PART III: CONSUMER INFORMATION

Pr BONEFOS®
clodronate disodium

This leaflet is part III of a three-part "Product Monograph" published when BONEFOS was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about BONEFOS. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

BONEFOS is used:

- for the management of hypercalcemia due to malignancy (high blood calcium in adult patients who have cancer), and
- as an adjunct in the management of osteolytic bone metastases (bone destruction when cancer cells have spread to the bone)

What it does:

BONEFOS belongs to a group of medicines called bisphosphonates. BONEFOS binds tightly to bone and blocks the function of cells which re-absorb bone. This strengthens the bones, and thus helps to relieve bone pain and prevent future problems with your bones (such as fractures). It also prevents the release of too much calcium into the blood (hypercalcemia).

When it should not be used:

You should not take BONEFOS if any of the following conditions apply to you.

- You have severe kidney disease.
- You have severe stomach or bowel problems.
- You are pregnant or breastfeeding.
- You are being treated with another bisphosphonate.
- You have an allergy to bisphosphonates, clodronate disodium, or to any ingredient in the formulation or component of the container of BONEFOS.

What the medicinal ingredient is:

Clodronate disodium

What the important nonmedicinal ingredients are:

Capsules: calcium stearate, colloidal anhydrous silica, gelatin, iron oxide (red and yellow), lactose, talc, titanium dioxide.

Solution for injection: sodium hydroxide, water for injection.

What dosage forms it comes in:

Capsules: Each yellow BONEFOS capsule contains 400 mg of clodronate disodium. BONEFOS capsules are provided in plastic bottles containing 120 capsules.

Solution for Injection: BONEFOS solution for injection is available in 5 mL glass ampoules containing anhydrous clodronate disodium 60 mg/mL. The solution must be diluted prior to infusion.

WARNINGS AND PRECAUTIONS

BEFORE starting treatment with BONEFOS talk to your doctor if:

- you suffer from kidney problems, as your dose may need to be reduced.
- you have stomach or bowel problems.
- you are pregnant or planning to become pregnant. BONEFOS should not be given during pregnancy.
- you are breast-feeding. Mothers being treated with BONEFOS should not breast-feed their children.
- you have ever had an allergic reaction to BONEFOS (or similar medicines called bisphosphonates) or any other ingredients of the drug or components of the container.
- you are presently taking another bisphosphonate.
- you have any dental problems or any dental procedures planned in the future.
- you have sores in the mouth.

Osteonecrosis (pronounced OSS-tee-oh-ne-KRO-sis) of the jaw, a rare condition that involves the loss or breakdown of the jaw bone, has been reported in patients with cancer receiving bisphosphonates. The majority of the cases were associated with dental procedures such as tooth extraction.

Your doctor may check if you:

- smoke
- have or have had issues with your teeth and/or gum disease
- have dentures that do not fit well
- have other relevant medical conditions at the same time such as a low red blood cell count (called anemia) or if your blood cannot form clots in the normal way.

Other possible factors that may increase the risk of osteonecrosis of the jaw include:

- chemotherapy;
- radiation therapy;
- steroid therapy (eg, cortisone);
- underlying cancer;
- infection; and
- poor oral hygiene.

If any of these risk factors applies to you, you should have a dental exam prior to starting treatment with BONEFOS. Be sure to tell your dentist about your cancer diagnosis and

treatments. If your medical situation changes to include any of these risk factors, contact your doctor. Your doctor may tell you to stop taking BONEFOS until your medical situation improves (ie, sores in your mouth are healed or risk factors improve).

Unusual fractures of the thigh bone have been reported with the use of bisphosphonates.

Contact your doctor if you feel any pain, weakness or discomfort in your thigh, hip or groin as this may be an early sign of a possible fracture of the thigh bone.

Visual (ocular) disturbances have been reported with bisphosphonate therapy. These include inflammation, infection, and/or irritation of the eye. Patients with visual disturbances other than uncomplicated conjunctivitis should be referred to an ophthalmologist for evaluation. Contact your doctor if you experience inflammation, infection and/or irritation of the eye.

The effect of BONEFOS on the ability to drive or use machines is not known.

Since there is no clinical experience in children, BONEFOS is only recommended for use in adult patients.

INTERACTIONS WITH THIS MEDICATION

Before you start treatment with BONEFOS, be sure to tell your doctor about any other prescription or over-the-counter medicines that you are using or intend to use.

