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PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine is dispensed with a doctor's prescription only

Bonefos® 800 mg
Tablets

Each tablet contains:
Disodium clodronate 800 mg

Inactive ingredients and allergens: see section 6 "Further Information".

Read this leaflet carefully in its entirety before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.
The medicine is not intended for children.

Essential information about Bonefos 800 mg
- Be sure to swallow the medicine in the morning on an empty stomach and to abstain from eating and drinking anything other than water for one hour after taking the medicine. (see section 2 "Use of the medicine and food" and section 3 "How should you use the medicine?").
- During the course of treatment with Bonefos 800 mg, it is important to be sure to drink lots of water.
- If you are suffering from impaired kidney function or kidney failure, the doctor must monitor you and adjust the dose for you (see section 2 "Special warnings regarding use of the medicine" and section 3 "Dosage recommendations for patients with kidney failure").
- Contact the doctor if you have pain, weakness or discomfort in the thigh, hip or groin (see section 2 "Special warnings regarding use of the medicine").

1) WHAT IS THE MEDICINE INTENDED FOR?
Bonefos 800 mg is used to treat bone dissolution or destruction (osteolysis) in patients suffering from increased bone breakdown as a result of tumors, and for treatment of hypercalcemia (excess blood calcium) in case of a malignant disease (cancer).

Therapeutic group:
Bisphosphonates.

2) BEFORE USING THE MEDICINE:

☒ Do not use the preparation if:
- you are sensitive (allergic) to the active ingredient or to any of the other ingredients included in the medicine, see section 6 for inactive ingredients in the medicine.
- you are currently being treated with other bisphosphonate medicines.
- Do not use this medicine if you have severe kidney failure.

Special warnings regarding use of the medicine:
- During treatment with Bonefos 800 mg, it is important to be sure to drink enough fluids, especially if you are suffering from high blood calcium levels (hypercalcemia) or from severe kidney problem (kidney failure).
  Use Bonefos 800 mg carefully in patients with kidney failure.
- Osteonecrosis of the jaw bones, usually characterized by tooth removal and/or local infection, including infection of the bone or bone marrow – can occur in cancer patients receiving combination therapy that includes bisphosphonates for treatment of bone brittleness as a result of metastases in the bone. Most patients who developed osteonecrosis also received, in addition to bisphosphonates, anticancer treatment which included chemotherapy and steroids.
- If you are at risk of osteonecrosis of the jaw bones (e.g., as a result of cancer, anticancer treatment – chemotherapy, radiotherapy or corticosteroids, or poor dental hygiene), the doctor may recommend that you undergo preventive dental treatment before commencing treatment with Bonefos 800 mg. During treatment with Bonefos 800 mg, avoid invasive dental treatments.
- Atypical femoral fractures have been observed in patients treated with bisphosphonates, especially in patients using bisphosphonates to prevent bone thinning (osteoporosis) for a prolonged period.
- Contact the doctor if you have pain, weakness or discomfort in the thigh, hip or groin. These may be early signs of femoral fractures. If you suspect that you have a femoral fracture, the doctor will consider whether to continue the treatment with bisphosphonates.

❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking:
- Bisphosphonates (see section 2 "Before using the medicine" in the box "Do not use the preparation if").
- Non-steroidal anti-inflammatory drugs (NSAIDs), especially diclofenac – may increase the risk for kidney failure.
- Aminoglycosides (antibiotic) - may increase the risk of low blood calcium levels (hypocalcemia).
- Estramustine phosphate (for treatment of prostate cancer) – Bonefos 800 mg may increase the estramustine phosphate level in the blood.
- Antacids, iron supplements, or any other iron- or calcium-containing (or any divalent cation) preparation – do not use together with Bonefos 800 mg tablets.

❗ Use of the medicine and food
Take Bonefos 800 mg with plain water only, and on an empty stomach. Abstain from drinking (aside from water), eating or taking other oral medicines for one hour after taking Bonefos 800 mg, since this may interfere with the absorption of Bonefos 800 mg.

❗ Pregnancy and breastfeeding
If you are pregnant or breastfeeding, planning to become pregnant or think you may be pregnant, consult the doctor or pharmacist before using this medicine.
It is not known if Bonefos 800 mg crosses the placenta in women. There are data that Bonefos 800 mg crosses the placenta in animals. However, it is not known if the active ingredient can harm the fertility of women or the fetus. Bonefos 800 mg is not recommended for pregnant women and for women of child-bearing age without using an effective contraceptive.
It is not known if Bonefos 800 mg passes into breast milk. Risk to a breastfeed baby cannot be ruled out. Stop breastfeeding during treatment with Bonefos 800 mg.

❗ Driving and use of machines
The effect of Bonefos 800 mg on ability to drive or operate machinery is unknown.

❗ Children
Do not use Bonefos 800 mg in children.

3) HOW SHOULD YOU USE THE MEDICINE?
Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure.
The dosage and the treatment regimen will be determined by the doctor only.

