

Xgeva® (denosumab) injection J0897

When requesting Xgeva® (denosumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications^{1,2}

- Prevention of skeletal-related events in individuals with bone metastases from solid tumors
- 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
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

Approved Off-label Compendial uses³

- Breast cancer: for prevention of skeletal-related events in an individual with bone metastases and an expected survival of ≥ 3 months
- Prostate cancer: for prevention of skeletal-related events in men with castration-recurrent disease who have bone metastases
- Giant cell tumor of bone:
 - As a single agent or combined with interferon alfa or radiation therapy for localized disease
 - As a single agent for metastatic disease
- To reduce the risk of fractures and improve bone mineral density in postmenopausal women with breast cancer receiving adjuvant endocrine therapy

Coverage Guidelines

For all indications, the individual meets the following safety criteria for approval:

- The individual has a serum calcium or corrected calcium greater than the lower limit of normal per laboratory reference.¹
- If the individual is a female of childbearing potential, pregnancy has been ruled out.¹

The individual meets **all** of the following criteria for approval:

- The individual has one of the following diagnoses:
 - Bone metastases from a solid tumor¹
 - If the primary cancer diagnosis is breast cancer, then the individual must have an expected survival of 3 months or greater.³
 - If the primary cancer diagnosis is prostate cancer, then the individual must have castration recurrent disease (ie, disease no longer responsive to androgen deprivation therapy).³
 - The primary cancer diagnosis is **not** multiple myeloma or other non-solid (hematologic) tumor¹

- Giant cell tumor of bone
 - Xgeva® (denosumab) is being used in an adult or skeletally mature adolescent in one of the following clinical scenarios:
 - As a single agent or combined with interferon alfa or radiation therapy for localized disease³
 - As a single agent for metastatic disease³
- Hypercalcemia of malignancy¹
 - The individual has tried and had an inadequate response to intravenous bisphosphonate therapy.¹
- To reduce the risk of fractures and improve bone mineral density in postmenopausal (natural or induced) individuals with breast cancer³
 - The individual is at high risk for fracture, defined as:
 - Baseline bone mineral density (BMD) T-score by DXA less than or equal to -2.5⁴
 - History of an osteoporotic (fragility) fracture⁴
 - Baseline BMD T-score by DXA between -1 and -2.5 if the FRAX® 10-year fracture probability for major osteoporotic fracture is $\geq 20\%$ or the 10-year probability of hip fracture is $\geq 3\%$ ⁴
 - The patient is receiving adjuvant endocrine therapy³

Approval duration: 12 months

Additional Information for Prescribers¹

Our prescribers are alerted to the following safety concerns as educational points/reminders:

- Osteonecrosis of the jaw can occur in individuals receiving Xgeva® (denosumab). An oral examination should be performed prior to starting Xgeva® (denosumab). Symptoms should be monitored and invasive dental procedures avoided during Xgeva® (denosumab) treatment.
- Atypical femoral fracture has been reported with Xgeva® (denosumab). Individuals with thigh or groin pain should be evaluated to rule out a femoral fracture.
- Individuals with increasing renal dysfunction, most commonly with severe dysfunction (CrCl < 30 mL/min or receiving dialysis), and with inadequate/no calcium supplementation, are at increased risk of hypocalcemia.
- Xgeva® (denosumab) can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Correct hypocalcemia prior to initiating therapy. Monitor calcium levels during therapy, especially in the first weeks of initiating therapy, and adequately supplement all individuals with calcium and vitamin D.

References

1. Xgeva[®] prescribing information. Thousand Oaks, CA: Amgen Inc.: March 2016.http://pi.amgen.com/~media/amgen/repositorysites/pi-amgen-com/xgeva/xgeva_pi.ashx. Accessed March 23, 2017.
2. Klasco RK (Ed): DRUGDEX[®] System. Thomson Micromedex, Greenwood Village, CO. Accessed March 23, 2017. <http://www.micromedexsolutions.com>
3. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium[®]) Accessed March 23, 2017. http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=158 Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[™]). ©2017 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines[™] and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.
4. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4176573/pdf/198_2014_Article_2794.pdf. Accessed March 24, 2017.

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