PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]Prolia® (*PRO-lee-ah*)

denosumab injection

Single-use Prefilled Syringe

Read this carefully before you start taking **PROLIA** 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 **PROLIA**.

What is PROLIA used for?

Prolia is used for the treatment

- of osteoporosis (thinning and weakening of the bone) in women after menopause who
  - have an increased risk for fractures or;
  - cannot use other osteoporosis medicines, or other osteoporosis medicines did not work well.
- to increase bone mass in men with osteoporosis at high risk for fracture.
- to increase bone mass and may reduce fractures that occur when medication to reduce testosterone levels are taken for the treatment of prostate cancer that has not spread to other parts of the body (nonmetastatic).
- to increase bone mass in women who are receiving certain treatments for breast cancer, which has not spread to other parts of the body (nonmetastatic) and at high risk of fracture.
- to increase bone mass to treat osteoporosis in both women and men at high risk for fracture related to the use of corticosteroid medicines, such as prednisone.
- to increase bone mass to prevent osteoporosis in both women and men at high risk for fracture related to starting corticosteroid medicines, such as prednisone.

What is osteoporosis?

Bone is constantly changing. There are special cells in the body called osteoclasts whose primary function is to remove bone. There is another type of cell called osteoblasts, which are bone-forming cells. In normal bone, there is a balance between the actions of these two cells. In people with osteoporosis, this balance no longer exists. Instead, the cells that remove bone work overtime, removing bone faster than new bone can be created. The result is bone that is thinner, weaker and more likely to break. Osteoporosis may occur without any pain or other symptoms. Sometimes the first symptom of osteoporosis is a fragility fracture, a broken bone that may be caused by a minor fall, or simple activities such as lifting groceries or getting out of bed. A fragility fracture can significantly increase the risk of future fractures. Aside from prescribing PROLIA, your doctor can guide you in other ways to manage your bone health.

Surgery or medicines that stop the production of estrogen or testosterone used to treat patients with breast or prostate cancer can also lead to bone loss. This may cause some bones to become weaker and break more easily.

Corticosteroids, like prednisone, can also cause thinning and weakening of the bone increasing your chance of broken bones.

How does PROLIA work?

PROLIA works differently than other osteoporosis medications. It is a RANK ligand inhibitor. RANK ligand is a protein which activates the cells that break down bone (osteoclasts). PROLIA blocks RANK ligand to stop the cells that break down bone. This action strengthens your bones by increasing bone mass and lowers the chance of breaking bones of the hip, spine, and nonspinal sites.

What are the ingredients in PROLIA?

Medicinal ingredients: denosumab.

Nonmedicinal ingredients: sorbitol, acetate, polysorbate 20, water for injection and sodium hydroxide. The prefilled syringe is not made with natural rubber latex.

PROLIA comes in the following dosage forms:

PROLIA is a liquid for injection, available in a prefilled syringe.

PROLIA is a clear, colourless to slightly yellow solution. Do not use if the solution is cloudy.

Do not use PROLIA if you:

- are allergic to denosumab or any other ingredient of PROLIA. Allergic reactions (eg, rash, hives, or in rare cases, swelling of the face, lips, tongue, throat, or trouble breathing) have been reported.
- have low calcium levels in your blood (hypocalcemia).
- are less than 18 years of age (see also **What is Prolia used for** above and **Other warnings you should know about** below).
- are pregnant or breastfeeding.
- are a woman before menopause [unless you have been diagnosed with breast cancer or are taking PROLIA for the treatment or prevention of osteoporosis related to the use of corticosteroid medicines (see also **What is Prolia used for** above and **Other warnings you should know about** below)].
- are currently taking denosumab, under the brand name XGEVA.
- do not have access to a health professional or trained injector.

Other warnings you should know about:

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

There is an increased risk of skin infection (cellulitis) with PROLIA therapy, most commonly on the leg. See a doctor urgently if you develop swollen, red, hot or painful skin, with or without fever.

You should take calcium and vitamin D supplements as recommended by your healthcare professional.

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

- Have low blood calcium.
- Cannot take daily calcium and vitamin D.
- Had parathyroid or thyroid surgery (glands located in your neck).
- Have been told you have trouble absorbing minerals in your stomach or intestines (malabsorption syndrome).
- Have kidney problems or are on kidney dialysis.
- Have ever had an allergic reaction to PROLIA.
- Plan to have dental surgery or teeth removed.
- Have a history of cancer.
- Are pregnant or could become pregnant.

