



# SIGMA sums it up:

Answers to questions about osteoporosis and denosumab therapy



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## Who is SIGMA?



SIGMA (Special Interest Group on Menopause and Aging) is the Canadian Menopause Society. We are a multidisciplinary group of family physicians, specialists and healthcare professionals who are interested in menopausal health. Our mission is to advance the health of women at and beyond the menopause transition through education initiatives and knowledge transfer.

SIGMA is a hub of menopausal knowledge with the ability to transfer information on a wide range of issues. It networks with menopause clinic(s) and menopause practitioners across Canada to share knowledge; to act as advocate(s) for menopausal health in Canada; and to provide up-to-date knowledge to our patients. SIGMA strives to have one voice in Canada that speaks for the women in Canada.

SIGMA is linked internationally to the North American Menopause Society (NAMS) and to the International Menopause Society (IMS). SIGMA members also liaise with the Society of Obstetricians and Gynecologists of Canada (SOGC), the Canadian College of Family Practice (CCFP), Osteoporosis Canada (OC) and the Federation of Medical Women of Canada (FMWC).

For references and additional information, please visit us at [www.sigmamenopause.com](http://www.sigmamenopause.com).



### Question 1: What is osteoporosis?

Osteoporosis is a condition that affects bone strength. Bones become thin and weak, increasing the chances of a broken bone (fracture). Some of the most common breaks due to osteoporosis include fractures of the hip, spine, arm, wrist, pelvis and rib. While most people can maintain bone health through a healthy diet, and by taking calcium and vitamin D supplements, individuals who have higher risk factors for breaking bones may benefit from additional medication. Anti-osteoporosis medications (together with calcium and vitamin D supplements) can reduce the risk of bone breakage by up to 70%.



### Question 2: Why is it important to treat osteoporosis with medications?

Weak or fragile bones that result in a broken bone can significantly affect the independence and quality of life for individuals with osteoporosis, especially the elderly. Fortunately, there are methods for predicting if someone has a higher risk of breaking a bone. By examining bone density, previous history of bone breakages and other risk factors using an innovative tool developed by the World Health Organization called a FRAX, we can estimate your 10-year risk of breaking a bone, and the need for preventive medication. Osteoporosis medication may be recommended for people who have osteoporosis (bone mineral density of less than -2.5), a previous "osteoporosis" fracture (hip, spine, arm, wrist, pelvis and rib) or a higher fracture risk.

### Question 3: What is Prolia (denosumab) and what is it used for?

Denosumab, which is the active ingredient in Prolia, is an antibody that slows down the weakening of bones. Denosumab targets the protein (called RANK Ligand) in the body that signals the cells (called osteoclasts) that break down bone, preventing these cells from forming and being activated. A single Prolia injection benefits bone health for a full six months. The results of clinical trials undertaken in the past five years have reported patients successfully using Prolia to strengthen their bones. It is also well tolerated and safe. Prolia injections continue to show a positive, beneficial effect on bone over long periods of time. Clinical trials are continuing to determine the longer term benefits of Prolia and to make sure the drug remains safe with long-term use.

#### Question 4:

### What is the difference between how Prolia and a bisphosphonate (Actonel, Fosamax) act on bone?

Most osteoporosis or bone therapies are called antiresorptive therapies. This means they slow down the weakening of bones. However, each type of bone therapy targets the bone cells, called osteoclasts, differently. Bisphosphonates, which your doctor would prescribe, such as Actonel (risedronate) or Fosamax (alendronate), attach to the surface of the bone and slow down the activity of the cells, called osteoclasts, that break down the bone – much like a car slowing down when going through a construction zone. The antibody denosumab, the active ingredient in Prolia, along with estrogen and other similar bone therapies of this kind, reduces the number of the cells (osteoclasts) that break down or remove bone – like having a flag person stop traffic in a construction zone. While bisphosphonates are effective because of their ability to slow the activity of osteoclasts and cause these cells to die prematurely, Prolia reduces the signalling that leads to the formation of these bone-weakening cells in the first place.



#### Question 5:

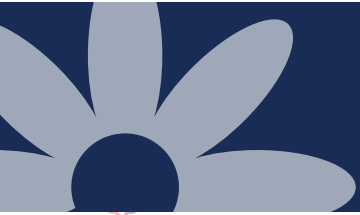
### What is a subcutaneous injection? Why does Prolia need to be injected?

