prolia® (denosumab) injection

For women with postmenopausal osteoporosis at high risk for fracture

Help strengthen and protect your bones from the risk of fracture

Indication

Prolia® is a prescription medicine used to treat osteoporosis in women after menopause who are at high risk for fracture or cannot use another osteoporosis medicine or other osteoporosis medicines did not work well.

Important Safety Information

What is the most important information I should know about Prolia?

If you receive Prolia, you should not receive XGEVA® (denosumab). Prolia contains the same medicine as XGEVA.

Please see additional Important Safety Information on page 8.

Prolia can cause serious side effects (including):

Increased risk of severe low calcium levels in your blood (hypocalcemia). Prolia may lower the calcium levels in your blood. If you have low blood calcium before you start receiving Prolia, it may get worse during treatment. Your low blood calcium must be treated before you receive Prolia. Talk to your doctor before starting Prolia. Your doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you take Prolia. Take calcium and vitamin D as your doctor tells you to.

If you have advanced chronic kidney disease (may or may not be on kidney dialysis), Prolia may increase your risk for severe low calcium levels in your blood, which could result in hospitalization, life-threatening events and death. A mineral and bone disorder associated with kidney disease called chronic kidney disease-mineral bone disorder (CKD-MBD) may increase your risk for severe low calcium levels in blood. Before you start Prolia and during treatment, your doctor may need to do certain blood tests to check for CKD-MBD.

Postmenopausal osteoporosis INCREASES YOUR RISK for a fracture

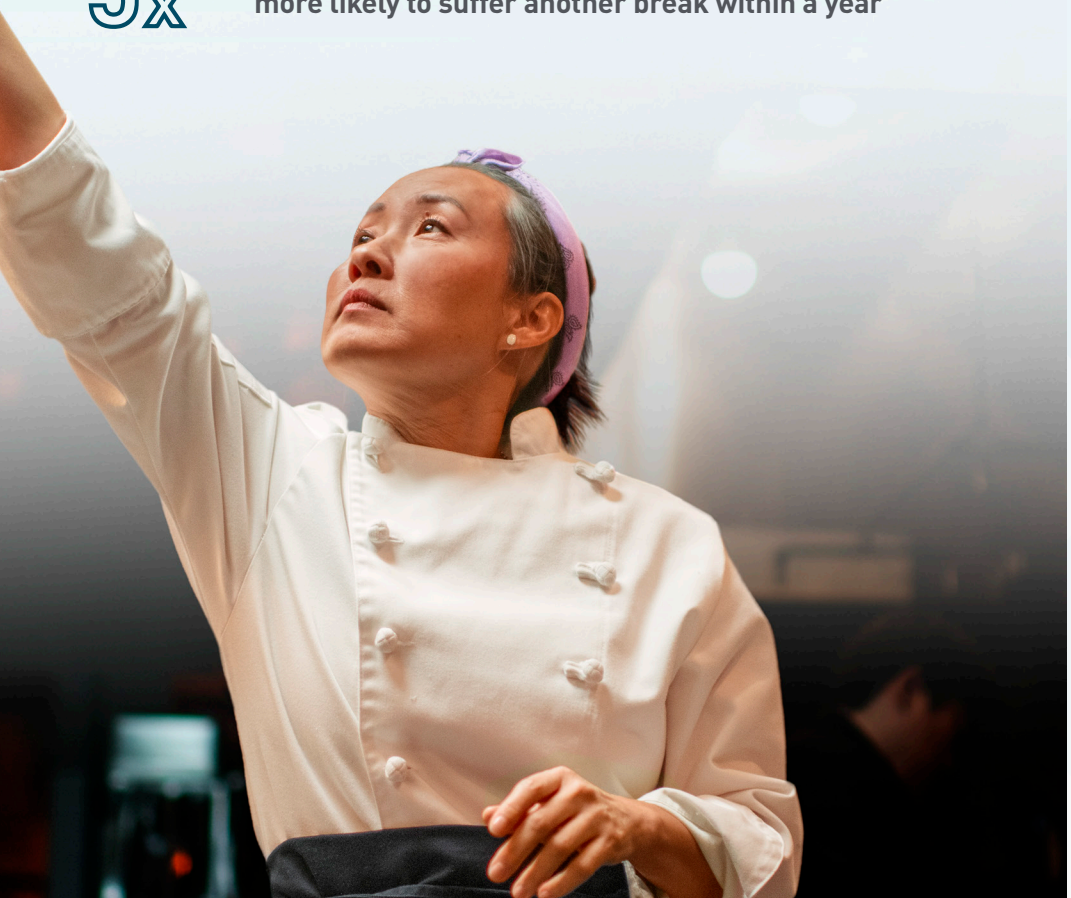
After menopause, **your body loses more bone than it replaces**, leaving bones brittle and at greater risk for fracture

