Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Zoledronic acid (Zometa®)	MP-RX-FP-130-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Zoledronic acid (Zometa®), a bisphosphonate agent approved by the Food and Drug Administration (FDA) for the treatment of hypercalcemia of malignancy, patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

Background Information

Zoledronic acid is a bisphosphonate and acts primarily on bone. It is an inhibitor of osteoclast-mediated bone resorption. Zoledronic acid inhibits osteoclastic activity and induces osteoclast apoptosis. Zoledronic acid also blocks the osteoclastic resorption of mineralized bone and cartilage through its binding to bone. Zoledronic acid inhibits the increased osteoclastic activity and skeletal calcium release induced by various stimulatory factors released by tumors.

Zometa is administered as an intravenous infusion and has a warning for Embryo-Fetal Toxicity.

Hypercalcemia of Malignancy

Zometa is indicated for the treatment of hypercalcemia of malignancy defined as an albumin-corrected calcium (cCa) of greater than or equal to 12 mg/dL [3.0 mmol/L] using the formula: cCa in mg/dL = Ca in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL]).

Multiple Myeloma and Bone Metastases of Solid Tumors

Zometa is indicated for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

Approved Indications

Zometa is approved by the FDA for the treatment of hypercalcemia of Malignancy, patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy.

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Other Uses

- The safety and efficacy of Zometa has not been established for use in hyperparathyroidism or non-tumor-related hypercalcemia.
- Off label indication: Drug-induced osteopenia, secondary to androgen-deprivation therapy in prostate cancer patients (prophylaxis).

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J3489	Injection, zoledronic acid, 1 mg

ICD-10	Description
C00.0-C80.2	Malignant neoplasms
C81.00-C81.99	Hodgkin lymphoma
C82.00-C86.6	Non-Hodgkin lymphoma
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms
D00.00-D09.9	In situ neoplasms
E83.52	Hypercalcemia
Z85.00-Z85.9	Personal history of malignant neoplasm

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Medical Necessity Guidelines

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.

Zoledronic acid (Zometa®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Requests for Zometa (zoledronic acid) may be approved for any of the following indications:

I. Bone metastases documented on imaging or bone pain associated with imaging-documented metastases from breast, prostate, lung, kidney, thyroid, or other solid tumors, **OR**
II. Hypercalcemia of malignancy, treatment; **OR**
III. Multiple myeloma; **OR**
IV. Breast cancer, prevention of bone loss secondary to adjuvant hormone therapy (such as aromatase inhibitors) (NCCN 2A); **OR**
V. Prevention of osteoporosis during androgen deprivation therapy in prostate cancer (NCCN 2A); **OR**
VI. Bone disease associated with Langerhans Cell Histiocytosis (NCCN 2A)

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Zoledronic acid (Zometa®), therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following information is provided:

A. Documentation of Serum Creatinine and Creatinine Clearance calculated based on actual body weight using Cockcroft-Gault formula, **AND**
B. Documentation of serum calcium levels or documentation that patient is taking calcium and Vitamin D supplementation.

C. Authorization Duration

i. Initial Approval Duration: Up to 12 months
ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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Requests for zoledronic acid may not be approved when the above criteria are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Indication	Recommended Dosing Schedule
Hypercalcemia of malignancy	• 4 mg as a single-use intravenous infusion • 4 mg as retreatment after a minimum of 7 days
Multiple myeloma and Bone Metastasis of Solid Tumors	• 4 mg as a single-use intravenous infusion every 3-4 weeks for patients with creatinine clearance of greater than 60 mL/min.
Exceptions	
• Treatment in patients with severe renal impairment is not recommended. • Monitor serum creatinine before each dose.	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Drug Facts and Comparisons. Facts and Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 2023. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.

6. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on June 21, 2023.
    a. Histiocytic Neoplasms. V1.2022. Revised May 20, 2022.

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

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 03/31/2025	Validation of information to ensure is up to date. Word formatting editing and indentation alignment.	4/16/2025	5/6/2025
Policy Inception	New Medical Policy creation	4/18/2024	6/28/2024