XGEVA®
(denosumab) injection
120 mg/1.7 mL vial

PRIOR AUTHORIZATION CONSIDERATIONS FOR XGEVA®

Patients may still receive XGEVA® under a step therapy policy*

Indication

XGEVA® is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors.

Important Safety Information

- XGEVA® is contraindicated in patients with pre-existing hypocalcemia and clinically significant hypersensitivity to XGEVA®. XGEVA® can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Osteonecrosis of the jaw and atypical femoral fracture have been reported. Clinically significant hypercalcemia following treatment discontinuation in patients with Giant Cell Tumor of Bone and in patients with growing skeletons has been reported. Multiple vertebral fractures following discontinuation of treatment have been reported. XGEVA® can cause fetal harm.

Please click here for additional Important Safety Information.

PATIENTS MAY STILL RECEIVE XGEVA® UNDER SOME STEP THERAPY POLICIES*

Tips for Navigating the Step Therapy Process for XGEVA®

- Key considerations for new solid tumor and multiple myeloma patients:
  - Identify appropriate candidates for therapy
  - Review payer-specific policy for coverage criteria
  - Ensure appropriate documentation is recorded/attached

Examples of documentation that may be helpful to include in prior authorization (PA) submissions:

DOCUMENTATION EXAMPLES THAT A PLAN MAY REQUIRE

CONSIDERATIONS	EVENT/CONDITION/APPLICABLE CODE(S)*
HISTORY WHILE TAKING BISPHOSPHONATES, INCLUDING	• Skeletal-related event(s), such as[1]: » Radiation to bone (Z51.0, Z92.3[2]) » Pathologic fracture (M84.40XA–M84.68XS, M48.50XA–M48.58XS, Z87.311[2]) » Surgery to bone (Z48.89[2]) » Spinal cord compression (C72.0, D33.4, G95.9[2])
RENAL FUNCTION	• Current renal function status (eg, creatinine clearance)[3,4] (N18.1–N18.9, I12.0–I13.2[2])
	• Dose reduction of IV bisphosphonates due to renal impairment[4]
INTOLERANCE TO BISPHOSPHONATES, INCLUDING	• Contraindication or hypersensitivity to any component of bisphosphonates[4] (T88.7XXA–T88.7XXS, Z88.8[2])
	• History of acute-phase reactions[4] (T88.7XXA–T88.7XXS, Z88.8[2])
	• History of severe and occasionally incapacitating bone, joint, and/or muscle pain[4] (R52[2])
ADDITIONAL CONSIDERATIONS	• Life expectancy[5]
	• Drug interactions with bisphosphonates[4] (T88.7XXA–T88.7XXS, Z88.8[2]) » Aminoglycosides: May have an additive effect to lower serum calcium for prolonged periods » Loop diuretics: Concomitant use with zoledronic acid may increase risk of hypocalcemia » Nephrotoxic drugs: Use with caution
	• Venous access[3] (I87.1, I87.2[2])
	• Oral or IV anticancer regimen[6]
	• Diagnoses, including: » Primary disease[5] (C90.00–C90.02, C40.00–C41.9, C61, Z85.46[2]) » Functional status[7] (Z73.6[2]) » Location and number of bone metastases and lesions[8] (C79.51[2])
	• Patients with asthma who are aspirin-sensitive[4]

* Information is provided as a courtesy only and is not comprehensive or instructive. Coding and coverage policies can change without warning and vary by plan. The healthcare provider is solely responsible for determining coverage, coding, and reimbursement. Amgen does not guarantee coverage or reimbursement.

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MANY PAYER POLICIES ALSO REFERENCE NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®) WHEN DECIDING COVERAGE

Updated NCCN Guidelines®

Denosumab (XGEVA®) is the only category 1† preferred bone antiresorptive treatment option for patients **whose prostate cancer has metastasized to bone**[9]

Denosumab (XGEVA®) is an NCCN category 1-recommended bone antiresorptive treatment option for patients **whose breast cancer has metastasized to bone**[10]

†Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Support from every angle.

Amgen Assist 360™ is your single point of contact for the tools and resources you need to navigate through reimbursement and access challenges.

Example Letter of Medical Necessity

Example Letter of Appeal

XGEVA® Prescribing Information, if needed for PA submission

AMGEN ASSIST 360™

Support, Simplified

Visit AmgenAssist360.com or call 888-4ASSIST (888-427-7478)
Monday-Friday, 9 am to 8 pm ET.