A broken bone in postmenopausal women is a warning sign of osteoporosis. Be sure to **talk to your doctor if you've broken a bone after menopause**

2 out of 3 women with postmenopausal osteoporosis at high risk for fracture **will break a bone in their lifetime**

5x

After an osteoporosis-related bone break, **you're 5x more likely to suffer another break within a year**



Prolia® reduces the risk of fracture—

prolia® (denosumab) injection

Postmenopausal osteoporosis means your bones are more at risk of fracture—and breaking a bone could have potentially devastating consequences. In a 3-year clinical trial, Prolia reduced the risk of fracture at the spine, hip, and other bones. Ask your doctor how Prolia can help you.

Read on to see how Prolia can help strengthen and protect your bones

- **The impact of postmenopausal osteoporosis**
- **Key facts about Prolia**
- **Real-world evidence: Prolia vs alendronate (Fosamax)**
- **More data on the effectiveness of Prolia**

Important Safety Information (continued)

Most people with low blood calcium levels do not have symptoms, but some people may have symptoms. 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 your fingers, toes, or around your mouth

Prolia can cause serious side effects (including):

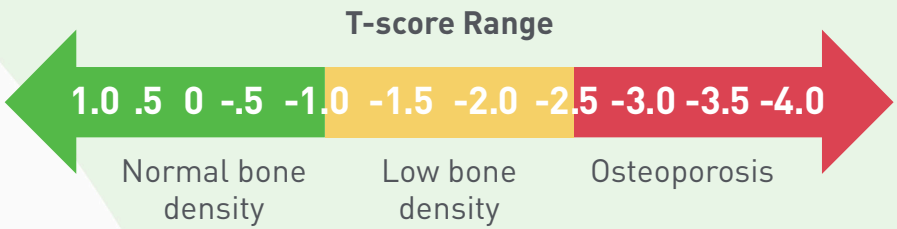
Possible serious side effects include serious allergic reactions, low blood calcium, severe jaw bone problems, unusual thigh bone fractures, increased risk of broken bones, including broken bones in the spine after stopping, skipping or delaying Prolia, serious infections, skin problems, severe bone, joint or muscle pain.

Please see additional Important Safety Information on page 8.

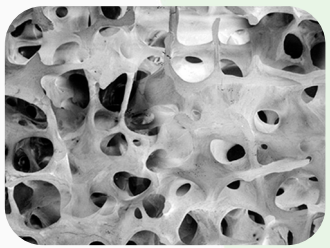
Bone density is an IMPORTANT FACTOR in your bone health

The bone mineral density (BMD) test is a way to measure your bone density by providing a T-score. **T-score is a measure of bone density,** which helps determine the severity of osteoporosis and **your risk for fracture.**

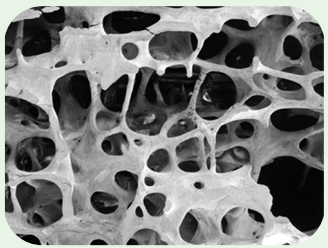
If you have been diagnosed with postmenopausal osteoporosis, your doctor may recommend a bone density scan **every 1 to 2 years** to monitor your progress on treatment.



