| UM-CDG-007 Bisphosphonate Drug Therapy | Approved By:<br>Director, Health Services | Effective Date:<br>11/10/2025 |
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***This Policy applies to all SECUR affiliates, associates, and subsidiaries.***

Approved by Courtney Gonzales, Director of Health Services on behalf of the Utilization Management Committee.

## PURPOSE

This coverage determination guideline serves to address bisphosphonate drug therapy, which are drugs that act to inhibit normal and abnormal bone reabsorption. These drugs are helpful in pain reduction, reversing hypocalcemia, and preventing and reducing fracture in a range of diseases that directly or indirectly impact bone modeling and remodeling. Bisphosphonates are available in both oral and parenteral forms. This coverage determination guideline will cover intravenous (IV) bisphosphonates: ibandronate sodium, pamidronate disodium, and zoledronic acid.

For SECUR Health Plan members, National Coverage Determinations (NCD) and Local Coverage Determinations (LCD) will be applied to requests when applicable. SECUR Health Plan Coverage Determination Guidelines (CDG) will be utilized in the absence of an appropriate NCD and/or LCD.

## DEFINITIONS

**None**

## POLICY

SECUR Health Plan considers intravenous bisphosphonate drug therapy medically necessary when administered as described in this coverage determination guideline and the use of intravenous bisphosphonate drug therapy must be supported in the documentation and must include:

1. The covered clinical diagnosis listed below, and
2. The indication for the intravenous bisphosphonate drug therapy, either:
   a) Member has demonstrated intolerance, adverse side effects, or contraindications for the US Food and Drug Administration (FDA) approved oral therapy dosing regimen, or insurmountable issues related to absorption, compliance, or dosing posture, or
   b) Member has failed oral bisphosphonate drug therapy with documentation of adequate trials or attempts of the FDA approved oral therapy resulted in fallen bone mass density and/or failure to suppress bone turnover.

The following are covered indications considered medically necessary by SECUR Health Plan for all intravenous bisphosphonates addressed in this coverage determination guideline, unless otherwise documented for a specific clinical medical condition or diagnosis noted.

1. Osteoporosis and Osteopenia
   Coverage for intravenous bisphosphonates include any of the following:
   a) Postmenopausal women and men age fifty or older who have had a hip and/or vertebral fracture,

including fragility fracture

b) Postmenopausal women and men age fifty or older who have had bone mineral density (BMD) values consistent with osteoporosis
c) Postmenopausal women and men age fifty or older who have T-scores from -1.0 to -2.5 and any one of the following:
   - History of fracture of proximal humerus, pelvis, or distal forearm
   - History of multiple fractures at other sites, excluding the face, feet, and hands
d) Pharmacologic therapy is recommended for members with osteopenia if the FRAX 10 year probability for major osteoporotic fracture is greater than 20% or the 10 year probability of hip fracture is greater than 3%.

2. Hypercalcemia associated with malignancy
   Osteoclastic hyperactivity resulting in excessive bone resorption is the underlying complication associated with metastatic bone disease and hypercalcemia associated with malignancy. Most instances occur in those with breast cancer, squamous cell tumors of the lung, head, and/or neck, renal cell carcinoma, and certain hematologic malignancies including multiple myeloma and certain lymphomas. Bisphosphonates in addition to hydration are indicated for moderate to severe hypercalcemia associated with malignancy with or without bone metastases.
3. Cancer Treatment Induced Bone Loss (CTIBL) in Breast and Prostate Cancer
   Breast Cancer
   Cytotoxic chemotherapy has two mechanisms inducing bone loss including a direct negative effect of the cytotoxic therapy on bone cells and many women who are postmenopausal have cytotoxic therapy effects on ovarian function that results in gonadal loss. Additionally, in premenopausal women, surgery and/or radiation therapy to the ovary results in bone loss. Hormone therapy in premenopausal and the aromatase inhibitors result in bone loss as well as gonadotropin releasing hormone (GnRH) antagonists/agonists, which shut off ovarian function resulting in estrogen depletion.

   Prostate Cancer
   Cytotoxic therapy again produces a negative impact not only on testicular function but also on bone. Surgical and hormone therapy results in androgen depletion and the depletion of estrogen and androgen results in a decrease in bone mineral density.

   National Comprehensive Cancer Network (NCCN) guidelines and supportive literature support the use of bisphosphonates in cancer treated individuals with concurrent adjuvant hormone therapy.
4. Bone metastases secondary to solid tumors, breast cancer, or prostate cancer.
5. For multiple myeloma, *coverage is limited to pamidronate disodium and zoledronic acid*.
6. Osteolytic lesions related to metastases.
7. Paget's Disease of bone (osteitis deformans)
   *Coverage is limited to pamidronate disodium and zoledronic acid.*
   Zoledronic acid injection is considered medically necessary for moderate to severe Paget's Disease of bone in men and women for any of the following:
   a) There is an elevation in serum alkaline phosphatase two times or higher than the upper limit of the age specific normal reference range
   b) There is risk for complication from the disease
   c) Induction of remission
   Zoledronic acid will be covered once per year for these members because after a single treatment, an extended period of remission is expected to be observed.
   If the member relapses after one year of remission, retreatment is considered medically necessary if the following occur:

a) Increase in serum alkaline phosphatase
b) Failure to achieve normalization of serum alkaline phosphatase
c) Significant symptom recurrence

