) Jurisdictions</b>		
<b>Jurisdiction</b>	<b>Applicable State/US Territory</b>	<b>Contractor</b>
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	Palmetto GBA, 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