References: 1. Ibrahim A, Scher N, Williams G, et al. Approval summary for zoledronic acid for treatment of multiple myeloma and cancer bone metastases. *Clin Cancer Res.* 2003;9(7):2394-2399. **2.** Optum360. *ICD-10-CM Expert for Physicians. The complete official code set*. 2019. **3.** Brown-Glaberman U, Stopeck AT. Role of denosumab in the management of skeletal complications in patients with bone metastases from solid tumors. *Biologics*. 2012;6:89-99. **4.** Zometa [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2018. **5.** Cigna. Cigna Denosumab Drug and Biologic Coverage Policy. https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/pharmacy/ph_1212_coveragepositioncriteria_denosumab.pdf. Accessed August 19, 2019. **6.** Curtis JR, Yun H, Matthews R, Saag KG, Delzell E. Adherence with intravenous zoledronate and IV ibandronate in the U.S. Medicare population. *Arthritis Care Res (Hoboken).* 2012;64(7):1054-1060. **7.** Smith MR. Osteoclast targeted therapy for prostate cancer: bisphosphonates and beyond. *Urol Oncol.* 2008;26(4):420-425. **8.** Fizazi K, Lipton A, Mariette X, et al. Randomized phase II trial of denosumab in patients with bone metastases from prostate cancer, breast cancer, or other neoplasms after intravenous bisphosphonates. *J Clin Oncol.* 2009;27(10):1564-1571. **9.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.4.2019. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed August 19, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **10.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.2.2019. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed August 19, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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Important Safety Information

Hypocalcemia

- Pre-existing hypocalcemia must be corrected prior to initiating therapy with XGEVA®. XGEVA® can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Monitor calcium levels, especially in the first weeks of initiating therapy, and administer calcium, magnesium, and vitamin D as necessary. Concomitant use of calcimimetics and other drugs that can lower calcium levels may worsen hypocalcemia risk and serum calcium should be closely monitored. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.
- An increased risk of hypocalcemia has been observed in clinical trials of patients with increasing renal dysfunction, most commonly with severe dysfunction (creatinine clearance less than 30 mL/minute and/or on dialysis), and with inadequate/no calcium supplementation. Monitor calcium levels and calcium and vitamin D intake.

Hypersensitivity

- XGEVA® is contraindicated in patients with known clinically significant hypersensitivity to XGEVA®, including anaphylaxis that has been reported with use of XGEVA®. Reactions may include hypotension, dyspnea, upper airway edema, lip swelling, rash, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue XGEVA® therapy permanently.

Drug Products with Same Active Ingredient

- Patients receiving XGEVA® should not take Prolia® (denosumab).

Osteonecrosis of the Jaw

- Osteonecrosis of the jaw (ONJ) has been reported in patients receiving XGEVA®, manifesting as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration, or gingival erosion. Persistent pain or slow healing of the mouth or jaw after dental surgery may also be manifestations of ONJ. In clinical trials in patients with cancer, the incidence of ONJ was higher with longer duration of exposure.
- Patients with a history of tooth extraction, poor oral hygiene, or use of a dental appliance are at a greater risk to develop ONJ. Other risk factors for the development of ONJ include immunosuppressive therapy, treatment with angiogenesis inhibitors, systemic corticosteroids, diabetes, and gingival infections.
- Perform an oral examination and appropriate preventive dentistry prior to the initiation of XGEVA® and periodically during XGEVA® therapy. Advise patients regarding oral hygiene practices. Avoid invasive dental procedures during treatment with XGEVA®. Consider temporarily interrupting XGEVA® therapy if an invasive dental procedure must be performed.
- Patients who are suspected of having or who develop ONJ while on XGEVA® should receive care by a dentist or an oral surgeon. In these patients, extensive dental surgery to treat ONJ may exacerbate the condition.

Atypical Subtrochanteric and Diaphyseal Femoral Fracture

- Atypical femoral fracture has been reported with XGEVA®. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution.
- Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. During XGEVA® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patients presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of XGEVA® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Hypercalcemia Following Treatment Discontinuation in Patients with Giant Cell Tumor of Bone (GCTB) and in Patients with Growing Skeletons

- Clinically significant hypercalcemia requiring hospitalization and complicated by acute renal injury has been reported in Xgeva-treated patients with GCTB and in patients with growing skeletons within one year of treatment discontinuation. Monitor patients for signs and symptoms of hypercalcemia after treatment discontinuation and treat appropriately.

Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation

- Multiple vertebral fractures (MVF) have been reported following discontinuation of treatment with denosumab. Patients at higher risk for MVF include those with risk factors for or a history of osteoporosis or prior fractures. When XGEVA® treatment is discontinued, evaluate the individual patient's risk for vertebral fractures.

Embryo-Fetal Toxicity

- XGEVA® can cause fetal harm when administered to a pregnant woman. Based on findings in animals, XGEVA® is expected to result in adverse reproductive effects.
- Advise females of reproductive potential to use effective contraception during therapy, and for at least 5 months after the last dose of XGEVA®. Apprise the patient of the potential hazard to a fetus if XGEVA® is used during pregnancy or if the patient becomes pregnant while patients are exposed to XGEVA®.

Adverse Reactions

- The most common adverse reactions in patients receiving XGEVA® with bone metastasis from solid tumors were fatigue/asthenia, hypophosphatemia, and nausea. The most common serious adverse reaction was dyspnea. The most common adverse reactions resulting in discontinuation were osteonecrosis and hypocalcemia.
- For multiple myeloma patients receiving XGEVA®, the most common adverse reactions were diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache. The most common serious adverse reaction was pneumonia. The most common adverse reaction resulting in discontinuation of XGEVA® was osteonecrosis of the jaw.

Please click here for full Prescribing Information.

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