

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

^P**XGEVA**[®] (*ex-jee-va*)

denosumab injection

Read this carefully before you start taking **XGEVA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **XGEVA**.

Serious Warnings and Precautions

- Osteonecrosis of the jaw (sore in mouth involving gums or jaw bones)

What is XGEVA used for?

- XGEVA is used for reducing the risk of developing cancer-related complications like broken bones and/or bone pain that need surgery or radiation.
- XGEVA is used for reducing the risk of developing cancer-related complications in patients with multiple myeloma. Multiple myeloma is a cancer of plasma cells (a type of white blood cell).
- XGEVA is used to treat giant cell tumour of bone, which cannot be treated by surgery or where surgery is not the best option in adults and adolescents (aged 13-17 years) whose bones have stopped growing.
- XGEVA is used to reduce high levels of calcium in the blood in cancer patients (hypercalcemia of malignancy) after other drugs called bisphosphonates did not work.

How does XGEVA work?

XGEVA works differently than other medications used to treat cancer patients whose disease has spread to their bones. It works as a RANK Ligand (RANKL) inhibitor. RANKL is a protein that promotes the breakdown of bone. XGEVA blocks RANKL to stop the breakdown of bone. This action strengthens your bones by increasing bone mass and lowers the chance of the cancer causing problems with your bones, such as fractures or severe pain requiring radiation treatment.

XGEVA reduces the amount of calcium in the blood by reducing the breakdown of bones. In patients with hypercalcemia of malignancy, the breakdown of bones can cause too much calcium in the blood.

What are the ingredients in XGEVA?

Medicinal ingredients: denosumab

Non-medicinal ingredients: acetate, polysorbate 20, sodium hydroxide, sorbitol and water for injection.

XGEVA comes in the following dosage forms:

XGEVA is a liquid for injection, with enough liquid in it for one shot. Each vial delivers 120 mg of denosumab. XGEVA is supplied in a carton containing 1 vial.

Do not use XGEVA if:

- you are allergic to denosumab or any other ingredient of XGEVA. Allergic reactions (eg, rash, hives, or in rare cases, swelling of the face, lips, tongue, throat, or trouble breathing) have been reported.
- you have hypocalcemia (low calcium levels in the blood), until your doctor corrects this condition.

What important information do I need to know about taking XGEVA?

XGEVA contains the same medicine as another drug called PROLIA, but at a different dose. If you are being treated with XGEVA, you should not be taking PROLIA or vice versa.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take XGEVA. Talk about any health conditions or problems you may have, including:

Hypocalcemia (low calcium levels in the blood)

XGEVA may lower levels of calcium in your blood. In the post-marketing setting, cases of low blood calcium with severe symptoms, including death, have been reported. If you have low blood calcium before you start receiving XGEVA, it may get worse during treatment. Your low blood calcium must be treated before you receive XGEVA. Most people with low calcium levels do not have symptoms, but some people may have symptoms. When the calcium levels in your blood go down, your body tries to correct the calcium levels by increasing the amount of a hormone made by your parathyroid glands (parathyroid hormone) in your blood. Call your doctor right away if you have symptoms of low blood calcium such as:

- Spasms, twitches, or cramps in your muscles.
- Numbness or tingling in fingers, toes or around the mouth.

Conditions which increase the risk of low blood calcium:

- If you cannot take daily calcium and/or vitamin D.
- If you have severe kidney disease or are on dialysis.

Your doctor will tell you to take calcium and vitamin D to help prevent low calcium levels in your blood while you take XGEVA, unless your blood calcium is high. Take calcium and vitamin D as your doctor tells you to.

Osteonecrosis of the Jaw (sore in mouth involving gums or jaw bones)

Severe jaw bone problems may happen when you take XGEVA. Your doctor should examine your mouth before you start XGEVA. Your doctor may tell you to see your dentist before you start XGEVA. It is important for you to practice good mouth care such as brushing and flossing your teeth regularly during treatment with XGEVA.

