Package leaflet: Information for the user

Prolia® ▼ 60 mg solution for injection in a pre-filled syringe
denosumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet
1. What Prolia is and what it is used for
2. What you need to know before you use Prolia
3. How to use Prolia
4. Possible side effects
5. How to store Prolia
6. Contents of the pack and other information

1. What Prolia is and what it is used for

What Prolia is and how it works

Prolia contains denosumab, a protein (monoclonal antibody) that interferes with the action of another protein, in order to treat bone loss and osteoporosis. Treatment with Prolia makes bone stronger and less likely to break.

Bone is a living tissue and is renewed all the time. Oestrogen helps keep bones healthy. After the menopause, oestrogen level drops which may cause bones to become thin and fragile. This can eventually lead to a condition called osteoporosis. Many women with osteoporosis have no symptoms, but they are still at risk of breaking bones, especially in the spine, hips and wrists.

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

What Prolia is used for

Prolia is used to treat:
• osteoporosis in women after the menopause (postmenopausal), reducing the risk of spinal, non-spinal and hip fractures.
• bone loss that results from a reduction in hormone (testosterone) level caused by surgery or treatment with medicines in patients with prostate cancer.

2. What you need to know before you use Prolia

Do not use Prolia

• if you have low calcium levels in the blood (hypocalcaemia).
• if you are allergic to denosumab or any of the other ingredients of this medicine (listed in section 6).
**Warnings and precautions**

Talk to your doctor or pharmacist before using Prolia

Please tell your doctor immediately if you develop a swollen, red area of skin, most commonly in the lower leg, that feels hot and tender (cellulitis), and possibly with symptoms of fever while being on treatment with Prolia.

Please tell your doctor if you have an allergy to latex (the needle cover on the pre-filled syringe contains a derivative of latex).

Tell your doctor if you have or have ever had severe kidney problems, kidney failure or have needed dialysis, which may increase your risk of getting low blood calcium if you do not take calcium supplements.

You should also take calcium and vitamin D supplements while being on treatment with Prolia. Your doctor will discuss this with you.

A dental examination should be considered before you start treatment with Prolia if you have cancer, are undergoing chemotherapy or radiotherapy, are taking steroids, do not receive routine dental care or have gum disease.

If you are under dental treatment or will undergo dental surgery, tell your dentist that you are being treated with Prolia.

It is important to maintain good oral hygiene when being on treatment with Prolia.

**Children and adolescents**

Prolia is not recommended for children and adolescents under 18 years of age. The use of Prolia in children and adolescents has not been studied.

**Other medicines and Prolia**

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. It is especially important that you tell your doctor if you are being treated with another medicine containing denosumab.

You should not take Prolia together with another medicine containing denosumab.

**Pregnancy and breast-feeding**

Prolia has not been tested in pregnant women. It is important to tell your doctor if you are pregnant; think you may be pregnant; or plan to get pregnant. Prolia is not recommended for use if you are pregnant.

If you become pregnant during Prolia treatment, please inform your doctor. You may be encouraged to enrol in Amgen’s Pregnancy Surveillance programme. Local representative contact details are provided in section 6 of this leaflet.

It is not known whether Prolia is excreted in breast milk. It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Prolia, considering the benefit of breast-feeding to the baby and the benefit of Prolia to the mother.
If you are nursing during Prolia treatment, please inform your doctor. You may be encouraged to enrol in Amgen’s Lactation Surveillance Program. Local representative contact details are provided in section 6 of this leaflet.

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**

Prolia has no or negligible influence on the ability to drive and use machines.

**Prolia contains sorbitol (E420)**

If you have been told by your doctor that you have an intolerance to some sugars (sorbitol E420), contact your doctor before taking this medicinal product.

**If you are on a controlled sodium diet**

This medicinal product contains less than 1 mmol sodium (23 mg) per 60 mg, i.e. essentially ‘sodium-free’.

3. **How to use Prolia**

The recommended dose is one pre-filled syringe of 60 mg administered once every 6 months, as a single injection under the skin (subcutaneous). The best places to inject are the top of your thighs and the abdomen. Your carer can also use the outer area of your upper arm. Each pack of Prolia contains a reminder card with stickers that can be removed from the carton. Use the peel-off stickers to mark the next injection date on your personal calendar and/or the reminder card to keep a record of the next injection date.

You should also take calcium and vitamin D supplements while being on treatment with Prolia. Your doctor will discuss this with you.

Your doctor may decide that it is best for you or a carer to inject Prolia. Your doctor or healthcare provider will show you or your carer how to use Prolia. For instructions on how to inject Prolia, please read the section at the end of this leaflet.

**If you forget to use Prolia**

If a dose of Prolia is missed, the injection should be administered as soon as possible. Thereafter, injections should be scheduled every 6 months from the date of the last injection.

**If you stop using Prolia**

To get the most benefit from your treatment, it is important to use Prolia for as long as your doctor prescribes it for you. Please talk to your doctor before you consider stopping the treatment.

