**CLINICAL GUIDELINES FOR MEDICAL NECESSITY**

**MEDICAL POLICY**

# Zoledronic Acid (Zometa®)

Version: 1.0

**EFFECTIVE DATE: 1/1/2024**

NantHealth® | Eviti®

## Please note the following:

## Zoledronic Acid (Zometa®)

**Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.**
**Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.**

## Zoledronic Acid (Zometa): Discussion

Osteoclastic hyperactivity resulting in excessive bone resorption is the underlying complication of metastatic bone disease and hypercalcemia associated with malignancy. [1] Zoledronic acid is in a class of drugs called bisphosphonates that work by inhibiting normal and abnormal bone reabsorption.[2,3] This action is helpful in reducing pain, reversing hypercalcemia, and preventing and reducing fractures in a range of diseases that directly or indirectly impact bone modeling and remodeling. [1] It slows down the breakdown of bone, increases bone density (thickness), and decreases the amount of calcium that is released from the bone into the bloodstream. [2]

The FDA-approved zoledronic acid for use in hypercalcemia of malignancy, multiple myeloma, and documented bone metastases of solid tumors along with standard antineoplastic therapy. The FDA-approved dosing for hypercalcemia of malignancy is 4 mg as a single-use intravenous infusion or 4 mg as a retreatment after a minimum of 7 days. The FDA dosing for multiple myeloma and bone metastasis from solid tumors is 4 mg as a single-use intravenous infusion. [3]

The National Comprehensive Cancer Network (NCCN) endorses zoledronic acid in the following cancer types: multiple myeloma, histiocytic neoplasms (Langerhans cell histiocytosis), cancer-treatment induced bone loss in breast and prostate cancer, and bone metastases from solid tumors. [4,5,6]

Zoledronic acid can cause osteonecrosis of the jaw (ONJ). [3,7] Baseline dental exams are recommended, and invasive dental work should be avoided when possible. [2,3,5,6]
Monitor the patient for renal dysfunction with the use of zoledronic acid. Patients being treated with zoledronic acid (Zometa) should not be treated with zoledronic acid (Reclast) or other bisphosphonates. [2,3]

## Zoledronic Acid: Definitions

- **Food and Drug Administration (FDA) -**The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of thirty-two leading cancer centers devoted to patient care, research, and education. The NCCN

guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

- **Osteonecrosis of the jaw (ONJ) -** A rare but potentially debilitating condition affecting the bone tissue when the jaw is no longer covered by the gums and starts to die. [7]

## Zoledronic Acid: Policy

Zoledronic acid will be considered for coverage when the following criteria are met:

### Bone Metastases from Solid Tumors

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Must be taken with calcium 1,200-1,500 mg and vitamin D 400-800 international units (IU) daily [3,5,6]; AND
4. Must have serum creatinine level and creatinine clearance assessed prior to each treatment [5,6]; AND
5. Must have documented bone metastases and one of the following:
   a) Metastatic castration-resistant prostate cancer with all the following:
      i. Has creatinine clearance greater than 30 mL/min
      ii. Is prescribed for the prevention of skeletal-related events
      iii. Patients should have progressed after treatment with at least one hormonal therapy [3,5]
   b) Invasive breast cancer and is prescribed for risk reduction of distant metastasis for 3-5 years in high-risk node-negative or node-positive tumors [6]
   c) Inflammatory breast cancer or invasive breast cancer and is prescribed in addition to systemic or endocrine therapy and the patient has expected survival of greater than or equal to 3 months [6]
   d) Bone metastases from all other solid tumors [1,3]

### Cancer Treatment - Induced Bone Loss (CTIBL) in Breast Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist and the following:
   a) Must be postmenopausal and receiving adjuvant aromatase inhibitor therapy [1,6]
   b) Prescribed to maintain or improve bone density and reduce risk of fracture [2,6]
   c) Must be taken with calcium 1200-1500 mg and vitamin D 400-800 international units (IU) daily [3,6]
   d) Must have serum creatinine level and creatinine clearance assessed prior to each treatment [6]

