

# Zoledronic acid: Zometa®; Reclast® (Intravenous)

Document Number: IC-0153

Last Review Date: 03/31/2023

Date of Origin: 06/21/2011

Dates Reviewed: 09/2011, 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 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, 07/2018, 07/2019, 07/2020, 04/2021, 04/2022, 07/2022, 04/2023

## I. Length of Authorization

### Zometa:

- Coverage is provided for 12 months and may be renewed (unless otherwise specified).

### Reclast:

- Prevention of osteoporosis in post-menopausal women: Coverage is provided for 24 months and may be renewed.
- All other indications: Coverage is provided for 12 months and may be renewed (unless otherwise specified).

## II. Dosing Limits

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

#### Zometa

Indication	Quantity Limit
Hypercalcemia of malignancy	4 mg bottle/vial per 7 days x 2 doses only
Multiple myeloma, bone metastases from solid tumors, osteopenia/osteoporosis in systemic mastocytosis, & prevention of skeletal related events in prostate cancer	4 mg bottle/vial every 21 days
Prevention of bone loss in breast cancer	4 mg bottle/vial every 168 days (6 months)
Prevention of androgen deprivation therapy-induced bone loss in prostate cancer	4 mg bottle/vial every 84 days (3 months)
Langerhans Cell Histiocytosis	4 mg bottle/vial every 28 days

#### Reclast

Indication	Quantity Limit
------------	----------------

Prevention of osteoporosis in post-menopausal women	5 mg solution every 730 days (24 months)
All other indications	5 mg solution every 365 days (12 months)

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

**Zometa**

Indication	Max Units
Hypercalcemia of malignancy	4 billable units per 7 days x 2 doses only
Multiple myeloma, bone metastases from solid tumors, osteopenia/osteoporosis in systemic mastocytosis, & prevention of skeletal related events in prostate cancer	4 billable units every 21 days
Prevention of bone loss in breast cancer	4 billable units every 168 days (6 months)
Prevention of androgen deprivation therapy-induced bone loss in prostate cancer	4 billable units every 84 days (3 months)
Langerhans Cell Histiocytosis	4 billable units every 28 days

**Reclast**

Indication	Max Units
Prevention of osteoporosis in post-menopausal women	5 billable units every 730 days (24 months)
All other indications	5 billable units every 365 days (12 months)

**III. Initial Approval Criteria <sup>1,2</sup>**

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

**Zometa**

**Universal Criteria <sup>1,31,37</sup>**

- Patient does not have hypocalcemia and will be adequately supplemented with calcium and vitamin D (*Note: excludes when use is for hypercalcemia of malignancy*); **AND**
- Patient must have a CrCl  $\geq$  30 mL/min; **AND**
- Will not be used in combination with Reclast, other bisphosphonates, denosumab, romosozumab, or parathyroid hormone analogs/related peptides; **AND**

Coverage is provided in the following conditions:

**Hypercalcemia of malignancy † Φ <sup>1</sup>**

- Patient has an albumin-corrected serum calcium level of > 12 mg/dL

### Multiple myeloma †<sup>1</sup>

**Bone metastases from solid tumors †<sup>1</sup>** (in conjunction with standard antineoplastic therapy)

**Prevention of skeletal related events in men with castration-resistant/recurrent prostate cancer ‡<sup>3</sup>**

**Prevention of bone loss associated with aromatase inhibitor therapy for breast cancer in postmenopausal women or premenopausal women on adjuvant ovarian suppression ‡<sup>3</sup>**

