POLICY NUMBER UM ONC_1190	**SUBJECT** Bone Modifying Agents (Aredia, Zometa, Xgeva/Prolia)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
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	**APPROVAL DATE** April 8, 2020	**EFFECTIVE DATE** April 24, 2020	**COMMITTEE APPROVAL DATES** (latest version listed last) 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	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**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** All	

I. PURPOSE

To define and describe the accepted indications for usage of Bone Modifying Agents (Aredia, Zometa, Xgeva/Prolia) in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century 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

1. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

a. 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**

b. 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**

c. 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: http://pathways.newcenturyhealth.com **AND**

d. Continuation requests of previously approved non-preferred medication are not subject to this provision **AND**

e. When available, generic alternatives are preferred over brand-name drugs.

2. NOTE: The preferred agent, per NCH Policies & NCH Pathway, is IV bisphosphonate (Zometa/Reclast or Aredia) over Xgeva/Prolia (denosumab) for bone metastases from solid tumors, for prevention/treatment of osteoporosis/bone loss, and as adjuvant therapy to decrease the risk of bone metastases in ER/PR+ breast cancer. Xgeva is an acceptable alternative for members with documented intolerance/contraindications/renal impairment and a CrCl of < 30 mL/min.

3. Hypercalcemia of Malignancy

a. Zometa, or Aredia are 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:

   i. Corrected Calcium (mg/dL) = Calcium + 0.8 x (4 – patient Albumin).

b. Xgeva (denosumab) may be used for the above indication if the member has failed, is intolerant to, or has a contraindication to IV bisphosphonates (zoledronic acid or pamidronate).

4. Multiple Myeloma

a. The member has multiple myeloma and Zometa or Aredia are being used in combination with anti-myeloma therapy.

b. Xgeva (denosumab) may be used for the above indication if the member has failed, is intolerant to, or has a contraindication to IV bisphosphonates (zoledronic acid or pamidronate).

5. Solid Tumors with Skeletal Metastases

a. Zometa or Aredia is being used for a member with a solid tumor and skeletal metastases documented on any imaging study.

b. Xgeva (denosumab) may be used for the above indication if the member has failed, is intolerant to, or has a contraindication to IV bisphosphonates (zoledronic acid or pamidronate).

DOSE ADJUSTMENTS FOR ZOLEDRONIC ACID FOR USE IN MYELOMA & 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

6. Breast Cancer

a. The member has non-metastatic breast cancer and 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.

b. Zoledronic acid is being used as a part of the adjuvant therapy regimen in combination with adjuvant endocrine treatment of early breast cancer in a postmenopausal woman or a premenopausal woman on ovarian suppression Note: Typical dosing in this setting is zoledronic acid 4 mg iv every 6 months.

c. Prolia (denosumab) may be used for the above indications if the member has failed, is intolerant to, or has a contraindication to Zoledronic acid.

7. Prostate Cancer

a. The member has prostate cancer and Zoledronic acid is being used for the following:

   i. Prevention or treatment of osteoporosis during androgen deprivation therapy for members who are 70 years or higher or are at high risk for fractures **AND**

ii. Prolia (denosumab) may be used for the above indication if the member has failed, is intolerant to, or has a contraindication to Zoledronic acid).

8. Giant Cell Tumor of Bone

a. The member has giant cell tumor of the bone and Xgeva (denosumab) is being used as a single agent or combined with interferon alfa/peginterferon or radiation therapy for localized disease **OR** as a single agent for metastatic disease.

III. EXCLUSION CRITERIA

1. Members with creatinine clearance < 60 mL/min without Zometa dose adjustment, see table above.
2. Dosing exceeds single dose limits for Zometa 4 mg, Aredia 90 mg, and Xgeva 120 mg, Prolia 60 mg.
3. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

IV. MEDICATION MANAGEMENT

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

V. APPROVAL AUTHORITY

1. Review – Utilization Management Department
2. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Zometa Product Information. Novartis, 2019.
2. Pamidronate Product Information. Areva Pharmaceuticals. Elizabethtown, KY. 2012.
3. Xgeva Product Information. Amgen. Thousand Oaks, CA. 2020.
4. Prolia Product Information. Amgen, September 2019.
5. Clinical Pharmacology Elsevier Gold Standard. 2020.
6. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.
7. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.
8. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2020.