

Drug Holidays: How long is long enough?

What is the problem?

All medications have risks along with benefits. As a patient, you always need to weigh the advantages of taking any drug against potential harm it may cause. Recently the issue of harm has surfaced with osteoporosis drugs because of two rare, but frightening problems associated with long-term use.

For osteoporosis drugs, namely bisphosphonates, the current question that we are wrestling with is how long is long enough to be on treatment and what may be too long.

What do we know?

Most scientific studies have been with alendronate (Fosamax), the most widely used osteoporosis drug that has been available since 1995. There are many other similar drugs in the class of bisphosphonates, and all seem to have similar risk to benefit profiles.

There are definite benefits to osteoporosis drugs. People who take osteoporosis drugs, regularly and correctly, reduce their risk of having a fracture by about one-third. This is particularly true in patients who are at high risk for having a fracture or who have very low bone density. For people at low risk, fracture protection is not well proven.

There are rare harms that can occur with long-term use of osteoporosis drugs. Estimates are that for each year of use about 1 of every 1,000 patients who take osteoporosis drugs has a harmful side effect. The risk of harm appears to increase the longer a patient stays on the drug, particularly after 4 to 5 years. We will focus on two harmful effects that have received a lot of news coverage recently.

Atypical fracture: One of the harmful effects is a tendency for patients to suffer a fracture, right in the middle of the long thighbone --- with hardly any injury. Many patients who have had these fractures report a deep, aching pain in the middle of the thigh several weeks to months before that bone breaks. The ache is not joint pain and not related to exertion or physical activity.

Osteonecrosis of the jaw: The other harmful effect is a condition where the bones that support the teeth break down and don't heal--- the medical term is osteonecrosis of the jaw (ONJ). ONJ usually occurs after dental procedures like implants or extractions and has been linked to high dosage bisphosphonates used in patients with cancer. ONJ tends to happen in patients who have poor dental health.

Both these harmful conditions are rare — about 1 in 1,000 osteoporosis drug users each year. This is a 0.001% chance and would be similar to reaching into a bag of 999 red balls and pulling out the one blue ball. For people at high risk of fracture, the chance of benefiting from the treatment is many times greater than the harm. Treatment will reduce the risk of a fracture.

What we don't know

- 1) We don't know exactly how much of the benefit stays after the drug has been stopped. Researchers believe there is continuing advantage from the drug for a few years.
- 2) We aren't sure exactly how long the drug benefit lasts in different bones – particularly the hip and the spine bones. Patients who were on a treatment for five years and off for five years did about as well as those staying on treatment for the entire ten years.
- 3) We aren't clear about when to restart an osteoporosis treatment after a drug holiday.

To help with these uncertainties, doctors are measuring bone metabolism with blood tests called bone turnover markers. As long as the results of the bone markers are low, it is logical that the drug is still having an effect in reducing fracture risk. The research on one bisphosphonate (alendronate) shows that the markers can stay low for 6-12 months after stopping treatment, but research into other osteoporosis drugs shows much shorter continued benefit after stopping. The carry-over effect depends on how long the drug remains in the bone and how much of it is released from bone back into the blood stream and eliminated from the body.

What can you do?

If you are on a bisphosphonate, you and your health care provider need to consider what you might gain or lose from stopping the treatment for a year or two.

For some people, it may be more risky to stop taking the drug than staying on it.

Would you benefit from a drug holiday?

To prepare for a visit with your doctor, weigh the following factors.

How long have you been on treatment?	0-2 yrs	3-4 yrs	5+ yrs
What was your fracture risk before you started taking the drug?	Low	Moderate	High
What is your fracture risk now?	Low	Moderate	High
What is your bone density?	Normal	Low bone mass	Osteoporosis
Have you broken a bone?	No		Yes

Should you take a holiday?	Yes	Maybe	No
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More answers in the **GREEN**: You could probably benefit from a drug holiday.

More answers in the **RED**: You probably should stay on treatment.

More answers in the **YELLOW**: You'll want to discuss carefully with your doctor.

How can you be sure?

Learn your fracture risk at www.americanbonehealth.org. This information will help you and your doctor determine whether or not you should be on a treatment that will help prevent fractures.

Always remember, there are other important [prevention strategies](#) to keep your bones strong.