**Prevention of bone loss associated with androgen deprivation therapy in men with prostate cancer ‡<sup>3</sup>**

**Treatment of osteopenia/osteoporosis in patients with systemic mastocytosis ‡<sup>3,26,33</sup>**

**Langerhans Cell Histiocytosis ‡<sup>3,34</sup>**

- Patient has multifocal bone disease OR unifocal isolated bone disease

### Reclast

#### Universal Criteria <sup>2,31,37</sup>

- Confirmation patient is receiving calcium and Vitamin D supplementation if dietary intake is inadequate; **AND**
- Patient must not have hypocalcemia; **AND**
- Patient must have a CrCl  $\geq$  35 mL/min and no evidence of acute renal impairment; **AND**
- Will not be used in combination with Zometa, other bisphosphonates, denosumab, romosozumab, or parathyroid hormone analogs/related peptides; **AND**

Coverage is provided in the following conditions:

#### **Treatment and prevention of postmenopausal osteoporosis †<sup>2,25,28,32,38,39</sup>**

- Patient experienced severe intolerance, ineffective response $\pm$ , or has contraindications\* to oral bisphosphonate therapy; **OR**
- Patient had a prior fragility fracture or is at especially high fracture risk

**Note:** *Patients discontinuing treatment with denosumab due to a reduction in fracture risk (i.e., no longer high or very high risk) require subsequent antiresorptive therapy in order to prevent accelerated bone mineral density loss and increase in fracture risk. Coverage is provided for **one administration** for this use prior to temporary discontinuation of intravenous antiresorptive therapy.*

#### **Treatment to increase bone mass in men with osteoporosis †<sup>2</sup>**

- Patient experienced severe intolerance, ineffective response±, or has contraindications\* to oral bisphosphonate therapy; **OR**
- Patient had a prior fragility fracture or is at especially high fracture risk

#### **Treatment and prevention of glucocorticoid-induced osteoporosis † 2**

- Patient experienced severe intolerance, ineffective response±, or has contraindications\* to oral bisphosphonate therapy; **OR**
- Patient had a prior fragility fracture or is at especially high fracture risk

#### **Treatment of Paget's disease of bone in men and women † 2**

- Serum alkaline phosphatase is two times or higher than the upper limit of the age-specific reference range; **OR**
- Patient is symptomatic; **OR**
- Patient is at risk for complications from their disease

#### **± Ineffective response is defined as one or more of the following: 28,30,37**

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

#### **\* Examples of contraindications to oral bisphosphonate therapy include the following: 29**

- o Documented inability to sit or stand upright for at least 30 minutes
- o Documented pre-existing esophageal disorder such as achalasia, esophageal stricture, esophageal varices, or Barrett's esophagus
- o Surgical anastomoses are present in the GI tract after certain types of bariatric surgery (e.g., Roux-en-Y gastric bypass)

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

## **IV. Renewal Criteria 1,2**

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 the initial criteria section; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: renal impairment, osteonecrosis of the jaw, atypical femoral fractures, hepatic impairment, hypocalcemia, incapacitating pain in the bone, joint, and/or muscle, etc.; **AND**

#### **Reclast 2,25,30,32**

- Disease response as indicated by the following:
  - o Osteoporosis indications:
    - Absence of fractures; **OR**
    - Increase in bone mineral density compared to pretreatment baseline; **AND**

- Patients who have received 3 years of bisphosphonate therapy should be re-evaluated with a DXA or serum marker for bone turnover [i.e., serum C-terminal crosslinking telopeptide (CTX)]; **AND**
- Those patients at low-to-moderate risk of fractures should be considered for a temporary discontinuation of bisphosphonate for up to 5 years (re-assess risk at 2 to 4 year intervals to determine if earlier re-initiation is necessary)
  - Paget's Disease: normalization of serum alkaline phosphatase (SAP) or a reduction of  $\geq 75\%$  from baseline in total SAP excess (defined as the difference between the measured level and midpoint of normal range)

**Zometa** <sup>1,27,30</sup>

- 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)
  - Hypercalcemia of Malignancy: May not be renewed
  - Prevention of bone loss/skeletal related events in cancer patients/Osteoporosis or Osteopenia in Systemic Mastocytosis:
    - Absence of fractures; **OR**
    - Increase in bone mineral density compared to pretreatment baseline
  - Langerhans Cell Histiocytosis:
    - Improvement in bone pain; **OR**
    - Improvement/resolution in active bone lesions compared to pretreatment baseline