PROLIA may interfere with normal bone and tooth development in fetuses, nursing babies, and children under 18 years of age. PROLIA is not indicated for use in patients under 18 years of age.

Do not take PROLIA if you are pregnant or could become pregnant as PROLIA may harm your unborn baby. Your healthcare provider should do a pregnancy test before you start treatment with PROLIA. You should use an effective method of birth control (contraception) during treatment with PROLIA and for at least 5 months after your last dose of PROLIA. If you become pregnant while taking PROLIA, stop taking PROLIA and tell your doctor right away.

Nursing mothers should not take PROLIA. It may also interfere with breastfeeding.

PROLIA may lower levels of calcium in the blood. If you are prone to low calcium levels, your doctor will monitor your blood, especially in the first few weeks after starting PROLIA. Severe low blood calcium levels may lead to hospitalization, life-threatening events, and death. Low blood calcium should be treated before receiving PROLIA. Symptoms of low blood calcium may include muscle spasms, twitches, cramps, numbness or tingling in hands, feet or around the mouth, and weakness. Some patients may not have any symptoms of low calcium. Tell your doctor if you have any of these symptoms. Tell your doctor if you have or have had severe kidney problems as this may increase your risk of getting low blood calcium.

Tell your doctor right away if you have symptoms of infection, including:

- Fever or chills
- Skin that looks red, swollen, hot or tender to touch
- Severe abdominal pain
- Frequent or urgent need to urinate or burning feeling when you urinate

Tell your doctor if you have any of the following symptoms of skin problems that do not go away or get worse:

- Redness
- Itching
- Rash
- Dry or leathery skin
- Open, crusted or peeling skin
- Blisters

After you start PROLIA:

- Take good care of your teeth and gums, and see your dentist regularly.
- If you have a history of dental problems (such as poorly fitting dentures or gum disease), see your dentist before starting PROLIA.
- Tell your dentist that you are taking PROLIA, especially if you are having dental work.

A dental condition called osteonecrosis of the jaw (ONJ) which can cause tooth and jawbone loss has been reported in patients treated with PROLIA. The risk of ONJ may increase with length of time on PROLIA. Tell your doctor and dentist immediately about any dental symptoms, including pain or unusual feeling in your teeth or gums, or any dental infections.

Some people have developed unusual fractures in their thigh bone. Contact your doctor if you experience new or unusual pain in your hip, groin, or thigh.

After your treatment with PROLIA is stopped, it is possible that broken bones in your spine may occur especially if you have a history of broken bones in the spine. Do not stop taking PROLIA without first talking with your doctor. If your PROLIA treatment is stopped, discuss other available treatment options with your doctor.

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 PROLIA:

In a drug interaction study, PROLIA (60 mg) did not interfere with the action of a drug called midazolam which is metabolized (broken down) by a certain liver enzyme called cytochrome P450 3A4. No drug interactions are expected with PROLIA and other drugs metabolised by this enzyme in women with postmenopausal osteoporosis.

You should discuss with your doctor any medications or vitamins or herbal products you are taking before using PROLIA.

How to take PROLIA:

PROLIA is administered as a single injection under the skin (subcutaneous) every 6 months. The injection can be in your upper arm, upper thigh, or abdomen. It can be given any time with or without food by a healthcare professional, by a trained injector, or a patient may self-inject if a healthcare professional determines that is appropriate.

Your prefilled syringe may be left outside the refrigerator to reach room temperature (up to 25°C) before injection. This will make the injection more comfortable. See instructions for injection.

Keep all medicines, including PROLIA, away from children.

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

Usual dose:

The usual dose of PROLIA is 60 mg administered once every 6 months. You should also take supplements of calcium and vitamin D.

Missed dose:

