PRIOR AUTHORIZATION POLICY

POLICY: Bone Modifiers – Zoledronic Acid (Zometa) Prior Authorization Policy
- Zometa® (zoledronic acid injection – Novartis, generic)

REVIEW DATE: 03/03/2021

OVERVIEW

Zoledronic acid injection (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 addition to standard antineoplastic therapy.

Prostate cancer should have progressed after treatment with at least one hormonal therapy.[1] Another formulation of zoledronic acid injection is available, Reclast®, but is not included in this policy.[2]

Other Uses With Supportive Evidence

Data are available with zoledronic acid injection (Zometa) regarding off-label uses. One example is to prevent bone loss in patients with breast cancer receiving aromatase inhibitor therapy. Aromatase inhibitor therapy prevents peripheral production and suppress estrogen levels and can lead to accelerated bone loss beyond what would naturally occur in women.[3,4] 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[5] states that zoledronic acid injection (Zometa) [4 mg every 6 months] is the preferred agent for prevention and treatment of aromatase inhibitor bone loss.[4] Zoledronic acid injection (Zometa) has been studied and shown benefits in postmenopausal women receiving adjuvant letrozole for breast cancer.[5,6]

Zoledronic acid injection (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. The National Comprehensive Cancer Network (NCCN) clinical practice guidelines regarding prostate cancer (version 2.2021 – February 17, 2021)[7] cite zoledronic acid as an option to increase bone density, a surrogate for fracture risk, during ADT for prostate cancer. Zoledronic acid injection (Zometa) has led to bone mineral density increases in patients with prostate cancer who are receiving androgen deprivation therapy.[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.

Zoldedronic acid injection (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 injection (Zometa) to be efficacious in preserving bone mineral density in premenopausal women with breast cancer who developed ovarian failure due to adjuvant chemotherapy.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of zoledronic acid injection (Zometa). 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 injection (Zometa) as well as the monitoring required for adverse events and long-term efficacy, approval requires zoledronic acid injection (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 injection (Zometa) is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Bone Metastases From Solid Tumors – Treatment** Approve for 1 year if the patients meets all of the following criteria (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/genitourinary cancer, and head and neck cancer.
   A) Patient has bone metastases; AND
   B) Patient with prostate cancer must have received at least one hormonal therapy; AND
   Note: 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.

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

3. **Multiple Myeloma – Treatment.** Approve for 1 year if the agent is prescribed by or in consultation with a hematologist or an oncologist.

Other Uses with Supportive Evidence

4. **Prevention of Bone Loss (To Increase Bone Mass) in Patients with Breast Cancer Receiving Aromatase Inhibitor Therapy**. Approve for 1 year if the patient meets the following criteria (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.

5. **Prevention of Bone Loss (To Increase Bone Mass) in Patients with Prostate Cancer Who are Receiving Androgen Deprivation Therapy (ADT).** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient has prostate cancer that is not metastatic to bone; AND
   B) Patient must meet 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), or Zoladex® (goserelin implant).

ii. Patient has undergone bilateral orchiectomy.

6. Prevention of Bone Loss (to Increase Bone Mass) in Premenopausal Patients with Breast Cancer Who Have Developed Ovarian Failure. Approve for 1 year if the patient meets the following criteria (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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of zoledronic acid (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® injection for intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; December 2018.
2. Reclast® injection [prescribing information]. East Hanover, NJ: Novartis; April 2020.
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-Cancer Care Ontario 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 2.2021 – February 17, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 1, 2021.
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.