Tell your doctor immediately about any dental symptoms, including pain or unusual feeling in your teeth or gums, or any dental infections. If possible, you should not undergo tooth

extraction or other dental procedures (excluding regular dental cleaning) while you are receiving treatment with XGEVA without talking to your doctor first.

If you do need dental work, tell your dentist that you are receiving XGEVA and tell your doctor that you are having dental work done.

Unusual Thigh Bone Fractures

Unusual fracture in the thigh bone may occur with some medicines, including XGEVA. Contact your doctor if you experience new or unusual pain in your hip, groin, or thigh.

High Calcium Levels in the Blood after Stopping Treatment with XGEVA

Some patients with giant cell tumour of the bone and some who are still growing during treatment with XGEVA, have developed high calcium levels in the blood weeks to months after stopping treatment.

Your doctor will monitor you for signs and symptoms of high levels of calcium, after you stop receiving XGEVA.

Risk of Broken Bones in the Spine After Stopping Treatment with XGEVA

Do not stop taking XGEVA without first talking with your doctor. After treatment with XGEVA is stopped, there may be an increased risk of having broken bones in your spine especially in people who have had a fracture or who have had osteoporosis (a condition in which bones become thin and fragile).

Skin Infections

Tell your doctor promptly if you develop a swollen, red area on your skin that feels hot and tender with symptoms of fever (cellulitis) while taking XGEVA.

Pregnancy or Breast-Feeding

XGEVA is not recommended for use in women who are pregnant or plan to become pregnant and nursing mothers. XGEVA may interfere with normal bone and tooth development in fetuses and nursing babies, and may interfere with breastfeeding.

XGEVA is not intended for use in pregnant women. You should not be given XGEVA if you are pregnant. A highly effective method of birth control should be used when taking XGEVA, or for at least 5 months after the last dose of XGEVA.

It is not known whether XGEVA is excreted into human milk.

Use in Children

XGEVA is not recommended for anyone under 18 years of age except for adolescents with giant cell tumour of bone whose bones have stopped growing. The use of XGEVA has not been studied in children and adolescents with other cancers that have spread to bone.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with XGEVA:

Before starting XGEVA, tell your doctor about all the medicines you take, including prescription and non-prescription drugs, vitamins and herbal supplements.

Interactions between XGEVA and other drugs have not been studied.

How to take XGEVA:

XGEVA is administered as a single injection under the skin (subcutaneous) once every four weeks. You should not inject XGEVA into the muscle (intramuscular), into your veins (intravenous) or between the layers of the skin (intra-dermal). The injection can be in your upper arm, upper thigh, or abdomen. The injection should be administered under the supervision of your doctor who is familiar with this drug. You may be able to give yourself XGEVA injections only if you have been trained in giving the injection and your doctor thinks you are capable of doing it correctly and if your doctor follows up with you as necessary.

Before injection, remove the vial from the refrigerator and allow it to reach room temperature (up to 25°C) in the original container. This will make the injection more comfortable. Do not shake. See instructions for injection.

Keep all medicines, including XGEVA, away from children.

Do not share XGEVA product with others, even if they have a similar disease.

INSTRUCTIONS FOR INJECTION

IMPORTANT: TO HELP AVOID CONTAMINATION AND POSSIBLE INFECTION DUE TO INJECTION, PLEASE READ AND FOLLOW THESE INSTRUCTIONS CAREFULLY.

How to prepare for XGEVA injection

XGEVA is available as a liquid in vials. When you receive your XGEVA, always check to see that:

- The name XGEVA appears on the package and vial label.
- The expiration date on the vial label has not passed. **Do not use a vial after the date on the label.**
- The XGEVA liquid in the vial is clear, colourless to slightly yellow.

Only use disposable syringes and needles. Use the syringes only once and dispose of them as instructed by your doctor or nurse.