A bone density T-score of -2.5 or lower is defined as osteoporosis. The lower the score, the greater your risk of fracture.



Normal bone
Bone density T-score of -1.0 and above



Bone with osteoporosis
Bone density T-score of -2.5 or lower

Bone images courtesy of David W. Dempster, PhD, 2000. Reproduced with permission.

Are you at risk of BREAKING A BONE?

If you have two or more of the below risk factors, you are at high risk of breaking a bone.

- ☐ T-score less than or equal to -2.5
- ☐ Low body weight
- ☐ Long-term steroid use such as prednisone
- ☐ Parent suffered hip fracture
- ☐ Rheumatoid arthritis
- ☐ Age 65 or older
- ☐ Previous fracture
- ☐ Excessive alcohol ≥3 drinks/day
- ☐ Cigarette smoking
- ☐ Diabetes

GET TO KNOW THE 1-2-3's of Prolia®

1 shot every 6 months can help strengthen and protect your bones

You should take calcium and vitamin D as directed by your doctor while you receive Prolia.

2 important benefits of Prolia:

helps reduce fracture risk

helps strengthen bones

3 years on Prolia reduced the risk of new spine fractures in women by 68%

In a 3-year study, **women not treated with Prolia had more new spine fractures (7.2%) compared to women treated with Prolia (2.3%)**. Study consisted of 7393 patients who received either Prolia or a placebo (a treatment containing no medicine). All patients received calcium and vitamin D.

In the same study, Prolia also significantly increased bone mineral density (BMD) compared to placebo.

Important Safety Information

After your treatment with Prolia is stopped, or if you skip or delay taking a dose, your risk for breaking bones, including bones in your spine, is increased. Do not stop, skip or delay taking Prolia without first talking with your doctor.

Please see additional Important Safety Information on page 8.

There are two kinds of scientific studies that help us learn about medicine:
CLINICAL TRIALS AND REAL-WORLD STUDIES

WHAT IS A CLINICAL TRIAL?

Clinical trials help establish a medicine's safety (side effects) and efficacy (how well that medicine works) in carefully controlled settings. Clinical trials may not represent what happens in real-world medical care or in the broader population living with the same disease.

Prolia® 3-Year Fracture Clinical Trial

In the Prolia 3-Year fracture trial, women taking Prolia for 3 years **reduced their risk of new spine fractures by 68%**. In this study of 7,393 patients, women not treated with Prolia had more new spine fractures (7.2%) compared to women treated with Prolia (2.3%).

WHAT IS A REAL-WORLD STUDY?

After FDA approval, patients begin using the medication as part of their routine medical care. Researchers gather evidence from real-world situations, which differ from carefully controlled clinical trials. This evidence is valuable for gaining a broader perspective on how the medication performs outside of a clinical trial. Evidence from a real-world study is meant to further our understanding of a medication, but is not meant to replace clinical trials.

Evidence from a real-world Prolia study

In the largest real-world study of postmenopausal women with osteoporosis, the rate of fractures in women taking Prolia was compared to the rate of fractures in women taking alendronate (commonly known as Fosamax). Information about fractures in these women was collected from January 2012-December 2019.

EVIDENCE FROM A REAL-WORLD STUDY

Compared to alendronate (Fosamax), Prolia lowered the overall risk of Major Osteoporotic Fracture by

39%

The overall risk of major osteoporotic fracture was 10.5% for women taking Prolia compared to 17.2% for women who took alendronate. Major Osteoporotic Fracture includes fractures such as the hip, spine, and arm bones.

Important Safety Information

The most common side effects of Prolia® are back pain, pain in your arms and legs, high cholesterol, muscle pain, and bladder infection.

Please see additional Important Safety Information on page 8.

For women with postmenopausal osteoporosis at high risk for fracture whose osteoporosis medication is not working well

More clinical trial data showing Prolia® IMPROVES BONE DENSITY

A 1-year study of over 500 women with postmenopausal osteoporosis found that those who switched from alendronate to **Prolia showed a significant increase in bone mineral density (BMD) at the hip and the lumbar spine** compared to women who stayed on alendronate, a commonly prescribed bisphosphonate (such as Fosamax).

