AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Zoledronic acid	Page:	1 of 7
Effective Date:	5/23/2025	Last Review Date:	4/2025

Applies to:	☒Illinois	☐Florida	☒Florida Kids
	☒New Jersey	☒Maryland	☐Michigan
	☒Pennsylvania Kids	☒Virginia	☐Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for zoledronic acid under the patient's prescription drug benefit.

Description:

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications: zoledronic acid 5mg[1,2]

- Treatment and prevention of osteoporosis in postmenopausal women
- Treatment to increase bone mass in men with osteoporosis
- Treatment and prevention of glucocorticoid-induced osteoporosis in patients expected to be on glucocorticoids for at least 12 months
- Treatment of Paget's disease of bone in men and women

Limitations of Use: Optimal duration of use has not been determined. For patients of low-risk for fracture, consider drug discontinuation after 3 to 5 years of use.

All other indications are considered experimental/investigational and not medically necessary.

Compendial Uses[9]

- For treatment-related bone loss in patients with prostate cancer receiving androgen deprivation therapy (ADT)

FDA-Approved Indications: zoledronic acid 4mg[1,2]

- 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= calcium (Ca) in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL]).
- 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.

Limitations of Use: The safety and efficacy of zoledronic acid 4mg in the treatment of hypercalcemia associated with hyperparathyroidism or with other non-tumor-related conditions have not been established.

Compendial Uses: zoledronic acid 4mg[3]

- Treatment in postmenopausal patients with breast cancer who are receiving adjuvant aromatase inhibition therapy to maintain or improve bone mineral density and reduce risk of fractures
- Treatment in postmenopausal patients with breast cancer who are receiving adjuvant therapy to reduce the risk of distant metastases
- Treatment for osteopenia or osteoporosis in patients with systemic mastocytosis
- Langerhans cell histiocytosis with bone disease

All other indications are considered experimental/investigational and not medically necessary.

Applicable Drug List:

Zoledronic acid

Policy/Guideline:

Documentation – zoledronic acid 5mg:
Submission of the following information is necessary to initiate the prior authorization review:

- Chart notes or medical record documentation indicating a history of fractures, T-score, and Fracture Risk Assessment Tool (FRAX) fracture probability (where applicable)
- Chart notes, medical record documentation, or claims history supporting use of androgen deprivation therapy.

Documentation – zoledronic acid 4mg:
Submission of the following information is necessary to initiate the prior authorization review: Chart notes, medical record documentation, or claims history supporting use of aromatase inhibitor therapy, if applicable.

Coverage Criteria – zoledronic acid 5mg:

Postmenopausal Osteoporosis, Treatment and Prevention[1-4]

Authorization of 12 months may be granted to postmenopausal members for treatment or prevention of osteoporosis when ANY of the following criteria are met:

- Member has a history of fragility fractures (e.g., low trauma fracture from force similar to a fall from standing position)
- Member has a pre-treatment T-score less than or equal to -2.5
- Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1)

Osteoporosis in Men[1-3,5]

Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:

- Member has a history of an osteoporotic vertebral or hip fracture
- Member has a pre-treatment T-score less than or equal to -2.5
- Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (see Appendix)

Glucocorticoid-Induced Osteoporosis[1,2,6]

Authorization of 12 months may be granted for members with glucocorticoid-induced osteoporosis when BOTH of the following criteria are met:

- Member is currently receiving or will be initiating glucocorticoid therapy at an equivalent prednisone dose of greater than or equal to 2.5 mg/day for at least 3 months
- Member meets ANY of the following criteria:
  - Member has a history of a fragility fracture (e.g., low trauma fracture from force similar to a fall from standing position)
  - Member has a pre-treatment T-score of less than or equal to -2.5
  - Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (see Appendix)

Paget's Disease of Bone[1,2,7]

Authorization of 1 month (one dose [5 mg]) may be granted for treatment of Paget's disease of bone.

Prostate Cancer[9]

Authorization of 12 months may be granted for members with prostate cancer for treatment-related bone loss when receiving androgen deprivation therapy (ADT) (e.g., gosarelin, leuprolide, triptorelin).

