Drug Policy:

Bone Modifying Agents [Pamidronate, Zoledronic Acid, Denosumab Products: Xgeva/Prolia (denosumab), Wyost/Jubbonti (denosumab-bbdz)]

POLICY NUMBER UM ONC_1190	**SUBJECT** Bone Modifying Agents [Pamidronate, Zoledronic Acid, Denosumab Products: Xgeva/Prolia (denosumab), Wyost/Jubbonti (denosumab-bbdz)]	**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 12/07/11, 06/01/13, 07/24/14, 12/04/14, 01/19/15, 07/26/16, 08/25/16, 06/12/17, 06/13/18, 07/10/19, 12/11/19, 04/08/20, 10/14/20, 01/13/21, 11/15/21, 12/08/21, 05/11/22, 08/10/22, 03/08/23, 05/10/23, 02/14/24, 08/14/24, 09/18/24	**APPROVAL DATE** September 18, 2024	**EFFECTIVE DATE** September 27, 2024	**COMMITTEE APPROVAL DATES** 12/07/11, 06/01/13, 07/24/14, 12/04/14, 01/19/15, 07/26/16, 08/25/16, 06/12/17, 06/13/18, 07/10/19, 12/11/19, 04/08/20, 10/14/20, 01/13/21, 11/15/21, 12/08/21, 05/11/22, 08/10/22, 03/08/23, 05/10/23, 02/14/24, 08/14/24, 09/18/24
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee	
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**	**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Bone Modifying Agents [Pamidronate, Zoledronic Acid, Denosumab Products: Xgeva/Prolia (denosumab), Wyost/Jubbonti (denosumab-bbdz)] usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Breast Cancer

1. The member has non-metastatic breast cancer and Bone Modifying Agents are being used for the prevention or treatment of osteoporosis when the member is receiving adjuvant aromatase inhibitor therapy and/or ovarian suppression/ablation OR
2. Bone Modifying Agents are being used as a part of the adjuvant therapy regimen in combination with adjuvant endocrine treatment for early breast cancer in a postmenopausal woman or a premenopausal woman on ovarian suppression/ablation. NOTE: Typical dosing in this setting is zoledronic acid 4 mg iv every 6 months.

C. Giant Cell Tumor of Bone

1. The member is an adult or adolescent 12 years of age or older with giant cell tumor of the bone and a Bone Modifying Agent will be used as a single agent for unresectable localized disease OR for metastatic disease.

D. Hypercalcemia of Malignancy

1. Bone Modifying Agents are being used in conjunction with hydration for hypercalcemia as defined as a corrected calcium of greater than or equal to 12 mg/dL (corrected for albumin level). The following formula is used to calculate the corrected calcium level:
   a. Corrected Calcium (mg/dL) = Calcium + 0.8 x (4 – patient Albumin).

E. Multiple Myeloma

1. The member has multiple myeloma and a Bone Modifying Agent is being used with or without anti-myeloma therapy.

F. Prostate Cancer

1. The member has prostate cancer and a Bone Modifying Agent is being used for the prevention or treatment of osteoporosis during androgen deprivation therapy for members who are 70 years of age or higher or are at high risk for fractures.

G. Solid Tumors with Skeletal Metastases

1. Bone Modifying Agents are being used for a member with a solid tumor and skeletal metastases documented on any imaging study.

DOSE ADJUSTMENTS FOR ZOLEDRONIC ACID FOR USE IN MYELOMA & SOLID TUMORS WITH SKELETAL METASTASES:

Creatinine Clearance in ml/min	Dose of Zoledronic Acid
>60	4 mg
50-60	3.5 mg
40-49	3.3 mg
30-39	3.0 mg
<30	Use is not recommended

III. EXCLUSION CRITERIA

A. Members with creatinine clearance less than 60 mL/min without zoledronic acid dose adjustment, see table above.

B. Dosing exceeds single dose limits for Zoledronic Acid 4 mg, Pamidronate 90 mg, Xgeva/Wyost 120 mg, and Prolia/Jubbonti 60 mg.

C. Investigational use of a Bone Modifying Agent with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Zoledronic Acid Product Information. Hospira, Inc. Lake Forest, IL 2021

B. Pamidronate Product Information. Hospira, Inc. Lake Forest, IL 2021

C. Xgeva Product Information. Amgen Inc. Thousand Oaks, CA. 2020.

D. Prolia Product Information. Amgen Inc. Thousand Oaks, CA. 2022.

E. Wyost prescribing information. Sandoz Inc. Princeton, NJ 2024

F. Jubbonti prescribing information. Sandoz Inc. Princeton, NJ 2024

G. Clinical Pharmacology Elsevier Gold Standard 2024.

H. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.

I. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

J. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.

K. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

L. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.