Setting up for an injection

1. Find a clean flat working surface, such as a table.
2. Remove the vial of XGEVA from the refrigerator. Allow XGEVA to reach room temperature (this takes about 15 to 30 minutes). Vials should be used only once. **DO NOT SHAKE THE VIAL.** Shaking may damage the XGEVA. If the vial has been shaken vigorously, the solution may appear foamy and it should not be used.
3. Assemble the supplies you will need for an injection:
 - XGEVA vial and sterile disposable syringe and a 27-gauge needle.
 - Two alcohol swabs and one cotton ball or gauze pad.
 - Puncture-proof disposal container.
4. Clean your work surface thoroughly and wash your hands with soap and warm water.

Selecting and preparing the injection site

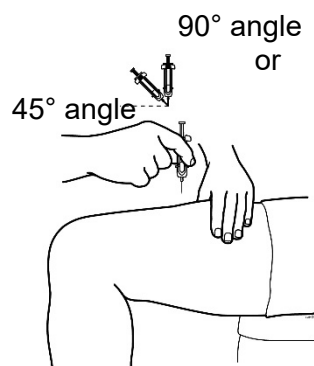
1. Choose an injection site. The recommended injection sites for XGEVA are:
 - The outer area of your upper arms.
 - The abdomen, except for the two-inch (5 cm) area around your navel.
 - The top of your thighs.

How to prepare the dose of XGEVA in vials

1. Take the cap off the vial. Clean the stopper with an alcohol swab.
2. Check the package containing the syringe. If the package has been opened or damaged, do not use that syringe. Dispose of that syringe in the puncture-proof disposal container. If the syringe package is undamaged, open the package and remove the syringe.
3. Keep the vial on your flat working surface and insert the needle straight down through the rubber stopper. Do not put the needle through the rubber stopper more than once.
4. Push the plunger of the syringe down and inject the air from the syringe into the vial of XGEVA. Keeping the needle inside the vial, turn the vial upside down. Make sure that the tip of the needle is in the XGEVA liquid.
5. Keeping the vial upside down, slowly pull back on the plunger to fill the syringe with XGEVA liquid. Withdraw the entire content of the vial.
6. Keeping the needle in the vial, turn the syringe needle up and check for air bubbles in the syringe. If there are air bubbles, gently tap the syringe with your fingers until the air bubbles rise to the top of the syringe. Then slowly push the plunger up to force the air bubbles out of the syringe.
7. Remove the syringe from the vial but **do not lay it down** or let the needle touch anything.

Injecting the dose of XGEVA

1. Hold the syringe in the hand you will use to inject XGEVA. With the other hand, clean the injection site with an alcohol swab. Use a circular motion from the inside to the outside of the injection site.
2. Pinch a fold of skin at the cleaned injection site.
3. Holding the syringe like a pencil, use a quick “dart-like” motion to insert the needle either straight up and down (90-degree angle) or at a slight angle (45 degrees) into the skin.



4. After the needle is inserted, let go of the skin. Inject the prescribed dose subcutaneously as directed by your doctor, nurse or pharmacist.
5. When the syringe is empty, pull the needle out of the skin and place a cotton ball or gauze over the injection site and press for several seconds.
6. Use a syringe, needle and vial only once. **DO NOT** put the needle cover (the cap) back on the needle. Discard the vial with any remaining XGEVA liquid.

Disposal of syringes, needles and vials

You should always follow the instructions given by your doctor, nurse, or pharmacist on how to properly dispose of containers with used syringes, needles and vials. There may be special provincial or local laws for disposal of used needles and syringes.

- Place all used needles, needle covers, syringes, and vials (empty or unused contents) into a “Sharps” container given to you by your doctor or pharmacist or in a hard-plastic container with a screw-on cap, or a metal container with a plastic lid, labelled “used syringes.” Do not use glass or clear plastic containers.
- When the container is full, tape around the cap or lid to make sure the cap or lid does not come off. **Do not throw the container in the household trash. Do not recycle.**
- **Always** keep the container out of the reach of children.