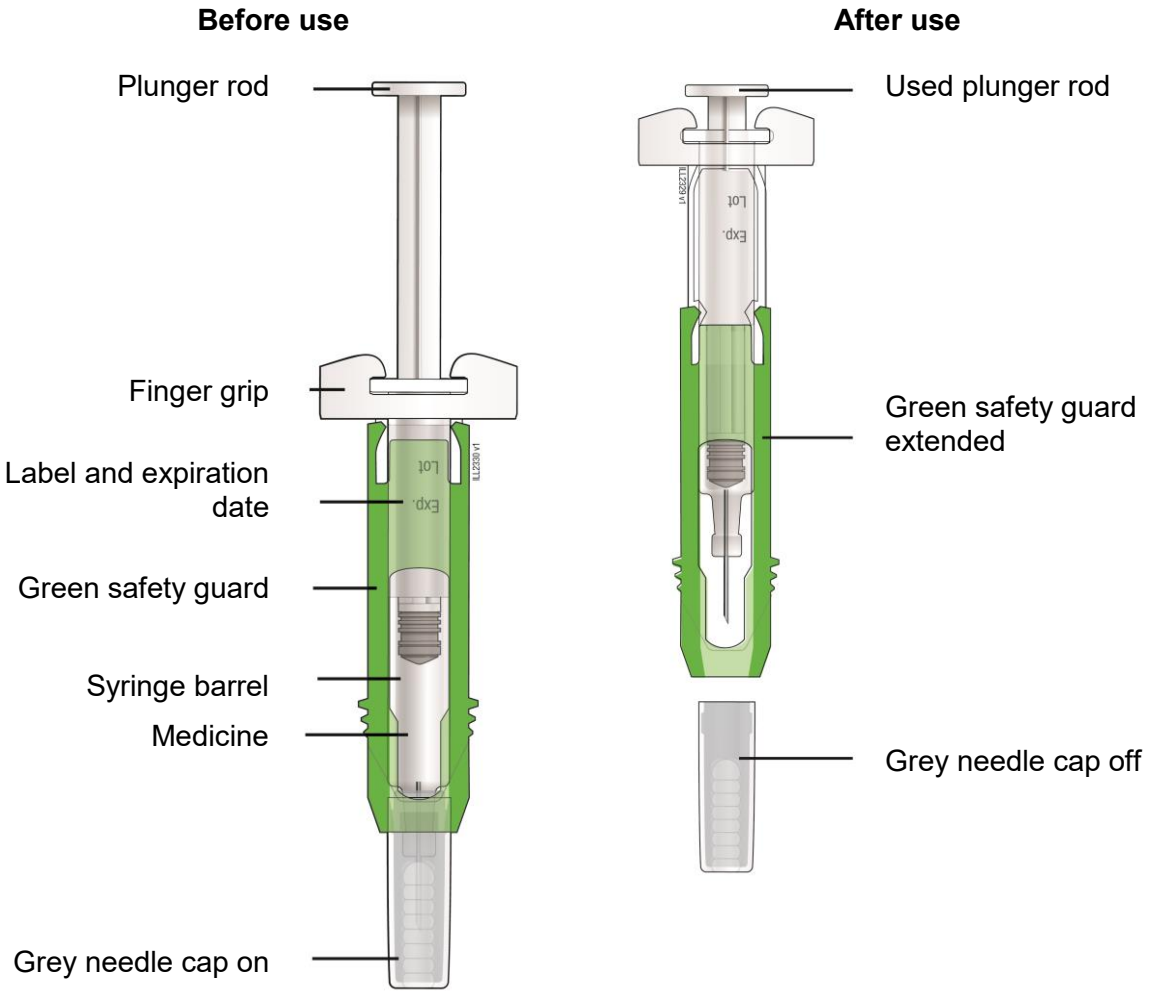
If you miss a dose you should receive your next dose as soon as convenient. Schedule your next dose 6 months from the date of your last injection.

Overdose:

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

The following instructions are for preparing and giving an injection of PROLIA using a single-use prefilled syringe with a manual needle guard:

Guide to parts



Important: The needle is covered by the grey needle cap before use.

Important:

Before you use a PROLIA prefilled syringe, read this important information:

Using the prefilled syringe

- Administration should be performed by an individual who has been trained in injection techniques. This includes patients who have been deemed appropriate by their healthcare professional to administer PROLIA.
- Make sure the name PROLIA appears on the carton and prefilled syringe label.
- Check the carton and prefilled syringe label to make sure the dose strength is 60 mg.

- Do NOT use a syringe after the expiration date on the label.
- Do NOT shake the syringe.
- Do NOT remove the grey needle cap from the syringe until you are ready to inject.
- Do NOT use the syringe if the carton is open or damaged.
- Do NOT use a syringe if it has been dropped on a hard surface. Part of the syringe may be broken even if you cannot see the break. Use a new syringe.
- Do NOT slide the green safety guard over the needle before you give the injection. This will "activate" or lock the green safety guard. Use another syringe that has not been activated and is ready to use.
- **The prefilled syringe is not made with natural rubber latex.**

Call your healthcare provider or Amgen Medical Information at 1-866-502-6436 if you have any questions.