Medicines that may interact with BONEFOS include:

- nonsteroidal anti-inflammatory drugs (NSAIDs), especially diclofenac;
- other bisphosphonates;
- other calcium-reducing agents, including corticosteroids, phosphate, calcitonin, mithramycin or loop diuretics (eg, furosemide);
- aminoglycoside antibiotics;
- estramustine phosphate;
- antacids; and
- dietary supplements containing calcium, iron, magnesium or aluminum.

BONEFOS capsules should be taken on an empty stomach, with a glass of plain water, at least 2 hours before or after food, because food may decrease the amount of BONEFOS absorbed by the body.

BONEFOS capsules should never be taken with milk or food containing calcium or other divalent cations because they interfere with the absorption of BONEFOS.

PROPER USE OF THIS MEDICATION

Usual dose:

Your doctor will determine the appropriate dose for you. Follow the dosing instructions exactly and ask your doctor or pharmacist if you are not sure.

BONEFOS for Injection:

- 300 mg/day is given as a slow infusion into a vein.

BONEFOS Capsules:

- Hypercalcemia due to malignancy: 1600 mg to 2400 mg (four to six capsules) daily. Maximum daily dose is 3200 mg (eight capsules). The daily dose can be taken once, or in two divided doses.
- Osteolytic bone metastasis due to malignancy: starting dose of 1600 mg (four capsules) daily. Maximum daily dose is 3200 mg (eight capsules).

BONEFOS capsules are to be taken on an empty stomach, with a glass of plain water, at least two hours before or after food or any other oral drugs.

BONEFOS capsules should be swallowed whole.

You will need to drink enough fluid or be hydrated during treatment with BONEFOS.

Overdose:

If you think you have taken or given more BONEFOS than you should, contact your doctor or a poison control centre immediately.

Missed Dose:

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to your regular dosing schedule.

Do not double dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, BONEFOS may have, in addition to its beneficial effects, some unwanted effects.

The following side effect has been reported very commonly:

- increased transaminases (a group of liver enzymes) within normal range

The following side effects have been reported commonly:

- nausea;

- vomiting;
- stomach pain;
- diarrhea; and
- increased liver enzyme levels more than twice the normal range without impaired liver function

The following side effects have been reported rarely:

- low blood calcium levels with symptoms (eg, muscle cramps or spasms);
- increased serum parathyroid hormone (a hormone of the small glands adjacent to the thyroid gland) associated with decreased serum calcium;
- increased blood alkaline phosphatase levels (in patients with metastatic disease, this may also be due to liver and bone disease); and
- skin rash due to drug-related allergy.

The following side effects were reported during postmarket experience:

- severe kidney damage (especially after rapid intravenous infusion of high doses of clodronate);
- airway constriction (due to a hypersensitivity reaction or in patients with acetylsalicylic acid-sensitive asthma);
- allergic skin reactions and overactivity of the parathyroid glands which control the amount of calcium in the blood;
- isolated cases of kidney failure, in rare cases with fatal outcome, have been reported, especially when NSAIDs, most commonly diclofenac, were used at the same time;
- severe bone, joint, and/or muscle pain (the onset of symptoms varied from days to several months after starting BONEFOS).

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / Effect		Talk with your doctor	
		Only if severe	In all cases
Unknown	Abnormal thigh bone fractures		✓
	Inflammation, infection and/or irritation of the eye		✓
	Symptoms of osteonecrosis of the jaw which may include: • pain, swelling or infection of the gums; • loosening of teeth; • poor healing of the gums; and • numbness or the feeling of heaviness in the jaw.		✓

This is not a complete list of side effects. For any unexpected effects while taking BONEFOS, contact your doctor or pharmacist.

HOW TO STORE IT

BONEFOS should be stored at room temperature (between 15°C and 30°C). Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

Canada Vigilance Program:

You can report any suspected adverse reactions associated with the use of heath products to the Canada Vigilance Program by one of the following 3 ways:

Report online at www.healthcanada.gc.ca/medeffect
Call toll-free at 1-866-234-2345
Complete a Canada Vigilance Reporting Form and:

- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, please contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or Canada.medinfo@bayer.com.

This document plus the full Product Monograph, prepared for health professionals, can be found at http://www.bayer.ca or by contacting the manufacturer at the above mentioned phone number and email address.

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