4. **Possible side effects**

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

Uncommonly, patients receiving Prolia may develop skin infections (predominantly cellulitis). Please tell your doctor immediately if you develop any of these symptoms while being on treatment with Prolia: swollen, red area of skin, most commonly in the lower leg, that feels hot and tender, and possibly with symptoms of fever.
Common side effects (affects 1 to 10 users in 100):

- painful urination, frequent urination, blood in the urine, inability to hold your urine,
- upper respiratory tract infection,
- pain, tingling or numbness that moves down your leg (sciatica),
- cloudy area in the lens of the eye (cataracts),
- constipation,
- rash,
- arm or leg pain (pain in extremity).

Uncommon side effects (affects 1 to 10 users in 1,000):

- fever, vomiting and abdominal pain or discomfort (diverticulitis),
- ear infection,
- skin condition with itching, redness and/or dryness (eczema).

Rare side effects (affects 1 to 10 users in 10,000):

- persistent pain and/or non-healing sores of the mouth or jaw,
- spasms, twitches, or cramps in your muscles, and/or numbness or tingling in your fingers, toes or around your mouth. These could be signs that you have low calcium levels in the blood (hypocalcaemia),
- allergic reactions (e.g. swelling of the face, lips, tongue or other parts of the body; rash, itching or hives on the skin).

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Prolia

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Store in the original carton in order to protect from light.
Do not shake excessively.

Your pre-filled syringe may be left outside the refrigerator to reach room temperature (up to 25°C) before injection. This will make the injection more comfortable. Once your syringe has been left to reach room temperature (up to 25°C), it must be used within 30 days.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Prolia contains

- The active substance is denosumab. Each 1 ml pre-filled syringe contains 60 mg of denosumab (60 mg/ml).
The other ingredients are acetic acid, glacial, sodium hydroxide, sorbitol (E420), polysorbate 20 and water for injections.

What Prolia looks like and contents of the pack

Prolia is a clear, colourless to slightly yellow solution for injection provided in a ready to use pre-filled syringe.

Each pack contains one pre-filled syringe with a needle guard.
Each pack contains one pre-filled syringe.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Manufacturer:
Amgen Technology Ireland (ADL)
Pottery Road
Dun Laoghaire
Co Dublin
Ireland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

Ireland
Amgen Limited
United Kingdom
Tel: +44 (0)1223 420305

United Kingdom
Amgen Limited
Tel: +44 (0)1223 420305

This leaflet was last revised in November 2012.

Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu/

Instructions for injecting with the Prolia pre-filled syringe with an automatic needle guard

This section contains information on how to use the Prolia pre-filled syringe. It is important that you or your carer do not give the injection unless training from your doctor or healthcare provider has been received. Always wash your hands before every injection. If you have questions about how to inject, please ask your doctor or healthcare provider for assistance.
Pre-filled syringe with clear needle guard

Use if the clear needle guard appears as shown below:

Do not use if the clear needle guard appears to be activated (spring is extended).

Before you begin

Read all instructions thoroughly before using the pre-filled syringe.

To reduce the risk of accidental needle sticks to users, each pre-filled syringe comes with a clear needle guard that is automatically activated to cover the needle after complete delivery of the pre-filled syringe content.

Do not attempt to activate the pre-filled syringe clear needle guard prior to injection.

Do not touch the needle guard tabs.
Do not use the pre-filled syringe if the grey needle cap has been removed or the clear needle guard has been activated (covering the needle).

How do you or the person injecting you use the Prolia pre-filled syringe?

Your doctor has prescribed a Prolia pre-filled syringe for injection into the tissue just under the skin (subcutaneous). You must inject the entire content (1 ml) of the Prolia pre-filled syringe and it should be injected once every 6 months as instructed by your doctor or healthcare provider.

Equipment:

To give an injection, you will need:
- one Prolia pre-filled syringe; and
- alcohol wipes or similar.

Before giving the injection

1. Remove the pre-filled syringe from the refrigerator. To remove the pre-filled syringe from the pack, grasp by the middle of the clear needle guard.

![Correct]

Do not pick up the pre-filled syringe by the plunger rod, grey needle cap or needle guard tabs. This could damage the device or activate the clear needle guard.

2. The pre-filled syringe may be left outside the refrigerator to reach room temperature. This will make the injection more comfortable.

3. Please note the following directions:
   a. Do not warm the pre-filled syringe in hot water or in the microwave.
   b. Do not leave the pre-filled syringe exposed to direct sunlight.
   c. Do not pick up the pre-filled syringe by the plunger rod, grey needle cap or needle guard tabs.
   d. Do not shake the pre-filled syringe excessively.
   e. Do not remove the grey needle cap from the pre-filled syringe until you are ready to inject.
   f. Do not attempt to activate the pre-filled syringe prior to injection.
   g. Do not attempt to remove the clear needle guard from the pre-filled syringe.

   Keep pre-filled syringes out of the sight and reach of children.

4. Check the following before continuing:
   a. Expiry date on the pre-filled syringe label (EXP). Do not use it if the date has passed the last day of the month shown.
b. **The appearance** of Prolia. It must be a clear, colourless to slightly yellow liquid. If it contains particles or is cloudy or discoloured, you must not use it.

c. You may notice a small bubble in the pre-filled syringe. You do not have to remove the air bubble before injecting. Injecting the liquid with the air bubble is harmless.