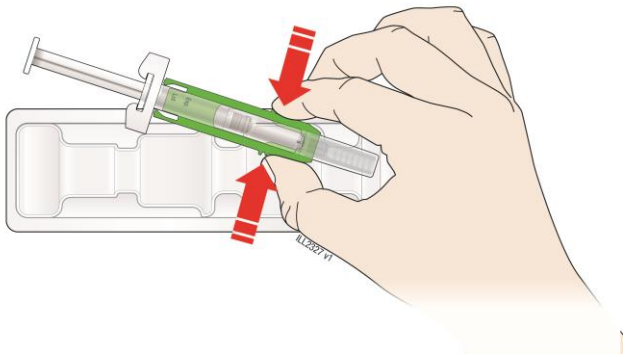
Step 1: Prepare

A. Remove the prefilled syringe carton from the refrigerator.

Remove the syringe tray from the carton. On a clean, well-lit surface, place the syringe tray at room temperature for 15-30 minutes before you give an injection.

- Do NOT use the prefilled syringe if the carton is damaged.
- Do NOT try to warm the prefilled syringe by using a heat source such as hot water or microwave.
- Do NOT leave the prefilled syringe in direct sunlight.
- Do NOT shake the prefilled syringe.

Open the tray by peeling away the cover. Grab the green safety guard to remove the prefilled syringe from the tray.

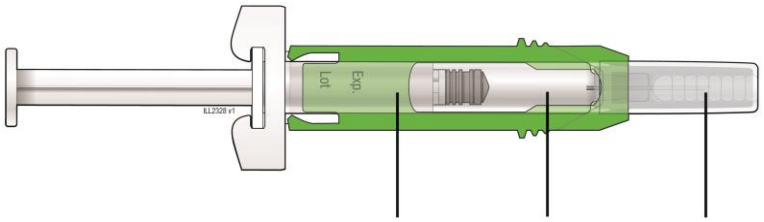


Grab Green Safety Guard

For safety reasons:

- Do NOT grab the plunger rod.
- Do NOT grab the grey needle cap.

B. Inspect the medicine and prefilled syringe.



Label and expiration date Medicine Grey needle cap

Always hold the syringe by the syringe barrel.

Make sure the medicine in the prefilled syringe is clear and colourless to pale yellow.

Do NOT use the prefilled syringe if:

- The medicine is cloudy or discoloured.
- Any part appears cracked or broken.
- The prefilled syringe has been dropped.
- The grey needle cap is missing or not securely attached.
- The expiration date printed on the label has passed.

In all cases, use a new prefilled syringe and call your healthcare professional or Amgen Medical Information at 1-866-502-6436.

C. Gather all materials needed for the injection.

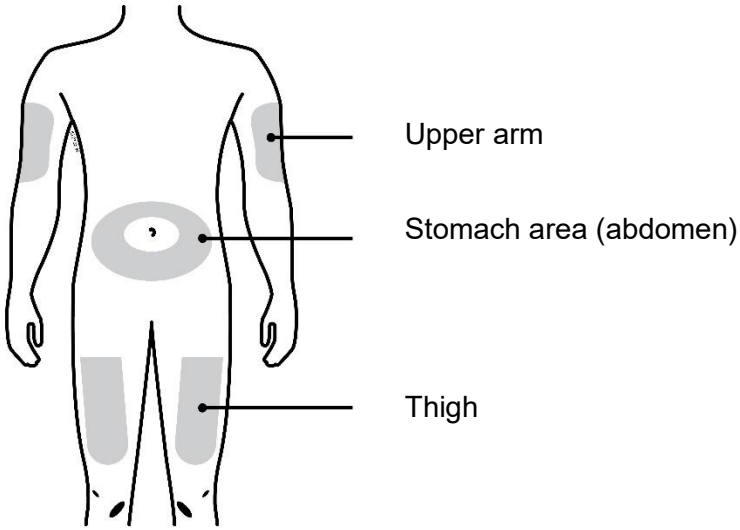
Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:

- Prefilled syringe
- Alcohol wipe
- Cotton ball or gauze pad
- Adhesive bandage
- Sharps disposal container

Step 2: Get ready

D. Prepare and clean the injection site



You can use:

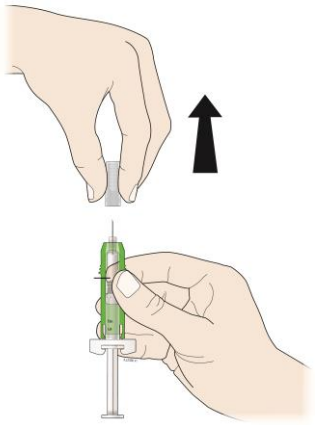
- Upper thigh
- Stomach area (abdomen), except for a 5 cm (2-inch) area right around the navel (belly button)
- Outer area of upper arm (only if someone else is giving you the injection).