## V. Dosage/Administration

**Zometa** <sup>1,6,10-12,13,27,35,36</sup>

Indication	Dose
Hypercalcemia of malignancy	4 mg IV x 1 dose, may be repeated after 7 days if serum calcium does not return to normal. Renal function must be carefully monitored in all patients receiving therapy and serum creatinine must be assessed prior to retreatment.
Prevention of aromatase inhibitor-induced bone loss in breast cancer	4 mg IV every 6 months
Prevention of androgen deprivation therapy-induced bone loss in prostate cancer	4 mg IV every 3 months
Prevention of skeletal related events in prostate cancer	4 mg IV every 3 weeks

Multiple myeloma & bone metastases from solid tumors	4 mg IV every 3 to 4 weeks <u>OR</u> 4 mg every 12 weeks
Treatment of osteopenia/osteoporosis in systemic mastocytosis	4 mg IV every 3 to 4 weeks
Langerhans Cell Histiocytosis	4 mg IV every month

\*decrease dose based upon CrCl (mL/min): 3.5 mg for CrCl 50-60; 3.3 mg for CrCl 40-49; 3 mg for CrCl 30-39

## Reclast <sup>2</sup>

Indication	Dose
Active Paget's Disease	5 mg IV x 1 dose
Prevention of osteoporosis in post-menopausal women	5 mg IV every 2 years
Prevention of glucocorticoid-induced osteoporosis	5 mg IV every year
Treatment of osteoporosis	5 mg IV every year

## VI. Billing Code/Availability Information

### HCPCS Code:

- J3489 - Injection, zoledronic acid, 1 mg; 1 billable unit = 1 mg

### NDC\*:

- Zometa 4 mg/100 mL single-dose ready-to-use bottle: 00078-0590-xx (obsolete)
- Zometa 4 mg/5 mL single-dose vial of concentrate: 00078-0387-xx (obsolete)
- Reclast 5 mg/100 mL ready-to-infuse solution: 00078-0435-xx

\*Generics available from various manufacturers

## VII. References

1. Zometa [package insert]. Stein, Switzerland; Novartis Pharmaceuticals; December 2018. Accessed March 2023. (obsolete)
2. Reclast [package insert]. East Hanover, NJ; Novartis Pharmaceuticals; April 2020. Accessed March 2023.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Zoledronic Acid. National Comprehensive Cancer Network, 2023. 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 2023.