Compared to those who stayed on alendronate, women who switched to Prolia had greater improvement in:

+0.85% increase vs alendronate

TOTAL HIP BMD

+1.18% increase vs alendronate

SPINE BMD

This study only evaluated bone mineral density. These results do not imply fracture risk reduction.

Important Safety Information

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BONE MATTERS®— the support you've been looking for

Once on treatment with Prolia, the Bone Matters support program can offer you resources to help strengthen and protect your bones. Keep your treatment on track by joining the Bone Matters program to access:

+ Bone-strengthening exercises
+ Calcium-rich recipes
+ Courtesy injection scheduling reminders

SIGN UP TO HELP YOU STAY ON TRACK WITH YOUR TREATMENT.
VISIT PROLIA.COM/SIGNUP OR CALL 877-4-PROLIA (877-477-6542)

Talk to your doctor about POTENTIAL BENEFITS VS POTENTIAL RISKS OF TREATMENT with Prolia®

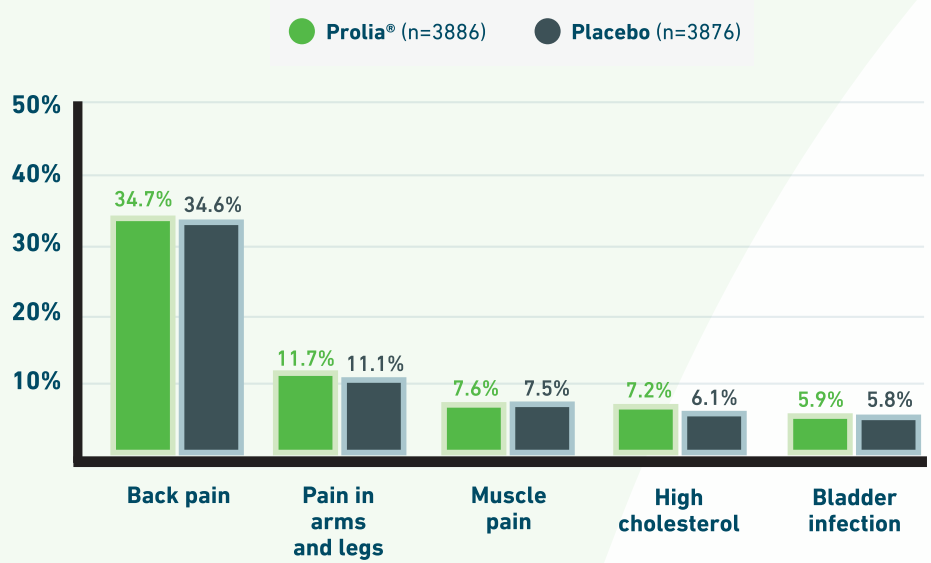
When starting a new treatment, it's always important to understand possible side effects. In the case of osteoporosis, it's also important to understand that not treating it could result in a higher risk of fracture. To find out if Prolia is right for you, discuss with your doctor the risks of side effects and the risks of not treating your osteoporosis.

"Since I've started on Prolia I feel like I've finally started to take control of my postmenopausal osteoporosis. Prolia has helped strengthen my bones, and I plan to stick with it."

Carole,
taking Prolia since 2015
Individual results may vary.

The most common SIDE EFFECTS OF PROLIA (greater than 5% and more common than placebo)

A 3-year clinical study tested the safety of Prolia in over 7700 women with postmenopausal osteoporosis aged 60 to 90 years. Approximately half of the women took Prolia, while the other half were untreated (given a placebo injection). **Below are the most common side effects of Prolia (greater than 5% and more common than placebo)** seen in this study.



These are not all of the possible side effects of Prolia.

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Indication

Prolia® (denosumab) is a prescription medicine used to treat osteoporosis in women after menopause who are at high risk for fracture or cannot use another osteoporosis medicine or other osteoporosis medicines did not work well.

