Drug Policy:

Bone Modifying Agents (Aredia, Zometa, Xgeva/Prolia)

POLICY NUMBER UM ONC_1190	**SUBJECT** Bone Modifying Agents (Aredia, Zometa, Xgeva/Prolia)		**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	**APPROVAL DATE** December 8, 2021	**EFFECTIVE DATE** December 31, 2021	**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	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1	**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 (Aredia, Zometa, Xgeva/Prolia) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH 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. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR
3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs.

B. NOTE: The preferred agent, per NCH Policies & NCH Pathway, is IV bisphosphonate Zometa/Reclast (zoledronic acid) or Aredia (pamidronate) over Xgeva/Prolia (denosumab) for all indications supported in this policy (except for Giant Cell Tumor of Bone). Xgeva/Prolia (denosumab) is an acceptable alternative for members with documented intolerance/contraindications to bisphosphonates, for example renal impairment and a CrCl of < 30 mL/min.

C. Hypercalcemia of Malignancy

1. Zometa (zoledronic acid) or Aredia (pamidronate) is being used in conjunction with hydration for hypercalcemia as defined as a corrected calcium of ≥ 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).

D. Multiple Myeloma

1. The member has multiple myeloma and Zometa (zoledronic acid) or Aredia (pamidronate) is being used with or without anti-myeloma therapy.

E. Solid Tumors with Skeletal Metastases

1. Zometa (zoledronic acid) or Aredia (pamidronate) is 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

F. Breast Cancer

1. The member has non-metastatic breast cancer and Zometa (zoledronic acid) is 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. Zometa (zoledronic acid) is 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 Zometa (zoledronic acid) 4 mg iv every 6 months.

G. Prostate Cancer

1. The member has prostate cancer and Zometa (zoledronic acid) 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.

H. 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 Xgeva (denosumab) will be used as a single agent for unresectable localized disease OR for metastatic disease.

III. EXCLUSION CRITERIA

A. Members with creatinine clearance < 60 mL/min without Zometa dose adjustment, see table above.

B. Dosing exceeds single dose limits for Zometa 4 mg, Aredia 90 mg, Xgeva 120 mg, and Prolia 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 definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of 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 2021.

B. Pamidronate Product Information 2021.

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

D. Prolia Product Information. Amgen Inc, Thousand Oaks, CA. 2021.

E. Clinical Pharmacology Elsevier Gold Standard 2021.

F. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2021.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2021.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2021.

I. 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.

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