4. Berenson JR, Boccia R, Lopez T, et al. Results of a Multicenter Open-Label Randomized Trial Evaluating Infusion Duration of Zoledronic Acid in Multiple Myeloma Patients (the ZMAX Trial). *J Support Oncol*. 2011;9(1):32-40.
5. Black DM, Delmas PD, Eastell R, et al. Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. *New Engl J Med*. 2007;356(18):1809-1822.
6. Eidtmann H, de Boer R, Bundred N, et al. Efficacy of Zoledronic Acid in Postmenopausal Women With Early Breast Cancer Receiving Adjuvant Letrozole: 36-Month Results of the ZO-FAST Study. *Ann Oncol*. 2010;21(11):2188-2194.
7. McClung M, Miller P, Recknor C, et al. Zoledronic Acid for the Prevention of Bone Loss in Postmenopausal Women With Low Bone Mass: A Randomized Controlled Trial. *Obstet Gynecol*. 2009;114(5):999-1007.
8. Michaelson MD, Kaufman DS, Lee H, et al. Randomized Controlled Trial of Annual Zoledronic Acid to Prevent Gonadotropin-Releasing Hormone Agonist-Induced Bone Loss in Men With Prostate Cancer. *J Clin Oncol*. 2007;25(9):1038-1042.
9. Reid DM, Devogelaer JP, Saag K, et al. Zoledronic Acid and Risedronate in the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis (HORIZON): A Multicentre, Double-Blind, Double-Dummy, Randomised Controlled Trial. *Lancet*. 2009;373(9671):1253-1263.
10. Smith MR, Eastham J, Gleason DM, et al. Randomized Controlled Trial of Zoledronic Acid to Prevent Bone Loss in Men Receiving Androgen Deprivation Therapy for Nonmetastatic Prostate Cancer. *J Urol*. 2003;169(6):2008-2012.
11. Bhoopalam N, Campbell SC, Moritz T, et al. Intravenous zoledronic acid to prevent osteoporosis in a veteran population with multiple risk factors for bone loss on androgen deprivation therapy. *J Urol*. 2009 Nov;182(5):2257-64. Epub 2009 Sep 16.
12. Bundred NJ, Campbell ID, Davidson N, et al. Effective inhibition of aromatase inhibitor-associated bone loss by zoledronic acid in postmenopausal women with early breast cancer receiving adjuvant letrozole: ZO-FAST Study results. *Cancer*. 2008 Mar 1;112(5):1001-10.
13. Brufsky A, Harker WG, Beck JT, et al. Zoledronic Acid Inhibits Adjuvant Letrozole-Induced Bone Loss in Postmenopausal Women With Early Breast Cancer, *J Clin Oncol* 2007, 25(7):829-36.
14. Himelstein AL, Qin R, Novotny PJ, et al. "CALBG 70604 (Alliance): A randomized phase III study of standard dosing vs longer interval dosing of zoledronic acid in metastatic cancer. *J Clin Oncol* 33, 2015 (suppl; abstr 9501).
15. 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.
16. 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.

17. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014.
18. 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.
19. Hortobagyi GN, Van Poznak C, Harker WG, et al. Continued Treatment Effect of Zoledronic Acid Dosing Every 12 vs 4 Weeks in Women With Breast Cancer Metastatic to Bone: The OPTIMIZE-2 Randomized Clinical Trial. *JAMA Oncol*. 2017 Jan 26. doi: 10.1001/jamaoncol.2016.6316.
20. Himelstein AL, Foster JC, Khatcheressian JL, et al. Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in Patients With Bone Metastases: A Randomized Clinical Trial. *JAMA*. 2017 Jan 3;317(1):48-58. doi: 10.1001/jama.2016.19425.
21. Dhesy-Third S, Fletcher GG, Blanchette PS, et al. Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: A Cancer Care Ontario and American Society of Clinical Oncology Clinical Practice Guideline. DOI: 10.1200/JCO.2016.70.7257 *Journal of Clinical Oncology* - published online before print March 6, 2017.
22. Hadji P, Aapro MS, Body JJ, et al. Management of Aromatase Inhibitor-Associated Bone Loss (AIBL) in postmenopausal women with hormone sensitive breast cancer: Joint position statement of the IOF, CABS, ECTS, IEG, ESCEO IMS, and SIOG. *J Bone Oncol*. 2017 Mar 23;7:1-12
23. 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.
24. Jeremiah MP, Unwin BK, Greenawald MH, et al. Diagnosis and Management of Osteoporosis. *Am Fam Physician*. 2015 Aug 15;92(4):261-8.
25. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline. *J Clin Endo Metab*, Vol 104, Iss 5, May 2019, pps 1595–1622, <https://doi.org/10.1210/jc.2019-00221>.
26. Rossini M, Zanotti R, Viapiana O, et al. Zoledronic acid in osteoporosis secondary to mastocytosis. *Am J Med*. 2014 Nov;127(11):1127.e1-4.
27. Chellapandian d, Makras P, Kaltsas G, et al. Bisphosphonates in Langerhans Cell Histiocytosis: An International Retrospective Case Series. *Mediterr J Hematol Infect Dis*. 2016 Jul 1;8(1):e2016033. doi: 10.4084/MJHID.2016.033. eCollection 2016.