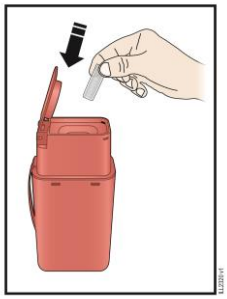
Clean the injection site with an alcohol wipe. Let the skin dry.

- Do NOT touch this area again before injecting.
- Do NOT inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

E. Hold the prefilled syringe by the syringe barrel. Carefully pull the grey needle cap straight off and away from the body.

Syringe barrel



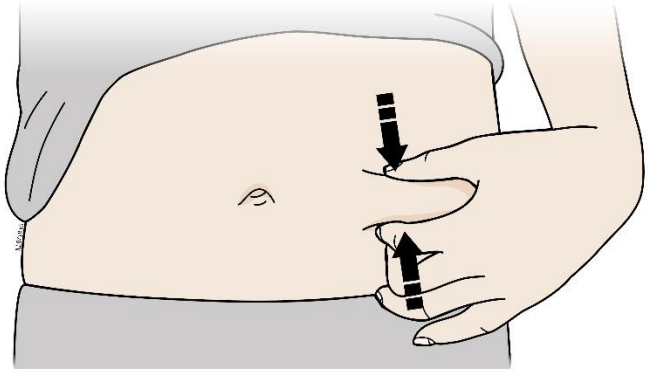


- Do NOT remove the grey needle cap from the prefilled syringe until you are ready to inject.
- Do NOT twist or bend the grey needle cap.
- Do NOT hold the prefilled syringe by the plunger rod.
- Do NOT put the grey needle cap back onto the prefilled syringe.

Important: Throw the grey needle cap into the sharps disposal container.

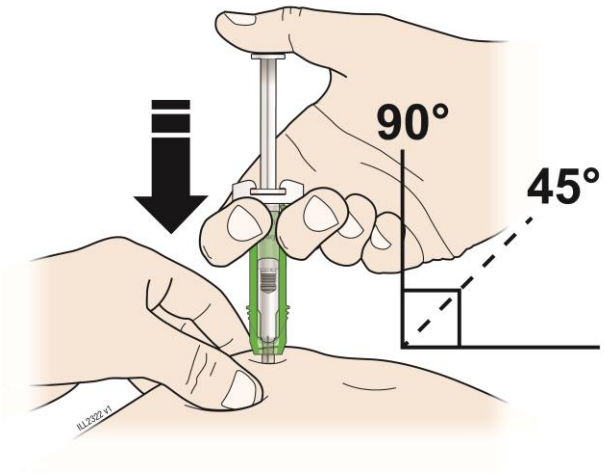
Step 3: Subcutaneous (under the skin) injection.

F. Pinch the injection site to create a firm surface.



Important: Keep skin pinched while injecting.

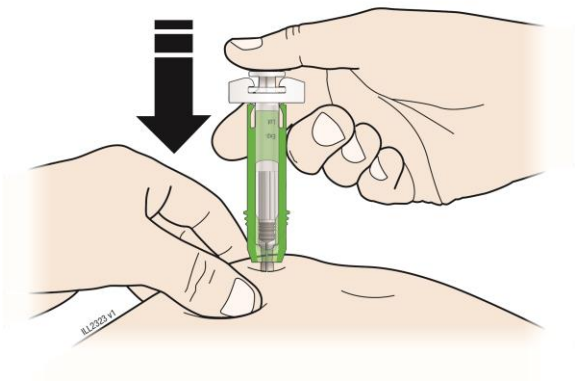
G. Hold the pinch. Insert the needle into the skin at 45 to 90 degrees.



H. Using slow and constant pressure, push the plunger rod until it reaches the bottom.

- Do NOT pull back the plunger rod while the needle is inserted.

When done, gently pull the syringe off of the skin.