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What is the most important information I should know about Prolia?

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Prolia® can cause serious side effects (including):

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If you have advanced chronic kidney disease (may or may not be on kidney dialysis), Prolia may increase your risk for severe low calcium levels in your blood, which could result in hospitalization, life-threatening events and death. A mineral and bone disorder associated with kidney disease called chronic kidney disease-mineral bone disorder (CKD-MBD) may increase your risk for severe low calcium levels in blood. Before you start Prolia and during treatment, your doctor may need to do certain blood tests to check for CKD-MBD.

Most people with low blood calcium levels do not have symptoms, but some people may have symptoms. Call your doctor right away if you have symptoms of low blood calcium such as:

- o spasms, twitches, or cramps in your muscles
- o numbness or tingling in your fingers, toes, or around your mouth

Serious allergic reactions have happened in people who take Prolia. 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 your face, lips, or tongue; rash; itching; or hives.

Severe jaw bone problems (osteonecrosis) may occur. Your doctor should examine your mouth before you start Prolia and may tell you to see your dentist. It is important for you to practice good mouth care during treatment with Prolia.

Unusual thigh bone fractures. Some people have developed unusual fractures in their thigh bone. Symptoms of a fracture include new or unusual pain in your hip, groin, or thigh.

Increased risk of broken bones, including broken bones in the spine, after stopping, skipping or delaying Prolia. Talk with your doctor before starting Prolia treatment. After your treatment with Prolia is stopped, or if you skip or delay taking a dose, your risk for breaking bones, including bones in your spine, is increased. Your risk for having more than 1 broken bone in your spine is increased if you have already had a broken bone in your spine. Do not stop, skip or delay taking Prolia without first talking with your doctor. If your Prolia treatment is stopped, talk to your doctor about other medicine that you can take.

Serious infections in your skin, lower stomach area (abdomen), bladder, or ear may happen. Inflammation of the inner lining of the heart (endocarditis) due to an infection may also happen more often in people who take Prolia. You may need to go to the hospital for treatment.

Prolia is a medicine that may affect the ability of your body to fight infections. People who have weakened immune systems or take medicines that affect the immune system may have an increased risk for developing serious infections.

Skin problems such as inflammation of your skin (dermatitis), rash, and eczema have been reported.

Bone, joint, or muscle pain. Some people who take Prolia develop severe bone, joint, or muscle pain.

Do not take Prolia if you: have low blood calcium; or are pregnant or plan to become pregnant, as Prolia may harm your unborn baby; or are allergic to denosumab or any ingredients in Prolia.

Before taking Prolia, tell your doctor about all of your medical conditions, including if you:

- Take the medicine XGEVA (denosumab)
- 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
- Are taking medicine that can lower your blood calcium levels
- Plan to have dental surgery or teeth removed
- Are pregnant or plan to become pregnant

  Females who are able to become pregnant:

  - o Your healthcare provider should do a pregnancy test before you start treatment with Prolia.
  - o 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.
  - o Tell your doctor right away if you become pregnant while taking Prolia.
- Are breast-feeding or plan to breast-feed

What are the possible side effects of Prolia?

It is not known if the use of Prolia over a long period of time may cause slow healing of broken bones. The most common side effects of Prolia are back pain, pain in your arms and legs, high cholesterol, muscle pain, and bladder infection.

These are not all the possible side effects of Prolia. 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 Prolia full Prescribing Information, including Medication Guide.

For women with postmenopausal osteoporosis at high risk for fracture

Talk to your doctor about strengthening your bones with Prolia®

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FDA-APPROVED FOR OVER

13

YEARS

OVER

18

MILLION WOMEN HAVE BEEN TREATED
WITH PROLIA® WORLDWIDE*

*Estimates of patients treated reflect global data since launch (June 2010–Sept 2022; US=approximately 26% of data). Patient counts are based on syringes sold and IQVIA prescription data.

START THE CONVERSATION

Click to get a downloadable Doctor Discussion Guide or visit Prolia.com/Guide

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