28. 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.
29. Rosen HN. (2022). Bisphosphonate therapy for the treatment of osteoporosis. In Rosen CJ, Schumacher KE (Eds.), *UptoDate*. Last updated: July 21, 2022. Accessed March 10, 2023. Available from [https://www.uptodate.com/contents/bisphosphonate-therapy-for-the-treatment-of-osteoporosis?sectionName=Contraindications%20to%20bisphosphonates&search=postmenopausal%20osteoporosis&topicRef=2064&anchor=H3422893804&source=see\\_link#H3422893804](https://www.uptodate.com/contents/bisphosphonate-therapy-for-the-treatment-of-osteoporosis?sectionName=Contraindications%20to%20bisphosphonates&search=postmenopausal%20osteoporosis&topicRef=2064&anchor=H3422893804&source=see_link#H3422893804)
30. 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.
31. 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.
32. 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.
33. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Systemic Mastocytosis 2.2022. National Comprehensive Cancer Network, 2023. 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 2023.
34. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Histiocytic Neoplasms 1.2022. National Comprehensive Cancer Network, 2023. 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 2023.
35. Gnant M, Mlineritsch B, Stoeger H, et al; Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria. Adjuvant endocrine therapy plus zoledronic acid in premenopausal women with early-stage breast cancer: 62-month follow-up from the ABCSG-12 randomised trial. *Lancet Oncol*. 2011 Jul;12(7):631-41. doi: 10.1016/S1470-2045(11)70122-X.
36. Saad F, Gleason DM, Murray R, et al; Zoledronic Acid Prostate Cancer Study Group. Long-term efficacy of zoledronic acid for the prevention of skeletal complications in patients with

metastatic hormone-refractory prostate cancer. *J Natl Cancer Inst.* 2004 Jun 2;96(11):879-82. doi: 10.1093/jnci/djh141.

37. 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.
38. 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.
39. Rosen HN. (2023) Overview of the management of osteoporosis in postmenopausal women. In: Rosen CJ, Schmader KE, (Eds). *UpToDate*. Last updated: Feb 27, 2023. Accessed March 10, 2023. Available from [https://www.uptodate.com/contents/overview-of-the-management-of-osteoporosis-in-postmenopausal-women?search=Overview%20of%20the%20management%20of%20osteoporosis%20in%20postmenopausal%20women.&source=search\\_result&selectedTitle=1~150&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/overview-of-the-management-of-osteoporosis-in-postmenopausal-women?search=Overview%20of%20the%20management%20of%20osteoporosis%20in%20postmenopausal%20women.&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1).
40. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Bisphosphonate Drug Therapy (L34648). Centers for Medicare & Medicaid Services. Updated on 08/19/2020 with effective date 08/27/2020. Accessed March 2023.
41. Wisconsin Physicians Service Insurance Corporation. Local Coverage Article (LCA): Billing and Coding: Bisphosphonate Drug Therapy (A56907). Centers for Medicare & Medicaid Services. Updated on 07/20/2022 with effective date 07/28/2022. Accessed March 2023.
42. First Coast Service Options, Inc. Local Coverage Determination (LCD) for Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications (L33270). Centers for Medicare & Medicaid Services, Inc. Updated on 1/15/2021 with effective date 01/21/2021. Accessed March 2023.
43. First Coast Service Options, Inc. Local Coverage Article (LCA): Billing and Coding: Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications (A57603). Centers for Medicare & Medicaid Services, Inc. Updated on 09/25/2020 with effective date 10/01/2020. Accessed March 2023.

