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

ELECTRONIC MEDICAL RECORD SYSTEM TIP SHEET

Finding patients with bone metastases from solid tumors and multiple myeloma who may be appropriate for a bone targeting agent can be an overwhelming process. Electronic Medical Records (EMR) capabilities can help identify these patients for follow-up evaluation and management. This tool provides examples of queries on EMR systems that may help identify appropriate patients for XGEVA® (denosumab) and should not be used for coding or reimbursement.*

*These examples are not intended to be instructive with respect to clinical decision-making or billing and coding. Healthcare providers are solely responsible for clinical decisions and ensuring the accuracy and validity of all billing and claims. This is not a guarantee of coverage or reimbursement for any product or service.

Indications

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

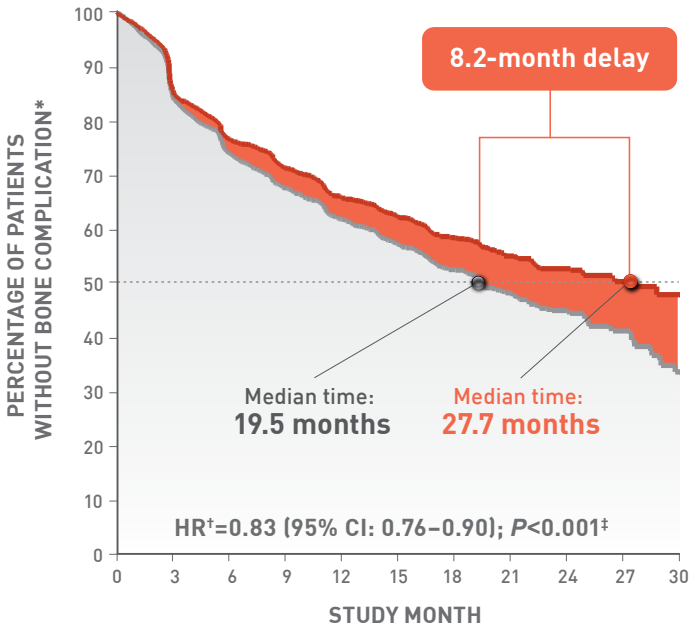
Please see Important Safety Information on pages 6-7.

FOR YOUR PATIENTS WITH BONE METASTASES FROM SOLID TUMORS

XGEVA® has been proven superior in delaying bone complications*:

8.2 months longer than zoledronic acid (ZA)[1]

Median time to first bone complication[1,*]



17%
RISK REDUCTION VS ZA

XGEVA® 120 mg Q4W (n=2,862)
zoledronic acid 4 mg Q4W (n=2,861)

- In a prespecified, integrated analysis of 3 pivotal trials in patients with solid tumors and bone metastases, XGEVA® prevented bone complications* for 27.7 months vs 19.5 months with ZA HR†=0.83 (95% CI: 0.76-0.90); *P*<0.001 for superiority[1]
- 5,723 patients were randomized 1:1 to receive Q4W either XGEVA® 120 mg SC + placebo IV or ZA 4 mg IV over 15 min + placebo SC[2,3]

MEDIAN TIME TO FIRST BONE COMPLICATION* (MONTHS)

TUMOR TYPE	XGEVA®	ZA	RISK REDUCTION XGEVA® vs ZA
Integrated Analysis[1] (n=5,723)	**27.7**	**19.5**	↓ **-17%** vs ZA
	HR†=0.83 (95% CI: 0.76-0.90); *P*‡<0.001 for superiority		
Breast cancer[2] (n=2,046)	**Minimum not reached§**	**26.4**	↓ **-18%** vs ZA
	HR†=0.82 (95% CI: 0.71-0.95); *P*‡=0.010 for superiority		
Prostate cancer[2] (n=1,901)	**20.7**	**17.1**	↓ **-18%** vs ZA
	HR†=0.82 (95% CI: 0.71-0.95); *P*‡=0.008 for superiority		
OST with MM[2] (n=1,776)	**20.5**	**16.3**	↓ **-16%** vs ZA
	HR†=0.84 (95% CI: 0.71-0.98); *P*‡<0.001, noninferiority; *P*‡=0.060, not significant for superiority		
OST without MM[4] (n=1,597)	**21.4**	**15.4**	↓ **-19%** vs ZA
	HR†=0.81 (95% CI: 0.68-0.96); **Post Hoc Analysis**		

*Bone complications, also known as skeletal-related events (SREs), are defined as radiation to bone, pathologic fracture, surgery to bone, and spinal cord compression.[2]
†Hazard ratio (HR) as the increase or decrease in likelihood of an event of interest (in this case a bone complication*) for one group relative to that in a comparator group.
‡*P* value for superiority.
§At 27 months (study end).
BTA, bone-targeting agent; CI, confidence interval; HR, hazard ratio; IV, intravenous; MM, multiple myeloma; OST, other solid tumors; Q4W, every 4 weeks; SC, subcutaneous; SRE, skeletal-related events; ZA, zoledronic acid.