Usual dose:

The usual dose of XGEVA is 120 mg administered once every 4 weeks. If you are being treated for giant cell tumour of bone or hypercalcemia of malignancy, you will receive an additional dose 1 week and 2 weeks after the first dose in the first month of treatment only.

You should also take supplements of calcium and vitamin D as instructed by your doctor.

Overdose:

If you think you, or a person you are caring for, have taken too much XGEVA, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose you should try to receive that dose as soon as you can. In order for XGEVA to work properly, XGEVA needs to be given every 4 weeks. Continue to schedule your doses every four weeks.

What are possible side effects from using XGEVA?

These are not all the possible side effects you may have when taking XGEVA. If you experience any side effects not listed here, tell your healthcare professional.

- Low blood calcium (hypocalcemia)
Symptoms of low blood calcium may include muscle spasms, twitches, cramps, numbness or tingling in fingers, toes or around the mouth
- Skin infection with swollen, red area of skin that feels hot and tender and may be accompanied by fever (cellulitis)
- Sore in mouth involving gums or jaw bones (osteonecrosis of the jaw)
- Shortness of breath (dyspnea)
- Low phosphate levels in the blood (hypophosphatemia)
- Allergic reactions (eg, rash, hives, or in rare cases, swelling of the face, lips, tongue, throat, or trouble breathing)
- Unusual thigh bone fractures (atypical femoral fracture)
- Rash that may occur on the skin or sores in the mouth (lichenoid drug eruption)
- Hair loss (alopecia)
- Pain, sometimes severe, in the muscles, joints, arms, legs or back
- High calcium levels in the blood (hypercalcemia) after stopping treatment in patients who are still growing while on treatment with XGEVA
- High calcium levels in the blood (hypercalcemia) after stopping treatment in patients with giant cell tumour of the bone
- Broken bones in your spine (multiple vertebral fractures) after stopping treatment with XGEVA

Serious side effects and what to do about them			
Symptom / effect ^a	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Low calcium levels in the blood [muscle spasms, twitches, cramps, numbness or tingling in fingers, toes or around the mouth] (hypocalcemia)		√	
COMMON			
Sore in mouth involving gums or jaw bones (osteonecrosis of the jaw)		√	
UNCOMMON			
Skin infection (mainly cellulitis) leading to hospitalization		√	
High calcium levels in the blood (hypercalcemia) after stopping treatment in patients with giant cell tumour of bone		√	
Unusual thigh bone fractures (atypical femoral fracture)		√	
RARE			
Allergic reactions [e.g. rash, hives, or in rare cases, swelling of the face, lips, tongue, throat, or trouble breathing] (drug hypersensitivity)		√	
High calcium levels in the blood (hypercalcemia) after stopping treatment in patients who are still growing while on treatment with XGEVA		√	
Broken bones in your spine following discontinuation of XGEVA (multiple vertebral fracture)		√	

^a Frequency reflects all adverse events

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Keep out of the reach and sight of children.

XGEVA should be stored in the refrigerator at 2°C to 8°C in the original carton to protect it from light. Do not freeze XGEVA. Do not shake XGEVA.

XGEVA may be removed from the refrigerator and allowed to reach room temperature (up to 25°C) to make the injection more comfortable.

Once removed from the refrigerator, XGEVA must not reach temperatures above 25°C and must be used within 30 days. If not used within 30 days, XGEVA should be discarded.

Do not use XGEVA after the expiry date which is printed on the carton and label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer required.

If you want more information about XGEVA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website [www.xgeva.ca], or
- Call Amgen Canada Medical Information at 1-866-502-6436, or
- Call the Victory Program at 1-888-706-4717.

This leaflet was prepared by Amgen Canada Inc.

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