

PREVENTING BROKEN BONES:

Your guide to understanding how XGEVA® can help prevent broken bones and three other serious bone problems* when cancer from solid tumors spreads to your bones.¹

*Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹



INDICATION

XGEVA® is a prescription medicine used to prevent fracture, spinal cord compression, or the need for radiation or surgery to bone in patients with multiple myeloma and in patients with bone metastases from solid tumors.

SELECT IMPORTANT SAFETY INFORMATION

Do not take XGEVA® if you have low blood calcium (hypocalcemia) or are allergic to denosumab or any of its ingredients. XGEVA® can significantly lower the calcium levels in your blood and some deaths have been reported. Severe jaw bone problems and unusual thigh bone fracture have been reported. Patients with Giant Cell Tumor of Bone and patients with bones that are not fully matured may develop high blood calcium levels after they stop taking XGEVA®, that can be serious. The risk of broken bones in the spine may increase after stopping XGEVA®. You should not become pregnant while taking XGEVA® because XGEVA® can harm your unborn baby.

Please see additional Important Safety Information on pages 18-19.

XGEVA®
(denosumab) injection

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Welcome

As someone with bone metastases (pronounced muh•TASS•tuh•seez), or “bone mets,” it’s important to understand how cancer can affect your bones.² This brochure explains how XGEVA® can help prevent serious bone problems if you have bone metastases from a solid tumor.¹

IMPORTANT SAFETY INFORMATION

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² *Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹

Why is bone protection important?



Cancer cells can break away from the tumor in an organ and spread throughout the body.²

After breaking away from a tumor, many cancer cells die without causing any problems. However, some cancer cells settle in a new location and begin to grow.²

When cancer spreads to the bone, it can weaken the bones. This can lead to serious bone problems, such as^{1,2}:

- Broken bones (fractures)
- A need for surgery to prevent or repair broken bones
- A need for radiation treatments to the bone
- Pressure on the spinal cord (spinal cord compression)

Serious bone problems* are common in people who have bone mets from certain solid tumors²

⁴ *Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹



About

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patients with
BREAST CANCER

and bone mets may have
a serious bone problem³



About

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patients with
PROSTATE CANCER

and bone mets may have
a serious bone problem³



About

6 of 10

patients with
LUNG CANCER

and bone mets may have
a serious bone problem³

Medicines like XGEVA[®] can help prevent serious bone problems if you have a bone met from a solid tumor¹

IMPORTANT SAFETY INFORMATION (CONT'D)

Do not take XGEVA[®] if you are allergic to denosumab or any of the ingredients of XGEVA[®].

Serious allergic reactions have happened in people who take XGEVA[®]. Call your doctor or go to your nearest emergency room right away if you have any symptoms of a serious allergic reaction, including low blood pressure (hypotension); trouble breathing; throat tightness; swelling of the face, lips, or tongue, rash; itching; or hives.

Please see additional Important Safety Information on pages 18-19.

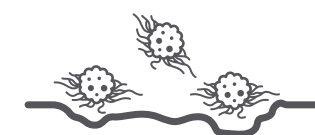
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How does XGEVA[®] work?



Normally, your body is continually breaking down and rebuilding your bone. This keeps your bones strong.²



When cancer spreads to bone, the bones break down faster.²

Over time, this makes bones weak and can lead to serious bone problems.^{2*}



XGEVA[®] works by stopping cells from becoming overactive and may interrupt the process of bone breakdown.^{1,4,5}

*Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹

IMPORTANT SAFETY INFORMATION (CONT'D)

What is the most important information you should know about XGEVA[®]?

Do not take XGEVA[®] if you take Prolia. XGEVA[®] contains the same medicine as Prolia[®] (denosumab).

Please see additional Important Safety Information on pages 18-19.

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How much of a difference can XGEVA® make?

In people with bone mets from breast cancer, prostate cancer, lung cancer, and other types of solid tumors^{1,6}:

XGEVA® delayed serious bone problems* for 27.7 months. This was **8.2 months longer** than another bone-targeting medicine, zoledronic acid, also known as ZA.^{1,6}

¹ *Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).

XGEVA® also decreased the chance of serious bone problems in people with bone mets in breast and prostate cancers^{1,7,8}

People with **BREAST CANCER** were
18% less likely
to have serious bone problems with XGEVA® than with ZA.^{1,7†}

People with **PROSTATE CANCER** were
18% less likely
to have serious bone problems with XGEVA® than with ZA.^{1,8†}

People with **LUNG CANCER** and other solid tumors

In a study of 1,776 patients with bone metastases from lung cancer and other solid tumors (excluding breast and prostate cancer) or multiple myeloma, XGEVA® was no less effective than ZA in lowering the chance of serious bone problems.¹

[†]In a study of 2,046 people with breast cancer.¹

[†]In a study of 1,901 men with prostate cancer.¹

IMPORTANT SAFETY INFORMATION (CONT'D)

Severe jaw bone problems (osteonecrosis)

Severe jaw bone problems may happen when you take XGEVA®. Your doctor should examine your mouth before you start, and while you are taking XGEVA®. Tell your dentist that you are taking XGEVA®. It is important for you to practice good mouth care during treatment with XGEVA®. In studies of patients with bone involvement, the rate of severe jaw problems was higher the longer they were being treated with XGEVA®.