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.

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CONSIDERATIONS FOR USING EMR TO SEARCH FOR PATIENTS WITH BONE METASTASES FROM SOLID TUMORS

ICD-10 and HCPCS codes listed below can help identify patients that may be appropriate for XGEVA®

Establishing evidence of bone metastases, SREs, reduced renal function, as well as confirming lack of BTA therapy, may require patient chart review.

Main search criteria define BTA eligible patients (A) and may be used in combination with additional search criteria (B-E).

MAIN SEARCH CRITERIA

A. Patients with solid tumors and bone metastases (which may be undetected and untreated)

ICD-10-CM codes may be used to identify patients with solid tumors; common examples include:[5]

- C50.011 – C50.929 for breast cancer
- C61 for prostate cancer
- C34.00 – C34.92 for lung cancer

To find patients with bone metastases, add the below criteria:

ICD-10-CM code for bone metastases (C79.51)[5] or Review chart and further bone imaging

ADDITIONAL SEARCH CRITERIA (consider including any one or more of the following in your search)

B. Patients who are NOT currently treated with bone-targeting agents

None of the following HCPCS codes for bone-targeting therapy within the past 4 weeks:

- J3489[6] for zoledronic acid and
- J2430[6] for pamidronate and
- J0897[6] for denosumab

C. Patients who are currently treated with ZA*

HCPCS code for zoledronic acid [J3489][6] within the past 4 weeks

D. Patients with evidence of a skeletal-related event (SRE)

Evidence of SRE:

- ICD-10-CM code for pathologic fracture (M84.40XA – M84.68XS, M48.50XA – M48.58XS)[5] or history of fracture (Z87.311)[5] or
- ICD-10-CM code for spinal cord compression (G95.9)[5] or
- History of radiation to the bone, bone surgery, and/or hospitalization for SRE

E. Patients with reduced renal function

Evidence of reduced renal function:

- ICD-10-CM code for chronic kidney disease (N18.1 – N18.9, I12.0 – I13.2)[5]

HCPCS = Healthcare Common Procedure Coding System; ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification.

Amgen is committed to protecting patient privacy and the Amgen field force is not permitted to access any protected health information. Therefore, any report with patient-specific data must not be handled by, shared with, or discussed by a healthcare professional with any agent of Amgen for any reason.

**XGEVA® has been proven superior in delaying median time to first bone complication in head-to-head trials versus zoledronic acid. Patients who had received IV bisphosphonates were excluded from the phase 3 studies. In a 2-year open-label extension of the trials, no new safety signals were observed in patients who transitioned to XGEVA®. See page 2 for study information.*

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FOR YOUR PATIENTS WITH MULTIPLE MYELOMA.[2]

XGEVA® offers consistent dosing across patients, regardless of renal function

- XGEVA® is a monoclonal antibody and is not cleared by the kidneys[1,2]
- The risk of hypocalcemia increases with decreasing renal function[2]
- In patients with renal impairment, closely monitor calcium levels and calcium and vitamin D intake[1,2]
- Patients with CrCl <30 mL/min were excluded from XGEVA® pivotal trials[1,2]

XGEVA® is a subcutaneously administered treatment option that complements a patient's primary MM treatment

- 83% of patients in a real-world setting receive either an oral or subcutaneous treatment for their primary multiple myeloma therapy[7,*]
- XGEVA® is the only subcutaneous, non-infusion, bone-targeting agent[2]

XGEVA® provided nearly 23 months of prevention (noninferior to ZA) against bone complications[†]

- Median time to first on-study bone complication[†] was 22.8 months and 24 months for XGEVA® and ZA, respectively
  HR[‡]=0.98 (95% CI: 0.85-1.14)[2]
- In a phase 3 study of newly-diagnosed multiple myeloma, 1,718 patients were randomized 1:1 to receive Q4W either XGEVA® 120 mg SC + placebo IV or ZA 4 mg IV over 15 min + placebo SC[2,3,8]

CI, confidence interval; CrCl, creatinine clearance; BTA, bone-targeting agent; MM, multiple myeloma; IV, intravenous; Q4W, every 4 weeks; SC, subcutaneous; ZA, zoledronic acid

*In a retrospective chart audit of 3,553 patients from Aug 2022 to Jul 2023.