Criteria for Initial Approval – zoledronic acid 4mg:

Hypercalcemia of Malignancy[1-3]

Authorization of 2 months may be granted for treatment of hypercalcemia of malignancy.

Multiple Myeloma[1-3]

Authorization of 12 months may be granted for treatment or prevention of skeletal-related events in members with multiple myeloma.

Bone Metastases From A Solid Tumor[1-3]

Authorization of 12 months may be granted for treatment or prevention of skeletal-related events in members with bone metastases from a solid tumor (e.g., breast cancer, non-small cell lung cancer, thyroid carcinoma, kidney cancer, prostate cancer).

Breast Cancer[3]

Authorization of 12 months may be granted for postmenopausal (natural or induced by ovarian suppression) members when either of the following criteria is met:

- The member is receiving adjuvant aromatase inhibition therapy for breast cancer and the requested medication will be used to maintain or improve bone mineral density and reduce the risk of fractures
- The member is receiving adjuvant therapy for breast cancer and the requested medication will be used for risk reduction of distant metastasis in high-risk node negative or node positive tumors

Systemic Mastocytosis[3]

Authorization of 12 months may be granted for treatment of osteopenia or osteoporosis in members with systemic mastocytosis.

Langerhans Cell Histiocytosis[3]

Authorization of 12 months may be granted for treatment of Langerhans cell histiocytosis with bone disease.

Continuation of Therapy – zoledronic acid 5mg:

Paget's Disease of Bone

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

All Other Indications

Authorization of 12 months may be granted for all members (including new members) who are currently receiving the requested medication through a previously authorized pharmacy or medical benefit, who meet either of the following criteria:

- Member has received less than 24 months of therapy and has not experienced clinically significant adverse events during therapy
- Member has received 24 months of therapy or more and meets both of the following criteria:
  - Member has experienced clinical benefit (i.e., improvement or stabilization in T-score since the previous bone mass measurement)
  - Member has not experienced any adverse effects

Continuation of Therapy – zoledronic acid 4mg:

Hypercalcemia of Malignancy

Authorization of 2 months may be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Appendix – zoledronic acid 5mg:

Fracture Risk Assessment Tool (FRAX)[6,8]

- High FRAX fracture probability: 10-year major osteoporosis-related fracture risk ≥ 20% or hip fracture risk ≥ 3%
- 10-year probability; calculation tool available at: https://frax.shef.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture (including fractures of the spine [clinical], hip, wrist, or humerus) and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg (prednisone equivalent) per day.

Approval Duration and Quantity Restrictions:

Initial and Renewal Approval:

- Zoledronic acid 5mg:
  - Paget's Disease of Bone: 1 month
  - All other indications: 12 months
- Zoledronic acid 4mg:
  - Hypercalcemia of Malignancy: 2 months
  - All other indications: 12 months

Quantity Level Limit: Reference Formulary for drug specific quantity level limits

References:

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1. Reclast [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2020.
2. Zoledronic acid injection [package insert]. Princeton, NJ: Fosun Pharma USA Inc.; February 2023.
3. LeBoff MS, Greenspan SL, Insogna KL, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022;33(10):2049-2102.
4. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2020 update. Endocr Pract. 2020;26(Suppl 1):1-46.
5. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocr Metab. 2012;97(6):1802-1822.
6. Humphrey MB, Russell L, Danila MI, et al. 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. Arthritis Rheumatol. 2023;75(12):2088-2102.
7. Singer FR, Bone HG, Hosking DJ, et al. Paget's disease of bone: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(12):4408-22.
8. FRAX® Fracture Risk Assessment Tool. © Centre for Metabolic Bone Diseases, University of Sheffield, UK. Available at: https://frax.shef.ac.uk/FRAX/. Accessed October 8, 2024.
9. The NCCN Drugs & Biologics Compendium® © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 8, 2024.

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1. Zometa [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.

2. Zoledronic acid [package insert]. Raleigh, NC: Fresenius Kabi; September 2023.
3. The NCCN Drugs & Biologics Compendium® © 2024 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 11, 2024.