8. Osteogenesis Imperfecta and Fibrous dysplasia of bone (McCune-Albright syndrome)
   *Coverage is limited to pamidronate disodium*.
9. Discontinuation of Denosumab (Prolia/Xgeva) Therapy
   *Coverage is limited to zoledronic acid.*
10. Treatment/Prevention of Glucocorticoid Induced Osteoporosis (GIOP) and Glucocorticoid Induced Bone Loss in Transplant Recipients
    *Coverage is limited to ibandronate sodium and zoledronic acid.*
    SECUR Health Plan will follow the 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid Induced Osteoporosis:
    a) Members taking glucocorticoids maintain a total calcium intake of 1000-1200 mg/day and vitamin D intake of 600-800 international units/day through either diet and/or supplements
    b) Members receiving high dose glucocorticoids and at moderate, high, or very high risk for fracture, intravenous therapy is a conditionally recommended treatment
    c) Members receiving high dose glucocorticoids with solid organ transplants, GFR greater than 35 mL/min, and no evidence of chronic kidney disease mineral induced bone disorder or hyperparathyroidism, intravenous therapy is a conditionally recommended treatment.

Summary Table of Covered Indications

| **Drug** | **Ibandronate (Boniva)*** | **Pamidronate (Aredia)*** | **Zoledronic Acid (Reclast)*** |
|---|---|---|---|
| **Route** | IV | IV | IV |
| **INDICATIONS** | | | |
| **Osteoporosis** | X | X | X |
| **Hypercalcemia of malignancy** | X | X | X |
| **Cancer Treatment - Induced Bone loss in Breast and Prostate Cancer** | | X | X |

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|---|---|---|---|
| **Bone metastases secondary to solid tumors, breast, and prostate cancer** | X | X | X |
| **Multiple Myeloma** | | X | X |
| **Osteolytic lesions due to metastases** | X | X | X |
| **Paget's Disease** | | X | X |
| **Osteogenesis Imperfecta** | | X | |
| **Fibrous dysplasia of bone (McCune-Albright syndrome)** | | X | |
| **Discontinuation of Denosumab (Prolia/Xgeva) Therapy** | | | X |
| **GIOP and Transplant** | X | | X |

References:

1. Kling JM, Clarke BL, Sandhu NP. Osteoporosis prevention, screening, and treatment: a review. *Journal of Women's Health*. 2014;23(7):563-572.
2. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2012;97(6):1802-22. doi: 10.1210/jc.2011-3045
3. Murad MH, Drake MT, Mullan RJ, et al. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *J Clin Endocrinol Metab*. 2012;97:1871–1880.

doi: 10.1210/jc.2011-3060
4. The North American Menopause Society (NAMS) Position Statement. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. *Menopause: The Journal of The North American Menopause Society*. 2021;28(9):973-997.
5. Camacho PA, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2020 Update. *Endocrine Practice*. 2020;26(Suppl 1):1-46.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Breast Cancer Version 3.2023 – March 3, 2023.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Prostate Cancer Version 1.2023 – September 16, 2022.
8. U.S. Food and Drug Administration (FDA) prescribing information for zoledronic acid injection: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021223s028lbl.pdf
9. Valachis A, Polyzos NP, Coleman RE, et al. Adjuvant therapy with zoledronic acid in patients with breast cancer: a systematic review and meta-analysis. *The Oncologist*. 2013;18:353-361.
10. 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. Journal of Clinical Oncology. 2022;40(7):787-803.
11. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomized trials. *The Lancet*. 2015;386(10001):1353-1361.
12. Leder BZ, Tsai JN, Jiang LA, Lee H. Importance of prompt antiresorptive therapy in postmenopausal women discontinuing teriparatide or denosumab: the denosumab and teriparatide follow-up study (DATA-follow-up). *Bone*. 2017;98:54-58.
13. Anastasilakis AD, Papapoulos SE, Polyzos SA, Appelman-Dijkstra NM, Makras P. Zoledronate for the prevention of bone loss in women discontinuing denosumab treatment: a prospective 2-year clinical trial. *Journal of Bone and Mineral Research*. 2019:2220-2228.
14. Makras P, Papapoulos SE, Polyzos SA, Appelman-Dijkstra NM, Anastasilakis AD. The three-year effect of a single zoledronate infusion on bone mineral density and bone turnover markers following denosumab discontinuation in women with postmenopausal osteoporosis. *Bone*. 2020;138:1-4.
15. Kendler DL, Body JJ, Brandi ML, et al. Osteoporosis management in hematologic stem cell transplant recipients: executive summary. *Journal of Bone Oncology*. 2021;28:1-4.
16. Kovvuru K, Kanduri SR, Vaitla P, et al. Risk factors and management of osteoporosis post-transplant. *Medicina*. 2020;56:1-18.
17. Ebeling PR. Approach to the patient with transplantation-related bone loss. *J Clin Endocrinol Metab*. 2009;94(5):1483-1490.
18. American College of Rheumatology. 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis.
19. Meyers C, Lisiecki J, Miller S, et al. Heterotopic ossification: a comprehensive review. *JBMR Plus*. 2019;3(4):1-19. doi: 10.1002/jbm4.10172
20. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: going from evidence to recommendations: the significance and presentation of recommendations. *Journal of Clinical Epidemiology*. 2013;66:719-725.
21. Local Coverage Determination (LCD) L34648, Bisphosphonate Drug Therapy, 2/10/2024 https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34648&ver=29