[†]Bone complications, also known as skeletal-related events (SREs), are defined as radiation to bone, pathologic fracture, surgery to bone, and spinal cord compression.

[‡]Hazard ratio (HR) is defined as the increase or decrease in likelihood of an event of interest (in this case, a bone complication[†]) for one group relative to a comparator group.

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.
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CONSIDERATIONS FOR USING YOUR EMR TO SEARCH FOR PATIENTS WITH MULTIPLE MYELOMA (MM)

The ICD-10 and HCPCS codes listed below can help identify patients that may be appropriate for XGEVA®

Confirming use of antimyeloma therapy and/ or lack of BTA therapy, as well as establishing evidence of SREs and/or reduced renal function, may require patient chart review.

Main search criteria define BTA eligible patients (A) and may be used in combination with additional search criteria (B-D).

MAIN SEARCH CRITERIA

A. Patients with MM receiving antimyeloma therapy

ICD-10-CM code for MM (C90.00 – C90.01)[5] AND Prescribed antimyeloma therapy

ADDITIONAL SEARCH CRITERIA (consider including any one or more of the following in your search)

B. Patients who are NOT currently treated with bone-targeting agents

None of the following HCPCS codes for bone-targeting therapy within the past 4 weeks:

- J3489[6] for zoledronic acid and
- J2430[6] for pamidronate and
- J0897[6] for denosumab

C. Patients with evidence of a skeletal-related event (SRE)

Evidence of SRE:

- ICD-10-CM code for pathologic fracture (M84.40XA – M84.68XS, M48.50XA – M48.58XS)[5] or history of fracture (Z87.311)[5] or
- ICD-10-CM code for spinal cord compression (G95.9)[5] or
- History of radiation to the bone, bone surgery, and/or hospitalization for SRE

D. Patients with reduced renal function

Evidence of reduced renal function:

- ICD-10-CM code for chronic kidney disease (N18.1 – N18.9, I12.0 – I13.2)[5]

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.

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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.

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Important Safety Information (continued)

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 Prescribing Information.

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4. Henry D, Vadhan-Raj S, Hirsh V, et al. Delaying skeletal-related events in a randomized phase 3 study of denosumab versus zoledronic acid in patients with advanced cancer: an analysis of data from patients with solid tumors. *Support Care Cancer*. 2014;22(3):679-687.
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SUPPORT SERVICES

AMGEN® Support+

We're right here, right when you need us

HCP Support Center

Our Amgen SupportPlus Representatives can assist with issues around patient coverage, prior authorizations, co-pay programs, and more.

Benefits Verification
- Verify patient's insurance plan coverage details

Prior Authorization Requirements
- Provide payer-specific prior authorization forms

Amgen SupportPlus Customer Portal
- A tool for managing patient benefits verification and more
- Submit, store, and retrieve benefit verifications electronically

Amgen® Access Specialists

An Amgen Access Specialist can provide live or virtual coverage and access resources to support your patients.

Contact your Amgen Access Specialist for live or virtual support that includes:
- Help with navigating prior authorization, appeals, and fulfillment processes
- Educating on payer requirements and necessary documentation for individual patient support
- Guidance on general reimbursement questions, including product coding and billing information
- Answers to general questions about Amgen SupportPlus programs and other available resources

Amgen® Nurse Partners

Dedicated Amgen Nurse Partners can offer supplemental support and provide information about resources to help patients access their prescribed medication.

Amgen Nurse Partners* can provide supplemental support, including:
- Guidance on resources that may help lower out-of-pocket medication costs
- Assistance to help your patients stay on track with their medication
- Answers to questions about Amgen SupportPlus

*Amgen Nurse Partners are only available to patients that are prescribed certain Amgen products. They are not part of your patient's treatment team and do not provide medical advice, nursing, or case management services. Amgen Nurse Partners will not inject patients with Amgen medications. Patients should always consult their healthcare provider regarding medical decisions or treatment concerns.

AMGEN Support+ | Co-Pay Program

Helping eligible patients save on out-of-pocket costs

The Amgen SupportPlus Co-Pay Program may help eligible patients with private or commercial insurance lower their out-of-pocket costs.

- Pay as little as **$0 out-of-pocket**† for each dose or cycle
- Can be applied to deductible, co-insurance, and co-payment†
- No income eligibility requirement

Encourage your patients with private or commercial insurance to check eligibility and enroll at AmgenSupportPlus.com/copay

†Eligibility criteria and program maximums apply. See AmgenSupportPlus.com/copay for full Terms and Conditions.

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