## Appendix 1 – Covered Diagnosis Codes

### Zometa

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

ICD-10	ICD-10 Description
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 reached 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 reached remission
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	Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.2	Malignant mast cell neoplasm

ICD-10	ICD-10 Description
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.7	Other specified malignant neoplasms of lymphoid, haematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified 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	Neoplasm of uncertain behavior of oral cavity and digestive organs
D38	Neoplasm of uncertain behavior of middle ear and respiratory and intrathoracic organs
D39	Neoplasm of uncertain behavior of female genital organs
D40	Neoplasm of uncertain behavior of male genital organs
D41	Neoplasm of uncertain behavior of urinary organs
D42	Neoplasm of uncertain behavior of meninges
D43	Neoplasm of uncertain behavior of brain and central nervous system
D44	Neoplasm of uncertain behavior of endocrine glands
D47.02	Systemic mastocytosis
D48	Neoplasm of uncertain behavior of other and unspecified sites
D49.0-D49.9	Neoplasms of unspecified behavior
E83.52	Hypercalcemia
M80.80XA- M80.88XS	Other osteoporosis with current pathological fracture
M81.6	Localized osteoporosis
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
M85.9	Disorder of bone density and structure, unspecified
M89.9	Disorder of bone, unspecified
M94.9	Disorder of cartilage, unspecified
Z79.810	Long term (current) use of selective estrogen receptor modulators (SERMs)

ICD-10	ICD-10 Description
Z85	Personal history of malignant neoplasm
Z85.3	Personal history of malignant neoplasm of breast
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

**Dual coding requirements:**

Prevention of bone loss in prostate cancer/ Prevention or treatment of osteoporosis in prostate cancer:

- Primary code: M85.80, M85.851, M85.852, M89.9 or M94.9 plus Z85.46 **and** Z79.899

Prevention of aromatase inhibitor induced bone loss in breast cancer:

- Primary code: M85.80, M85.851, M85.852, M89.9 or M94.9 plus: C50.011-C50.922 OR Z85.3 **and** Z79.810 OR Z79.811

**Reclast**

ICD-10	ICD-10 Description
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
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
M85.9	Disorder of bone density and structure, unspecified
M88.0	Osteitis deformans of skull
M88.1	Osteitis deformans of vertebrae
M88.811	Osteitis deformans of right shoulder
M88.812	Osteitis deformans of left shoulder
M88.819	Osteitis deformans of unspecified shoulder
M88.821	Osteitis deformans of right upper arm
M88.822	Osteitis deformans of left upper arm
M88.829	Osteitis deformans of unspecified upper arm
M88.831	Osteitis deformans of right forearm

ICD-10	ICD-10 Description
M88.832	Osteitis deformans of left forearm
M88.839	Osteitis deformans of unspecified forearm
M88.841	Osteitis deformans of right hand
M88.842	Osteitis deformans of left hand
M88.849	Osteitis deformans of unspecified hand
M88.851	Osteitis deformans of right thigh
M88.852	Osteitis deformans of left thigh
M88.859	Osteitis deformans of unspecified thigh
M88.861	Osteitis deformans of right lower leg
M88.862	Osteitis deformans of left lower leg
M88.869	Osteitis deformans of unspecified leg
M88.871	Osteitis deformans of right ankle
M88.872	Osteitis deformans of left ankle
M88.879	Osteitis deformans of unspecified ankle
M88.88	Osteitis deformans of other bone
M88.89	Osteitis deformans of multiple sites
M88.9	Osteitis deformans of unspecified bone
M89.9	Disorder of bone, unspecified
M94.9	Disorder of cartilage, unspecified
Z85.46	Personal history of malignant neoplasm of prostate

## 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), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

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

<b>Jurisdiction(s):</b> 5, 8	<b>NCD/LCD Document (s):</b> L34648
<a href="https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l34648&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP">https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l34648&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP</a>	

<b>Jurisdiction(s):</b> 5, 8	<b>NCD/LCD Document (s):</b> A56907
<a href="https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56907&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP">https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56907&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP</a>	
<b>Jurisdiction(s):</b> N	<b>NCD/LCD Document (s):</b> L33270
<a href="https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l33270&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP">https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l33270&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP</a>	
<b>Jurisdiction(s):</b> N	<b>NCD/LCD Document (s):</b> A57603
<a href="https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a57603&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP">https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a57603&amp;areaId=all&amp;docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP</a>	

<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