Department:	Pharmacy Management	**Original Approval:**	01/20/2016
Policy #:	PM135	**Last Approval:**	05/20/2019
Title:	Denosumab (Xgeva®)		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Denosumab (Xgeva): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Documentation that medication is being prescribed by or in consultation with a specialist -Medication list (current and past) -Diagnosis -Age -Radiographic or imaging studies -Dosing and duration requested -Initial/Extended approval -Labs/Diagnostics**.**

BACKGROUND

Xgeva, a receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor, is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. Xgeva is also indicated for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. Xgeva is also indicated for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. Another injectable formulation of denosumab is available, Prolia®, but it is not included in this policy.[2] The prescribing information for Xgeva notes that patients receiving Xgeva should not take Prolia.[1] Xgeva is available as a single-use vial that contains 120 mg of denosumab per 1.7 mL (70 mg/mL).

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	***Continue to criteria for approval below.***
Medicare Members	***Step-utilization of Part D drugs not required.***

Coverage of Xgeva is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Prevention of Skeletal-Related Events in Patients with Bone Metastases from Solid Tumors (e.g., Breast Cancer, Prostate Cancer, Non-Small-Cell Lung Cancer).**

Criteria. *Approve for 1 year if the patient meets the following criteria (A, B, C and D):*

- **A)** The patient is aged ≥ 18 years; AND
- **B)** The agent is prescribed by, or in consultation with, a hematologist or an oncologist; AND
- **C)** The patient has bone metastases; AND
- **D)** Patients with prostate cancer have received at least one hormonal therapy (e.g., Lupron Depot® [leuprolide for depot suspension], Eligard® [leuprolide acetate for injectable suspension], Trelstar® [triptorelin pamoate for injectable suspension], or Zoladex® [goserelin implant]).

Dosing. Approve 120 mg administered as a subcutaneous (SC) injection once every 4 weeks.

2. **Prevention of Skeletal-Related Events in Patients with Multiple Myeloma.[1]**

Criteria. Approve for 1 year if *the patientmeets the following criteria (A and B):*

- **A)** The patient is aged ≥ 18 years; AND
- **B)** The agent is prescribed by, or in consultation with, a hematologist or an oncologist.

Dosing. Approve 120 mg administered as a subcutaneous (SC) injection once every 4 weeks.

3. **Giant Cell Tumor of Bone.**

Criteria. Approve for 1 year.

Dosing. Approve 120 mg SC once every 4 weeks with loading doses on Day 8 and Day 15 of Month 1.[1,7]

4. **Hypercalcemia of Malignancy.**

Criteria. Approve for 2 months if *the patientmeets the following criteria (A, B, AND C)*:

- **A)** The patient has a current malignancy; AND
- **B)** The patient meets one of the following (i or ii):
  - **i.** The patient has tried intravenous (IV) bisphosphonate therapy (e.g., zoledronic acid injection [Zometa], pamidronate injection [Aredia]); OR
  - **ii.** The patient has an estimated calculated creatinine clearance (CrCl) < 30 mL/min; AND
- **C)** The patient's albumin-corrected calcium (cCa) is ≥ 11.5 mg/dL.

Dosing. Approve 120 mg SC once every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.[1]

Conditions Not Recommended for Approval

Xgeva has not been shown to be effective or there are limited or preliminary data, or potential safety concerns, that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions are provided below.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

Enter all special considerations here.

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	1. Xgeva® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; June 2018. 2. Prolia® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; June 2018.	
CFR		
WAC	WAC 284-43-2050	
RCW		
Contract Citation	☒ WAH	
	☒ IMC	
	☒ MA	
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
01/13/2016	New	Kelly Force; Yusuf Rashid, RPh
01/20/2016	Approval	MMLT
01/12/2017	No revisions	Fran McGaugh
01/13/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern Sophia Yun, PharmD
07/25/2017	Approved	MMLT
03/09/2018	Reassigned from UM147 to PM135	Cindy Bush
05/04/2018	Transferred to new template	Cindy Bush
06/12/2018	Revised	Jennifer Farley, PharmD
06/14/2018	Approval	UM Committee
04/15/2019	Revised	Jennifer Farley, PharmD
05/20/2019	Approval	UM Pharmacy Subcommittee

Appendix A: Cockcroft-Gault Equation for Estimating Creatinine Clearance

There are many different methods that can be used to calculate an estimated creatinine clearance (CrCl). The Cockcroft-Gault is one formula that provides an estimate of CrCl using serum creatinine. It is only for adults. This formula tends to overestimate CrCl in obese persons and to underestimate it in those who are lean. The Cockcroft-Gault equation for calculating CrCl is as follows:

CrCl in adults **(men)** = $\frac{\text{(140 minus age [in years] X weight [in kg])}}{\text{(72 X serum creatinine [in mg/dL])}}$

For women, multiple the above results by 0.85. The steps, for clarity, are as follows:

1) Subtract the patient's age in years from 140.
2) Multiple by the patient's weight in kg (if weight is in pounds, divide by 2.2 to get kg).
3) Multiple the patient's serum creatinine (in mg/dL) by 72.
4) Divide the total from 2) by the total from 3).
5) If the patient is female, take the total from 4) and multiple by 0.85.

For example, a man who is 55 years of age, who weighs 160 pounds (72.7 kg), and with a serum creatinine 0.9 mg/dL, would have a calculated creatinine clearance of 95 mL/minute. For a woman with these same values, her CrCl would be 81 mL/minute

Appendix B: Calculating albumin-corrected calcium (cCa)

If cCa value is not given, the following equation can be used to calculate cCa:
cCa in mg/dL = measured Ca (mg/dL) + (0.8 X [4.0 g/dL – patient albumin [g/dL]).

For example, a patient with a serum calcium level of 10.3 mg/dL, but an albumin level of 3.0 g/dL, appears to have a normal serum calcium level. However, when corrected for the low albumin, the real serum calcium value is 11.1 mg/dL, calculated as (10.3 + 0.8 X 1.0).