In a subcutaneous injection, medication is injected just under the skin, and not into the muscle. The most common subcutaneous injection given is insulin, with many patients with diabetes injecting themselves. The advantage of an injection over having to swallow a medication is that the drug can be completely absorbed and there are no stomach side effects that sometimes happen with pills. Since the Prolia injection is only given every six months, it is best administered by a healthcare professional such as a doctor or nurse.

#### Question 6:

### What are the advantages to taking Prolia over other medications for osteoporosis?

Prolia has been approved by Health Canada for the treatment of postmenopausal osteoporosis. Prolia was also recommended by Osteoporosis Canada as a first-line medication for osteoporosis. The decision you and your doctor make to use Prolia will be based on how safe the drug is for you (especially if you have other health conditions), its effectiveness for your particular condition and your personal preference. In head-to-head trials, Prolia increased bone density significantly more than Fosamax with no greater side effects. The clinical trials also showed that most people preferred an injection every six months over a weekly pill and were more likely to continue with therapy over a two-year period.



### Question 7: How well does Prolia work to protect my bones?

Clinical trials comparing patients who took Prolia with those taking a placebo (no medication) clearly demonstrated the effectiveness of Prolia. In clinical trials, patients who took Prolia (as well as calcium and vitamin D) experienced approximately 70% less spine breaks, 40% less hip breaks, and 20% less non-spinal breaks (wrist, rib, pelvis), compared to people who only took calcium and vitamin D. These data are similar to the bone protection seen with other osteoporosis medications, making Prolia a good first choice for postmenopausal osteoporosis. Studies done with first-time users of an osteoporosis medication and in those switching from taking a bisphosphonate (such as Fosamax) to Prolia, showed that bone density significantly improved with Prolia.



### Question 8: How long has Prolia been studied and in how many people?

Prolia has been studied for eight years. The largest clinical trial of Prolia versus a placebo was conducted with 8,000 women and this trial is now being extended to 10 years. At this point, with five years of clinical data, studies show continued benefits of Prolia in preventing bone breaks and increasing bone density, with no increased side effects. These clinical trials have also not seen any increase in atypical fractures. Osteonecrosis of the jaw (ONJ) has rarely been reported in patients taking Prolia (see question below). Clinical studies involving patients taking Prolia will be followed for another five years.

### Question 9: What are the benefits and risks of taking Prolia?

If you are at risk of an osteoporosis break, then taking Prolia can reduce that risk by up to 70%. When compared with other osteoporosis medications, Prolia won't upset your system and is convenient. Many people prefer the two injections a year over a once-a-week pill. There are very few risks associated with taking Prolia. This drug is completely removed or gone from the body 6-12 months after the last injection. In the first three years of a five-year clinical trial there was only a small increase in the risk of skin infections and eczema, but this risk was not seen in the last two years of the study. You should be advised that if you decide to stop taking Prolia, as with most medications, its benefits will go away over time. If you choose to stop taking Prolia you should speak to your doctor about other osteoporosis medications.





### Question 10: How do I know Prolia is right and safe for me?

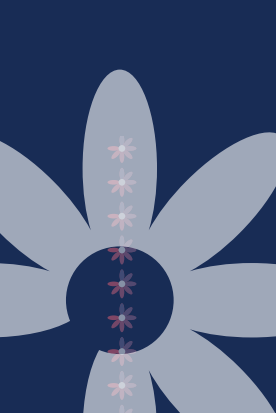
Osteoporosis Canada recommends Prolia as a first-choice therapy for the treatment of postmenopausal osteoporosis. Prolia is a good choice for anyone seeking good bone protection with few side effects. Before prescribing any osteoporosis medications your doctor will want to make sure that your bone loss is the result of osteoporosis and not another medical condition. This may require a physical exam and some simple laboratory tests (blood, urine). No special tests are needed before or during treatment with Prolia. Side effects as a result of Prolia cannot be predicted but they are rare and minor. You should contact your doctor if you experience any unusual symptoms while taking Prolia, such as skin infections or eczema.



### Question 11: If side effects occur, will they last the entire six months after injection? Is there anything that can be done to stop side effects that may occur while on therapy?

