CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Bone Modifiers – Zoledronic Acid (Zometa) Utilization Management Medical Policy
- zoledronic acid intravenous infusion – generic

REVIEW DATE: 03/18/2026

OVERVIEW

Zoledronic acid intravenous infusion (Zometa), a bisphosphonate, is indicated for the treatment of the following:[1]

- **Hypercalcemia of malignancy**.
- **Multiple myeloma and 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.

Limitations of Use: The safety and efficacy of zoledronic acid injection in the treatment of hypercalcemia associated with hyperparathyroidism or with other non–tumor-related conditions have not been established.[1]

Of note, zoledronic acid intravenous infusion is also available under the brand name (Reclast®) but is not included in this policy.[2]

Guidelines/Other Uses with Supportive Evidence

Data are available with zoledronic acid intravenous infusion (Zometa) for off-label uses.

Zometa is used to prevent bone loss in patients with breast cancer receiving aromatase inhibitor therapy.[3] Aromatase inhibitor therapy prevents peripheral production and suppresses estrogen levels and can lead to accelerated bone loss beyond what would naturally occur in women.[3,] This can place the patient at an increased risk for having a fracture. A review on the management of aromatase inhibitor-associated bone loss in postmenopausal women with breast cancer states that zoledronic acid intravenous infusion (Zometa) [4 mg every 6 months] is the preferred agent for prevention and treatment of aromatase inhibitor bone loss.[4,5]

Zoledronic acid intravenous infusion (Zometa) has been studied and shown benefits in postmenopausal women receiving adjuvant letrozole for breast cancer.[5,6] Zoldedronic acid intravenous infusion (Zometa) has utility in premenopausal patients with breast cancer who have developed ovarian failure. Chemotherapy-induced ovarian failure is an adverse effect associated with some adjuvant chemotherapy and can lead to rapid bone loss.[10,11]

Studies have demonstrated zoledronic acid intravenous infusion (Zometa) to be efficacious in preserving bone mineral density in premenopausal women with breast cancer who developed ovarian failure due to adjuvant chemotherapy. The National Comprehensive Cancer Network (NCCN) guidelines for breast cancer (version 2.2026 – February 27, 2026) also recommend bisphosphonates as adjuvant therapy for postmenopausal women with breast cancer.[13]

Zoledronic acid intravenous infusion (Zometa) has also been utilized to prevent bone loss in patients with prostate cancer who are receiving androgen deprivation therapy (ADT). ADT is associated with a variety of adverse events, including osteoporosis. NCCN guidelines regarding prostate cancer (version 5.2026 –

January 23, 2026) cite zoledronic acid as an option to increase bone density, a surrogate for fracture risk, during ADT for prostate cancer.[7] Zoledronic acid intravenous infusion (Zometa) has led to bone mineral density increases in patients with prostate cancer who are receiving ADT.[8,9] A clinical practice guideline for osteoporosis in men from the Endocrine Society[9] recommends pharmacological treatment for osteoporosis for men with prostate cancer receiving ADT who have a high risk of fracture.

The American Society of Clinical Oncology and the Cancer Care Ontario group updated guidelines for use of adjuvant bisphosphonates and other bone-modifying agents in breast cancer (2022). The guideline recommends adjuvant bisphosphonate therapy in postmenopausal patients with primary breast cancer who are candidates to receive adjuvant systemic therapy.[12]

The NCCN guidelines for histiocytic neoplasms (version 2.2025 – November 21, 2025) recommended zoledronic acid for patients with Langerhans Cell Histiocytosis with bone disease (category 2A).[14]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of zoledronic acid intravenous infusion (Zometa). Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with zoledronic acid intravenous infusion (Zometa) as well as the monitoring required for adverse events and long-term efficacy, approval requires zoledronic acid intravenous infusion (Zometa) to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of zoledronic acid intravenous infusion (Zometa) is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Bone Metastases from Solid Tumors – Prevention of Skeletal-Related Events.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   Note: Some examples of cancer in this clinical scenario include breast cancer, prostate cancer, non-small cell lung cancer, renal cell cancer, small cell lung cancer, colorectal cancer, bladder cancer, gastrointestinal cancer, genitourinary cancer, and head and neck cancer.
   A) Patient has bone metastases; AND
   B) Patient with prostate cancer must have castration-resistant prostate cancer; AND
   Note: This includes patients who have progressed after treatment with hormonal therapy or after surgical castration (e.g., bilateral orchiectomy). Examples of hormonal therapies for prostate cancer include Lupron Depot (leuprolide for depot suspension), Eligard (leuprolide acetate for injectable suspension), Trelstar (triptorelin pamoate for injectable suspension), and Zoladex (goserelin implant).
   C) The medication is prescribed by or in consultation with a hematologist or an oncologist.

Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 weeks.

---

2. **Hypercalcemia of Malignancy.** Approve for 1 month if the patient meets BOTH of the following (A and B):
   A) Patient has a current malignancy; AND
   B) Patient has an albumin-corrected calcium (cCa) ≥ 11.5 mg/dL.

   Dosing. Approve up to 4 mg administered intravenously for up to two doses with the second dose given a minimum of 7 days from the first dose.