Please see additional Important Safety Information on pages 18-19.

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How can XGEVA[®] help protect me from serious bone problems?*

- XGEVA[®] is a prescription medicine used to prevent fracture, spinal cord compression, or the need for radiation or surgery to bone in patients with multiple myeloma and in patients with bone metastases from solid tumors.¹

It's important to remember to take XGEVA[®] only as directed by your doctor.

*Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹

How will I receive XGEVA[®]?

XGEVA[®] is given as a shot once every 4 weeks at your doctor's office. The shot is given under the skin and does not involve an infusion through a vein.¹

- XGEVA[®] can be injected into your upper arm, upper thigh, or stomach area¹
- It is important to take XGEVA[®] at the recommended treatment schedule¹
- Talk to your doctor about whether scheduling appointments in advance may help with your treatment regimen

What should I know before I start taking XGEVA[®]?

- You may be told to take vitamin D and calcium supplements to help prevent low calcium levels in the blood¹
- Sticking to the treatment schedule your doctor prescribes will help give you the best chance of avoiding serious bone problems¹

IMPORTANT SAFETY INFORMATION (CONT'D)

Unusual thigh bone fracture

Unusual thigh bone fracture has been reported. Symptoms of a fracture include new or unusual pain in your hip, groin, or thigh.

Please see additional Important Safety Information on pages 18-19.

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How long will I need to take XGEVA®?

Take XGEVA® as prescribed by your doctor

- Your healthcare team may want you to continue treatment even if you do not have symptoms commonly associated with serious bone problems,* such as pain²
- Continuing to use XGEVA® can provide ongoing protection against serious bone problems¹
- Do not stop treatment with XGEVA® without talking to your doctor first¹
- Talk to your doctor to see what's right for you

What if I miss a dose of XGEVA®?

- If you have missed a dose, it is important to talk to your doctor and healthcare team for help getting back on track with XGEVA® treatment¹
- Sticking to the treatment schedule your doctor provides will help give you the best chance of avoiding serious bone problems¹

*Serious bone problems are defined as broken bones (fractures), the need for surgery to prevent or repair broken bones, the need for radiation treatments to the bone, and pressure on the spinal cord (spinal cord compression).¹

IMPORTANT SAFETY INFORMATION (CONT'D)

Risk of high calcium levels in patients with Giant Cell Tumor of Bone and in patients who are still growing

Patients with a type of cancer called Giant Cell Tumor of Bone and patients with bones that are not fully matured are at a greater risk to develop high blood calcium levels after they stop taking XGEVA®, that can be serious.

Please see additional Important Safety Information on pages 18-19.



Here are some tips to help you stay on track with your treatment plan:

- Record appointments in your calendar
- Schedule future appointments in advance
- Ask family or friends for help getting to your doctor's office

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What else should I know?

Speak to your doctor

Your doctor is a good source of information about XGEVA[®]. Below are some questions you can ask that will help get the conversation started with your doctor.

- What is XGEVA[®]?
- Why was I prescribed XGEVA[®]?
- How does XGEVA[®] work?
- How is XGEVA[®] given?
- What are possible side effects?
- How long should I be on XGEVA[®]?
- How often will I receive injections?
- How long will it take to inject XGEVA[®]?
- What should I know before I take XGEVA[®]?

IMPORTANT SAFETY INFORMATION (CONT'D)

Possible harm to your unborn baby

You should not become pregnant while taking XGEVA[®]. Tell your doctor right away if you are pregnant, plan to become pregnant, or suspect you are pregnant. XGEVA[®] can harm your unborn baby.

Please see additional Important Safety Information on pages 18-19.

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What financial resources are available?

XGEVA FIRST STEP™ Program

The XGEVA FIRST STEP™ Program can help eligible commercially insured patients reduce out-of-pocket costs for XGEVA®.

To enroll your practice in the XGEVA FIRST STEP™ program, please call 1-888-65-STEP1 (1-888-657-8371).



This program is not open to patients receiving prescription reimbursement under any federal, state, or government-funded healthcare program, such as Medicare, Medicare Advantage, Medicare Part D, Medicaid, Medigap, Veterans Affairs (VA), the Department of Defense (DoD), or TRICARE®, or where otherwise prohibited by law.



IMPORTANT SAFETY INFORMATION

Do not take XGEVA® if you have low blood calcium (hypocalcemia). Your low blood calcium must be treated before you receive XGEVA®. XGEVA® can significantly lower the calcium levels in your blood and some deaths have been reported. Take calcium and vitamin D as your doctor tells you to. Tell your doctor right away if you experience spasms, twitches, cramps, or stiffness in your muscles or numbness or tingling in your fingers, toes, or around your mouth.