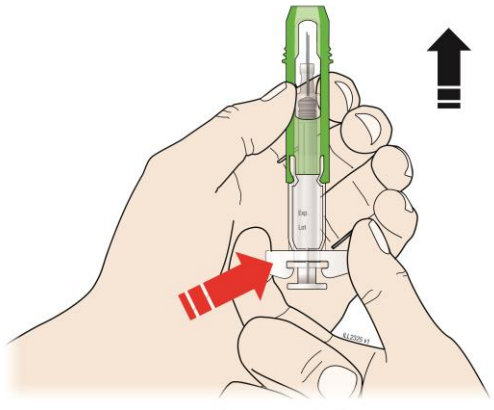
Important: When you remove the syringe, if it looks like the medicine is still in the syringe barrel, this means you have not received a full dose. Call your healthcare professional right away.

Step 4: Finish

I. 

Before you finish!

For your safety, pull the green safety guard until it clicks and covers the needle.



GRAB HERE

Once extended, the green safety guard will lock into position and will not slide back over the needle.

Keep your hands away from the needle at all times.

J. Discard (throw away) the used prefilled syringe.

- Put the used prefilled syringe in a sharps disposal container right away after use. Do NOT throw away (dispose of) the syringe in the household trash.
- If you do not have a sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes.
- Do NOT reuse the prefilled syringe.
- Do NOT recycle the prefilled syringe or sharps disposal container or throw them into household trash.

Important: Always keep the sharps disposal container out of the reach of children.

K. Examine the injection site.

If there is blood, press a cotton ball or gauze pad on the injection site. Do NOT rub the injection site. Apply an adhesive bandage if needed.

What are possible side effects from using PROLIA?

Like all medicines, PROLIA can cause side effects, although not everybody gets them.

These are not all the possible symptoms or side effects you may experience; if you are concerned about any effects you experience you should contact your healthcare professional.

Possible side effects include:

- Pain, sometimes severe, in the muscles, joints, arms, legs or back.
- 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.
- Allergic reactions (eg, rash, hives, or in rare cases, swelling of the face, lips, tongue, throat, or trouble breathing).
- Allergic reaction that can damage blood vessels mainly in the skin (eg, purple or brownish-red spots, hives or skin sores)
- Severe allergic reaction (drug reaction with eosinophilia and systemic symptoms [DRESS] syndrome) with skin rash/blisters, fever and/or increase in a type of white blood cell (eosinophils) with possible organ damage, such as liver, kidney, or lung.
- Skin condition with itching, redness and/or dryness (eczema). Injection site reactions were uncommon.
- Rash that may occur on the skin or sores in the mouth (lichenoid drug eruption).
- Hair loss (alopecia).
- Skin infection with swollen, red area of skin, that feels hot and tender and may be accompanied by fever (cellulitis).
- Common cold (runny nose or sore throat).
- Broken bones in the spine after stopping PROLIA (multiple vertebral fractures).

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON (≥ 1%, in 1 to 10% of patients)			
Skin condition with itching, redness and/or dryness (eczema)	X		
UNCOMMON (≥ 0.1%, < 1%)			
Skin infection (mainly cellulitis) leading to hospitalization, erysipelas (serious and rapid skin infection commonly on the face or legs)		X	
Bladder infection, pancreatitis (inflamed pancreas causing severe stomach pains), and ear infection		X	
Broken bones in the spine after stopping PROLIA treatment (multiple vertebral fractures)		X	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE (≥ 0.01%, < 0.1%)			
Low calcium levels in the blood (muscle spasms, twitches, cramps, numbness or tingling in hands, feet or around the mouth, and weakness)		X	
Endocarditis (inflammation of the inner lining of the heart)		X	X
Sore in mouth involving gums or jaw bones (osteonecrosis of the jaw)		X	X
Allergic reaction (feeling faint, trouble breathing/wheezing, throat tightness, swelling of face, lips or tongue, rash, hives)		X	X
Unusual thigh bone fractures (atypical femoral fracture)		X	

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.

When prescribed PROLIA, you will likely need to fill your prescription at a pharmacy. Store PROLIA in your refrigerator at 2°C to 8°C until your injection appointment with your health professional or trained injector. Do not freeze.

When removed from the refrigerator, PROLIA must be kept at room temperature (up to 25°C) in the original carton and must be used within 30 days.

Store in original carton in order to protect from light.

Do not use PROLIA 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 PROLIA:

- Talk to your healthcare professional
- Find the full product monograph, that is prepared for health 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.amgen.ca, or by calling toll free at: 1-866-50-AMGEN (1-866-502-6436) or visit www.prolia.ca.

This leaflet was prepared by Amgen Canada Inc.

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