5. **Wash your hands thoroughly.**

6. **Put all of the equipment you need within reach** on a comfortable, well-lit and clean surface.

Where should you give the injection?

The best places to inject are the top of your thighs and the abdomen. Your carer can also use the outer area of your upper arms.

How do you give the injection?

1. Clean your skin by using an alcohol wipe.

2. To avoid bending the needle, carefully pull the grey needle cap from the needle **straight off**. **Do not** touch the needle or push the plunger.

3. **Pinch (without squeezing) the skin** using your thumb and forefinger. **Insert the needle into the skin as shown by your doctor or healthcare provider.**

4. Push the plunger with a slow constant pressure, always keeping the skin pinched.

   Push the plunger all the way down as far as it will go to inject all the liquid. The clear needle guard will not activate unless you empty the pre-filled syringe.
5. While the plunger is still pressed all the way down, remove the needle from the skin, then release the plunger and allow the syringe to move up until the entire needle is covered by the clear needle guard. If the needle guard is not activated, an incomplete injection may have occurred.

Call your doctor or healthcare provider if you think you have not received the full dose.

**Do not** put the grey needle cap back on the needle.

6. If you notice a spot of blood, you may gently dab with a cotton ball or tissue. Do not rub the injection site. If needed, you may cover the injection site with a plaster.

**Do not** use any Prolia that is left in the syringe.

**Remember:** Only use each pre-filled syringe for one injection. If you have any problems, please ask your doctor or healthcare provider for help and advice.

**Disposing of used syringes**

- **Do not put the grey needle cap back on used syringes.**
- Keep used syringes out of the reach and sight of children.
- **The used syringe should be disposed** of in accordance with local requirements. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.
Instructions for injecting with the Prolia pre-filled syringe

This section contains information on how to use the Prolia pre-filled syringe. **It is important that you or your carer do not give the injection unless training from your doctor or healthcare provider has been received.** Always wash your hands before every injection. If you have questions about how to inject, please ask your doctor or healthcare provider for assistance.

Before you begin

Read all instructions thoroughly before using the pre-filled syringe.

**DO NOT** use the pre-filled syringe if the needle cover has been removed.

How do you use the Prolia pre-filled syringe?

Your doctor has prescribed a Prolia pre-filled syringe for injection into the tissue just under the skin (subcutaneous). You must inject the entire content (1 ml) of the Prolia pre-filled syringe and it should be injected once every 6 months as instructed by your doctor.

Equipment:

To give an injection, you will need:

1. A new Prolia pre-filled syringe; and
2. Alcohol wipes or similar.

What to do before you give a subcutaneous injection of Prolia

1. **Remove the pre-filled syringe from the refrigerator.**
   **DO NOT** pick up the pre-filled syringe by the plunger or needle cover. This could damage the device.

2. The pre-filled syringe may be left outside the refrigerator to reach room temperature. This will make the injection more comfortable.
   **DO NOT** warm it in any other way, for example, in a microwave or in hot water.
   **DO NOT** leave the syringe exposed to direct sunlight.

3. **DO NOT** shake the pre-filled syringe excessively.

4. **DO NOT** remove the needle cover from the pre-filled syringe until you are ready to inject.

5. Check the expiry date on the pre-filled syringe label (EXP).
   **DO NOT** use it if the date has passed the last day of the month shown.

6. Check the appearance of Prolia. It must be a clear, colourless to slightly yellow solution. The solution should not be injected if it contains particles or if it is discoloured or cloudy.

7. Find a comfortable, well-lit, clean surface and put all the equipment within reach.

8. Wash your hands thoroughly.
Where should you give the injection?
The best places to inject are the top of your thighs and the abdomen. Your carer can also use the outer area of your upper arms.

How do you give the injection?

1. Disinfect the skin by using an alcohol wipe.

2. To avoid bending the needle, gently pull the cover from the needle straight off without twisting, as shown in pictures 1 and 2. **DO NOT** touch the needle or push the plunger.

3. You may notice a small air bubble in the pre-filled syringe. You do not have to remove the air bubble before injecting. Injecting the solution with the air bubble is harmless.

4. Pinch (without squeezing) the skin between your thumb and forefinger. Put the needle fully into the skin as shown by your doctor or healthcare provider.

5. Push the plunger with a **slow** constant pressure, always keeping the skin pinched. Push the plunger all the way down as far as it will go to inject all the solution.

6. Remove the needle and let go of the skin.

7. If you notice a spot of blood you may gently dab it away with a cotton ball or tissue. Do not rub the injection site. If needed, you may cover the injection site with a plaster.

8. Only use each pre-filled syringe for one injection. **DO NOT** use any Prolia that is left in the syringe.

**Remember:** if you have any problems, please ask your doctor or healthcare provider for help and advice.

Disposing of used syringes

- **DO NOT** put the cover back on used needles.
- Keep used syringes out of the reach and sight of children.
- The used syringe should be disposed of in accordance with local requirements. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.