Only a few side effects specific to this medication have been reported. Cancer patients who were given 12 times the regular dose of Prolia to help protect their bones, experienced very few side effects. Antibody therapy is very specific and targets only the one body process: in this case only the cells that break down or remove bone, so other side effects are unlikely. Although there is no way of reversing the effects of Prolia once injected, there would not be reason to do so. Infrequent cases of skin infection and eczema improve with the usual medications and having these side effects may not require discontinuation of Prolia. There have been no allergic reactions reported to the therapy. However, the cap on the syringe is made of latex and should be handled with care by individuals with latex allergies.





### Question 12:

## What is hypocalcemia, and how common is it with Prolia?

Hypocalcemia is the word used to describe the condition of low calcium levels in the blood. Very low blood calcium levels in the blood may cause muscle spasm, heart rhythm problems, and convulsions. No increase in the occurrence or frequency of low blood calcium levels was seen in clinical trials with Prolia. In these studies, all the participants were given calcium and vitamin D supplements. It is recommended that you take adequate calcium supplements (1200 mg from diet and supplement combined) and vitamin D (800-2000 IU daily) before beginning any osteoporosis therapy.

### Question 13:

## Are there any risks for developing cancer associated with Prolia?

Some antibody therapies (for example, those used in the treatment of rheumatoid arthritis and other autoimmune diseases) carry risks for infection and cancer. However, these antibody therapies are very different from Prolia because they are directed toward the immune system. Prolia targets a protein that occurs naturally in your body, called RANK Ligand, which acts as a signal that leads to bones being broken down. When Prolia is present in the system the signal is stopped and fewer bone-removing cells (called osteoclasts) are formed.



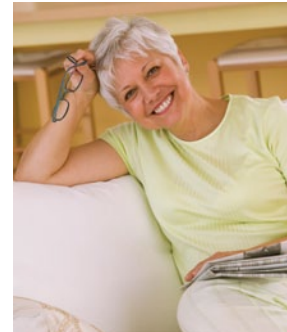
### Question 14:

## Is there a risk of osteonecrosis of the jaw (ONJ) or atypical femoral fracture with Prolia therapy?

ONJ is a delay (more than eight weeks) in healing of the jaw after a tooth extraction or dental surgery. In osteoporosis studies there was no increase in dental problems or delayed dental healing. ONJ in patients taking the intravenous bisphosphonate (Aclasta® [zoledronic acid]) or Prolia, compared to those who were not given any medication (placebo).

ONJ is generally seen in about 1% of patients who are given very high doses of intravenous bisphosphonate (Aclasta is given at 15 times the dose used for osteoporosis) for the treatment of bone cancer. The risk of ONJ is similar in patients given high doses of Prolia for bone cancer (12 times the dose used for osteoporosis treatment).

Atypical femoral/hip breaks have not been seen in the clinical trials with Prolia. Femoral or hip breaks are reduced in patients on long-term bisphosphonate therapy but should a fracture of the hip occur, it may occur lower on the thigh bone (atypical fracture) than in patients not on bisphosphonate therapy.





### Question 15:

How long do I have to take Prolia?  
Can I eventually take a break from  
treatment with Prolia?

Osteoporosis is usually a lifelong health condition that increases a person's risk of a fracture or bone break. Just like other chronic medical problems, medications must be continued as long as the condition exists. Stopping Prolia injections will result in a person's bone density returning to pretreatment levels after about one year and the benefits and likely protection from future fractures will be lost. However, in some people, the risk of bone breakage may decrease with time and their doctor may decide to monitor bone density and risk while discontinuing osteoporosis medications.

Sometimes, after long-term bisphosphonate therapy, such as Actonel and Fosamax, bone density remains stable. Your doctor may decide to stop the bisphosphonate therapy and rely on its long-term effects to control bone cell activity and maintain bone health. These "drug holidays" are not recommended with Prolia therapy since the drug does not remain "stuck" to the bone like bisphosphonates.

### Question 16:

Are there any considerations when  
Prolia is injected?