---

3. **Multiple Myeloma – Prevention of Skeletal-Related Events.** Approve for 1 year if the medication is prescribed by or in consultation with a hematologist or an oncologist.

   Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 weeks.

Other Uses with Supportive Evidence

---

4. **Breast Cancer – Adjuvant Therapy.** Approve for 1 year if the patient is post-menopausal.

   Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 months.

---

5. **Langerhans Cell Histiocytosis.** Approve for 1 year if the patient has bone disease.

   Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 months.

---

6. **Prevention of Bone Loss (To Increase Bone Mass) in a Patient with Breast Cancer Receiving Aromatase Inhibitor Therapy.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient has breast cancer that is not metastatic to bone; AND
   B) Patient is receiving an aromatase inhibitor therapy.
   Note: Examples of aromatase inhibitor agents include anastrozole, letrozole, and exemestane.

   Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 6 months.

---

7. **Prevention of Bone Loss (to Increase Bone Mass) in a Patient with Prostate Cancer Receiving Androgen Deprivation Therapy (ADT).** Approve 1 year if the patient meets BOTH of the following (A and B):
   A) Patient has prostate cancer that is not metastatic to bone; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient is currently receiving androgen deprivation therapy; OR

Note: Examples of androgen deprivation therapies include Lupron Depot (leuprolide for depot suspension), Eligard (leuprolide acetate for injectable suspension), Trelstar (triptorelin pamoate for injectable suspension), and Zoladex (goserelin implant).

ii. Patient has undergone bilateral orchiectomy.

Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 months.

---

8. Prevention of Bone Loss (to Increase Bone Mass) in a Premenopausal Patient with Breast Cancer Who Have Developed Ovarian Failure. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is premenopausal; AND

B) Breast cancer is not metastatic to bone; AND

C) Patient received adjuvant chemotherapy that led to ovarian failure.

Dosing. Approve up to 4 mg administered intravenously no more frequently than once every 3 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of zoledronic acid intravenous infusion (Zometa) is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zometa® intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; December 2018.
2. Reclast® intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; February 2026.
3. Van Poznak C, Somerfield MR, Barlow WE, et al. Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology (ASCO)-Cancer Care Ontario (CCO) focused guideline update. *J Clin Oncol*. 2017;35(35):3978-3986.
4. Hadji P, Aapro MS, Body JJ, et al. Management of aromatase inhibitor-associated bone loss in postmenopausal women with breast cancer: practical guidance for prevention and treatment. *Ann Oncol*. 2011;22:2546-2555.
5. Brufsky AM, Harker WG, Beck JT, et al. Final 5-year results of Z-FAST trial: adjuvant zoledronic acid maintains bone mass in postmenopausal breast cancer patients receiving letrozole. *Cancer*. 2012;118(5):1192-1201.
6. Coleman R, De Boer R, Eidtmann H, et al. Zoledronic acid (zoledronate) for postmenopausal women with early breast cancer receiving adjuvant letrozole (ZO-FAST study): final 60-month results. *Ann Oncol*. 2013;24:398-405.
7. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 5.2026 – January 23, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 23, 2026.
8. Ryan CW, Huo D, Demers LM, et al. Zoledronic acid initiated during the first year of androgen deprivation therapy increases bone mineral density in patients with prostate cancer. *J Urol*. 2006;176(3):972-978.
9. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2012;97:1802-1822.
10. Shapiro CL, Halabi S, Hars V, et al. Zoledronic acid preserves bone mineral density in premenopausal women who develop ovarian failure due to adjuvant chemotherapy: final results from CALGB trial 79809. *Eur J Cancer*. 2011;47:683-689.
11. Hershman DL, McMahon DJ, Crew KD, et al. Zoledronic acid prevents bone loss in premenopausal women undergoing adjuvant chemotherapy for early-stage breast cancer. *J Clin Oncol*. 2008;26(29):4739-4745.
12. Eisen A, Somerfield MR, Accordino MK, et al. Use of adjuvant bisphosphonates and other bone-modifying agents in breast cancer: ASCO-OH (CCO) guideline update. *J Clin Oncol*. 2022;40:787-800.
13. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – February 27, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2026.
14. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 2.2025 – November 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	It was noted that Zometa (brand name) is no longer available. **Breast Cancer – Adjuvant Therapy:** This was added as a new indication of use. Criteria are to approve if the patient is postmenopausal. **Bone Metastases From Solid Tumors – Prevention of Skeletal-Related Events:** The indication was changed to as stated. Previously it was "Bone Metastases from Solid Tumors – Treatment". **Multiple Myeloma – Prevention of Skeletal-Related Events:** The indication was changed to as stated. Previously it was "Multiple Myeloma – Treatment".	03/22/2023
Annual Revision	No criteria changes.	03/13/2024
Annual Revision	**Langerhans Cell Histiocytosis:** This new condition of approval was added to the Other Uses with Supportive Evidence section. Dosing was added.	03/19/2025
Annual Revision	**Dosing:** The verbiage "or less" and "by intravenous infusion" were replaced with "up to" and "administered intravenously", respectively.	03/18/2026