CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Zoledronic Acid (Zometa®)

Version: 2.0

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 bone metastases of solid tumors.[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.[4,5,6,11,12,13]

Zoledronic acid can cause osteonecrosis of the jaw (ONJ) which is a rare but potentially debilitating condition affecting the bone tissue when the jaw is no longer covered by the gums and starts to die.[3,7] Baseline dental exams are recommended and invasive dental work should be avoided when possible. Monitor the patient for renal dysfunction, serum creatinine level and creatinine clearance with the use of zoledronic acid. Patients being treated with zoledronic acid should not be treated with other zoledronic acid drugs, i.e. Reclast or 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 more than 30 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.

Zoledronic Acid: Policy

Note: 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.

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

Bone Metastases of Solid Tumors

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Meets all the following:
   a) Co-administer oral calcium supplements and a multiple vitamin containing Vitamin D daily
   b) Single-dose intravenous infusion for patients with creatinine clearance of >60 ml/min
   c) Given in conjunction with standard antineoplastic therapy.[3]

Breast Cancer (Ductal carcinoma in situ)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Meets all 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) Co-administer oral calcium supplements and a multiple vitamin containing vitamin D daily.[6]

Breast Cancer (Invasive and Inflammatory)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Postmenopausal patients along with calcium and vitamin D supplementation with one of the following:

a) 3-5 years with high-risk node-positive or node negative tumors receiving adjuvant therapy for risk reduction of distant metastasis
b) Adjuvant aromatase inhibition therapy to maintain or improve bone mineral density and reduce risk of fractures; AND

4. Used with calcium and vitamin D supplementation in addition to systemic therapy or endocrine therapy for bone metastasis in patients with expected survival of ≥3 months and adequate renal function.[6]

Prostate Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Progressed after treatment with at least one hormonal therapy; AND
4. Co-administer oral calcium supplements and a multiple vitamin containing vitamin D daily[3]; OR

For **NCCN** required criteria coverage:

5. Treatment-related bone loss in patients receiving androgen deprivation therapy when the absolute fracture risk warrants drug therapy; OR
6. Has high fracture risk and is receiving prevention or treatment of osteoporosis during androgen deprivation therapy (ADT)[1,5]; OR
7. Prevention of symptomatic skeletal-related events (SREs) in M1 castration-resistant prostate cancer (CRPC) if bone metastases is present.[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

For **NCCN** required criteria coverage:

3. First-line or subsequent treatment for one of the following:
   a) Unifocal LCH with isolated bone disease
   b) 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

For **FDA** required criteria coverage:

3. Single dose infusion; retreat after a minimum of 7 days.[3]

Multiple Myeloma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. In combination with primary myeloma therapy.[2,4]

Systemic Mastocytosis

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Treatment for osteopenia and osteoporosis.[10]

Thyroid Carcinoma (Papillary, Follicular, Oncocytic, Medullary and Anaplastic)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. For bone metastases.[11]

Non-Small Cell Lung Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. For bone metastases.[12]

Kidney Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. For bony metastases.[13]

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 November 6, 2024.
2. Zoledronic Acid Injection. https://medlineplus.gov/druginfo/meds/a605023.html. Accessed November 6, 2024.
3. Zoledronic Acid (Zometa®) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021223s041lbl.pdf. Accessed November 6, 2024.
4. National Comprehensive Cancer Network Guidelines. Multiple Myeloma. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed November 6, 2024.
5. National Comprehensive Cancer Network Guidelines. Prostate Cancer. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 6, 2024.
6. National Comprehensive Cancer Network Guidelines. Breast Cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 6, 2024.
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 November 6, 2024.
8. National Comprehensive Cancer Network Guidelines. Histiocytic Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 6, 2024.
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 November 6, 2024.
10. National Comprehensive Cancer Network Guidelines. Systemic Mastocytosis. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed November 6, 2024.
11. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 6, 2024.

12. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 6, 2024
13. National Comprehensive Cancer Network Guidelines. Kidney Cancer. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 6, 2024.

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
C34.9	Non-small cell lung cancer
C64.9	Malignant neoplasm of the kidney, unspecified
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
C73	Thyroid carcinoma
C90.00	Multiple myeloma
C96.6	Unifocal Langerhans-cell histiocytosis
D47.02	Systemic mastocytosis
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, 11/6/2024
3	Policy Revision Dates:	11/6/2024
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	11/2/2023, 11/20/2024
6	Revision Changes:	11/6/2024 - Added indications for thyroid carcinoma, systemic mastocytosis, NSCLC, and kidney cancer