## Cancer Treatment-Induced Bone Loss (CTIBL) in Prostate Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist and the following:
   a) Be taken with calcium 1200-1500 mg and vitamin D 400-800 international units (IU) daily [3,5]
   b) Has high fracture risk and is receiving prevention or treatment of osteoporosis during androgen deprivation therapy (ADT) [1,5]
   c) Must have serum creatinine level and creatinine clearance assessed prior to each treatment [5]

## Histiocytic Neoplasms - Langerhans Cell Histiocytosis (LCH)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist and the following:
   a) Serum creatinine level and creatinine clearance assessed prior to each treatment [3]
   b) Is receiving for first-line or subsequent treatment and has one following:
      i) Unifocal LCH with isolated bone disease [8,9]
      ii) Multifocal bone disease [8,9]

## Hypercalcemia of Malignancy

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist and the following:
   a) Serum creatinine level and creatinine clearance assessed prior to each treatment
   b) An albumin-corrected calcium (cCa) of greater than or equal to 12 mg/dL[3]
   c) Should be adequately rehydrated prior to the administration of zoledronic acid [1,3]

## Multiple Myeloma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist and have the following:
   a) Serum creatinine level and creatinine clearance assessed prior to each treatment
   b) Vitamin D levels assessed periodically
   c) Zoledronic acid prescribed in addition to primary therapy [2,4]

## Note:

1. Coverage of zoledronic acid will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.
2. Dosage and Administration

## Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

## Zoledronic Acid: References


1. Bisphosphonate Drug Therapy. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34648&ver=26&keyword=zoledronic%20acid&keywordType=starts&areaId=all&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1. Accessed on August 2, 2023.
2. Zoledronic Acid Injection. https://medlineplus.gov/druginfo/meds/a605023.html. Accessed July 27, 2023.
3. Zoledronic Acid (Zometa®) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021223s041lbl.pdf. Accessed July 27, 2023.
4. National Comprehensive Cancer Network Guidelines. Multiple Myeloma (Version 3.2023). https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed July 31, 2023.
5. National Comprehensive Cancer Network Guidelines. Prostate Cancer (Version 3.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 8, 2023.
6. National Comprehensive Cancer Network Guidelines. Breast Cancer (Version 4.2023). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 31, 2023.
7. Ben-Air,-E. (2021). Study Explores Jaw Problem Linked to Zoledronic Acid, Finds Risk Factors. https://www.cancer.gov/news-events/cancer-currents-blog/2021/jaw-osteonecrosis-zoledronic-acid. Accessed August 1, 2023.
8. National Comprehensive Cancer Network Guidelines. Histiocytic Neoplasms (Version 1.2022). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 9, 2023.
9. Chellapandian D, Makras P, Kaltsas G, et al. Bisphosphonates in Langerhans cell histiocytosis: an international retrospective case series. Mediterr J Hematol Infect Dis 2016. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928520/. Accessed August 10, 2023.


## Zoledronic Acid: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

| CODE | DESCRIPTION |
|---|---|
| C79.51 | Secondary malignant neoplasm of bone |

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|---|---|
| C79.52 | Secondary malignant neoplasm of bone marrow |
| C90.00 | Multiple Myeloma |
| C96.6 | Unifocal Langerhans-cell histiocytosis |
| E83.52 | Hypercalcemia of Malignancy |
| J3489 | Zoledronic Acid (Zometa) |
| M85.80 | Other specified disorders of bone density and structure, unspecified site |

## Zoledronic Acid: Revision and Review History

| No. | Description | Date(s) |
|---|---|---|
| 1 | Original Effective Date: | 1/1/2024 |
| 2 | Policy Review Dates: | 10/2/2023 |
| 3 | Policy Revision Dates: | |
| 4 | Department Owner: | Medical Affairs |
| 5 | NH Advisory Committee Approval Dates: | 11/2/2023 |
| 6 | Revision Changes: | |