Do not take XGEVA® if you are allergic to denosumab or any of the ingredients of XGEVA®. Serious allergic reactions have happened in people who take XGEVA®. Call your doctor or go to your nearest emergency room right away if you have any symptoms of a serious allergic reaction, including low blood pressure (hypotension); trouble breathing; throat tightness; swelling of the face, lips, or tongue, rash; itching; or hives.

What is the most important information you should know about XGEVA®?

Do not take XGEVA® if you take Prolia. XGEVA® contains the same medicine as Prolia® (denosumab).

Severe jaw bone problems (osteonecrosis)

Severe jaw bone problems may happen when you take XGEVA®. Your doctor should examine your mouth before you start, and while you are taking XGEVA®. Tell your dentist that you are taking XGEVA®. It is important for

you to practice good mouth care during treatment with XGEVA®. In studies of patients with bone involvement, the rate of severe jaw problems was higher the longer they were being treated with XGEVA®.

Unusual thigh bone fracture

Unusual thigh bone fracture has been reported. Symptoms of a fracture include new or unusual pain in your hip, groin, or thigh.

Risk of high calcium levels in patients with Giant Cell Tumor of Bone and in patients who are still growing

Patients with a type of cancer called Giant Cell Tumor of Bone and patients with bones that are not fully matured are at a greater risk to develop high blood calcium levels after they stop taking XGEVA®, that can be serious.

Increased risk of broken bones in the spine after discontinuing XGEVA®

After your treatment with XGEVA® is stopped, your risk for breaking bones in your spine can increase, especially if you have a history of risk factors such as osteoporosis or prior fractures.

Possible harm to your unborn baby

You should not become pregnant while taking XGEVA®. Tell your doctor right away if you are pregnant, plan to become pregnant, or suspect you are pregnant. XGEVA® can harm your unborn baby.

Tell your doctor if you:

- Are taking a medicine called Prolia® (denosumab) because it contains the same medicine as XGEVA®
- Have symptoms of low blood calcium such as muscle stiffness or cramps
- Have symptoms of severe jaw bone problems such as pain or numbness
- Have ongoing pain or slow healing after dental surgery
- Have symptoms of high blood calcium such as nausea, vomiting, headache, and decreased alertness
- Are pregnant, plan to become pregnant, suspect you are pregnant, or breastfeeding

While taking XGEVA®, you should:

- Take good care of your teeth and gums and visit a dentist as recommended
- Tell your dentist that you are taking XGEVA®
- Tell your doctor if you plan to have dental surgery or teeth removed
- Talk to your doctor before you stop taking XGEVA® about your risk for broken bones in your spine
- Women of child bearing age should use highly effective contraception while taking XGEVA® and for at least 5 months after the last dose of XGEVA®

What are the possible side effects of XGEVA®?

In patients with bone metastases from solid tumors using XGEVA®, the most common side effects were tiredness/weakness, low phosphate levels in your blood, and nausea. The most common serious side effect of XGEVA® was shortness of breath.

In multiple myeloma patients receiving XGEVA®, the most common side effects were diarrhea, nausea, low red blood cells, low blood platelets and calcium levels, back pain, swelling of the lower legs or hands, upper respiratory tract infection, rash, and headache. The most common serious adverse reaction in multiple myeloma patients was pneumonia.

These are not all the possible side effects of XGEVA®. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see accompanying Prescribing Information.

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Helpful Resources for More Guidance

XGEVA® Website

www.xgeva.com

Lets Talk Bone Mets

www.letstalkbonemets.com

American Cancer Society

www.cancer.org

Cancer Support Community

www.cancersupportcommunity.org

National Cancer Institute

www.cancer.gov

Cancer Hope Network

www.cancerhopenetwork.org

Amgen does not endorse and is not responsible for the content included in these resources.

References: **1.** XGEVA® (denosumab) prescribing information, Amgen. **2.** American Cancer Society. Bone metastasis. American Cancer Society website. <https://www.cancer.org/content/cancer/en/treatment/understanding-your-diagnosis/advanced-cancer.html>. Revised May 2, 2016. Accessed June 5, 2017. **3.** Oster G, Lamerato L, Glass AG, et al. Natural history of skeletal-related events in patients with breast, lung, or prostate cancer and metastases to bone: a 15-year study in two large US health systems. *Support Care Cancer*. 2013;21(12):3279-3286. **4.** Mundy GR. Metastasis to bone: causes, consequences and therapeutic opportunities. *Nat Rev Cancer*. 2002;2(8):584-593. **5.** Roodman GD. Mechanisms of bone metastasis. *N Engl J Med*. 2004;350(16):1655-1664. **6.** Lipton A, Fizazi K, Stopeck AT, et al. Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: a combined analysis of 3 pivotal, randomised, phase 3 trials. *Eur J Cancer*. 2012;48(16):3082-3092. **7.** Stopeck AT, Lipton A, Body J-J, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. *J Clin Oncol*. 2010;28(35):5132-5139. **8.** Fizazi K, Carducci M, Smith M, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *Lancet*. 2011;377(9768):813-822.



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