Prolia is a human antibody and is not recognized any differently from other antibodies circulating in your system; therefore your body will not have a reaction to Prolia. There are no known reactions to Prolia, so on the day of your injection no fasting is required and you may take other medications as usual before and after your injection. No allergic reactions have been reported after an injection with Prolia and there is no need to remain at your doctor's office for a period of observation. However, the cap on the syringe is made of latex and should be handled with care by individuals with latex allergies.

### Question 17:

I missed my six-month dosing  
appointment. What should I do?

After six months, the effects of your last Prolia shot will begin to gradually decrease over several weeks to months. You will not feel any different if you miss a dose, and you can go ahead with the next dose at your earliest convenience. Even if you restart therapy with Prolia after a long time without treatment, the new injection will work for the prescribed six months: you do not need to "catch up" on doses.

Your osteoporosis therapy is part of a long-term plan, and it is recommended and safest to stay as close as possible to the treatment schedule you and your doctor have decided upon.

The ProVital™ Support Program is offered to help you stay on your dosing schedule. If you join this program, you will receive a reminder call from a nurse when you are due for your next injection. In addition to the ProVital Program, you may want to talk to your doctor about other strategies to help you keep to your schedule.

### Question 18:

How do I store my Prolia before it is  
injected, and what if I need to travel with it?

Your Prolia dose comes already loaded into a syringe ready for injection. The pharmacy stores the syringe and medication in the fridge until it is picked up. After you have picked up your Prolia, you can keep it in the package at room temperature for up to 30 days before it is injected. The drug and syringe should not be frozen or exposed to high temperatures (over 25°C), so it is recommended that you keep your medication in your home and not your car. If you are travelling with your Prolia you can keep it in the packaging at room temperature. However, if you need to keep your Prolia for longer than 30 days, it is recommended you speak with your pharmacist about safe storage.



### Question 19: Who should I inform that I am taking Prolia?

Prolia is a medication that reduces your chance of having a bone break due to osteoporosis. Even though it is administered every six months, it continues its effectiveness between injections. Since any medication may affect how another medication works, it is important to inform your healthcare provider about ALL medications you are taking, including Prolia. Take the time to find out about all of your medications, what they are used for and their possible side effects. It is best to keep a written or typed list of all your medications and when they are usually taken. Bring this list to all medical visits as it will inform your healthcare providers that you are already taking Prolia to protect your bones. If there is a chance that you might forget to get your Prolia shot, it is recommended that you tell your doctor or other healthcare provider so they can help you keep on schedule.

### Question 20: How will I remember to get my Prolia treatment every six months?

It is hard to remember to take medications every week let alone every six months. Start by writing the date of your next shot in your personal appointment calendar and ask a family member to write it down in their calendar as well. You may wish to sign up for the ProVital Support Program. Once you sign up, a nurse will call you to remind you of the date of your next dose as well as provide you with additional information about osteoporosis. If you wish to register for ProVital, call 1-877-776-1002. Your doctor's office may also have a reminder system already in place for advising patients of their next dose.

### Question 21: How much calcium and vitamin D do I need while taking medication for osteoporosis?

Calcium and vitamin D supplements are important for bone health and should be taken every day while you are taking medication for osteoporosis. Osteoporosis Canada's recommended calcium intake is 1200 mg of elemental calcium a day, from your diet and supplement combined. A diet without dairy products typically contains about 400 mg of calcium, and a cup of milk or yogurt contains about 300 mg. If you consume two servings of dairy each day, you will only need 200 mg of elemental calcium as a supplement.

Osteoporosis Canada recommends 800-2000 IU of vitamin D per day for patients with osteoporosis. Since the Tolerable Upper Intake Level (the maximum dose considered safe without need of medical monitoring) has recently been raised to 4000 IU per day, this means that taking up to 2000 IU of vitamin D daily should be safe for osteoporosis patients over the age of 50. Vitamin D can also be taken less frequently in larger doses, such as weekly (10,000-14,000 IU) or monthly (50,000 IU).

## Question 22: How does exercise help maintain strong bones?

Exercise in general is vital to your health. Being active helps prevent falls and maintain strong bones. Weight-bearing exercises help maintain your bone and muscle strength. Walking (or any other exercise where you are bearing your body's weight on your feet) is the best kind of weight-bearing exercise. Strong leg muscles developed from walking are important for preventing falls and bone breaks. Try to find an exercise that you and your partner or friends enjoy and make exercise a social event.



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