Dosage recommendations for patients with normal kidney function:
- For treatment of **hypercalcemia** due to cancer, you will usually receive Bonefos by way of infusion. However, if the doctor recommended Bonefos 800 mg tablets for oral use, the recommended initial dosage is 2,400 mg (3 tablets) or 3,200 mg (4 tablets) a day. In accordance with your response to treatment, the dosage may be gradually reduced to 1,600 mg a day to maintain normal blood calcium levels.
- For treatment of **osteolysis** in patients suffering from bone metastases, the recommended dosage is 1,600 mg (2 tablets) a day. If necessary, the dose can be increased to a maximum dosage of 3,200 mg (4 tablets) a day.

Dosage recommendations for patients with kidney failure:
- Do not use a dosage exceeding 1,600 mg a day for a prolonged period.
- The dosage is in accordance with kidney function, according to the following index:
  - Creatinine clearance values of 50-80 ml/min: 1,600 mg a day.
  - Creatinine clearance values of 30-50 ml/min: 1,200 mg a day.
  - Creatinine clearance values of 10-30 ml/min: 800 mg a day.
  - Creatinine clearance values of less than 10 ml/min: Do not use Bonefos 800 mg at all.

Do not exceed the recommended dose.

Directions for use:
- Since Bonefos 800 mg is secreted from the body via the kidneys, it is important to drink a lot (e.g., water) during treatment.
- The Bonefos 800 mg tablet can be halved to ease swallowing. However, the two halves must be swallowed at the same time. Do not dissolve the tablets in water or crush them before swallowing.
- If you have been prescribed a daily dose of 1,600 mg, take the tablets together once a day (do not split between morning and evening). Take the tablets in the morning on an empty stomach, with a glass of water.
- If you have been prescribed a dose higher than 1,600 mg, split the dosage. Take 2 tablets in the morning, according the directions above. The rest of the dose should be taken later in the day between meals, more than two hours after a meal and one hour before the next meal or a beverage that is not water.
- See section 2 "Before using the medicine" in the subsections "Use of the medicine and food" and "If you are taking other medicines" for additional important instructions.

Tests and follow-up:
Blood tests should be performed to monitor kidney function before commencing treatment and during the treatment period.

If you accidentally took a higher dosage, drink lots of fluids and contact the doctor; he will check your kidney function and your calcium levels.

If you forgot to take the medicine at the scheduled time, do not take a double dose. Take the next dose at the regular time and consult the doctor.

If you stop taking the medicine: Do not stop taking Bonefos 800 mg unless the doctor has told you to stop. If you are interested in discontinuing use of Bonefos 800 mg, consult the doctor beforehand regarding the expected ramifications.

How can you contribute to the success of this treatment?
Complete the treatment regimen recommended by the doctor.
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS:
As with any medicine, use of Bonefos 800 mg may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
Contact the doctor if you have pain, weakness or discomfort in the thigh, hip or groin. These may indicate a femural fracture (see section 2 "Before using the medicine" subsection "Special warnings regarding use of the medicine").
The most common side effect is diarrhea, usually mild, and occurs at high frequency at high dosages.

Additional side effects
Occurring frequently (between 1 and 10 in 100 patients):
Low blood calcium levels (without symptoms), diarrhea or nausea or vomiting (all usually mild), increased aminotransferase (a group of liver enzymes) levels, usually within the normal range.
Occurring very rarely (between 1 and 10 in 10,000 patients): low blood calcium levels (with symptoms), increased serum parathyroid hormone levels associated with decreased serum calcium levels, increased serum alkaline phosphatase levels (can be a result of a liver or bone disease in patients with metastatic cancer), increased aminotransferase (a group of liver enzymes) levels, more than two-fold higher than the normal range, without affecting liver function, skin reactions (hypersensitivity).
The following side effects have been reported after marketing of the medicine: Uveitis – swelling and itching of the middle layer of the eye, additional visual disorders have been reported with bisphosphonates, including conjunctivitis – swelling and inflammation on the inner side of the eyelid and episcleritis – swelling and inflammation of the tissue covering the white of the eye, and scleritis – swelling and inflammation of the white of the eye. Conjunctivitis has been reported in only one patient treated with Bonefos 800 mg in combination with another bisphosphanate preparation. Impaired respiration in asthma patients sensitive to aspirin, hypersensitivity manifested by a respiratory disorder, impaired kidney function or severe kidney damage after high dosages of Bonefos 800 mg, single cases of kidney failure, including rare cases that led to death, primarily upon use in combination with NSAIDs, primarily of the diclofenac type, single cases of osteonecrosis of the jaw, primarily in patients previously treated with amino-bisphosphonates, such as zoledronate and pamidronate.
Rare cases of severe pains in the bones, joints and/or muscles have been reported in patients who took Bonefos 800 mg. The onset of the symptoms varies from days to a few months after commencing treatment with Bonefos 800 mg. Atypical femural fractures have been reported in patients taking bisphosphanate, especially after long-term treatment for osteoporosis. These fractures may occur anywhere along the femur, even with no or minimal trauma to the area. Some patients experience pains in the thigh or groin. Fractures may occur in both femur bones. If there is suspicion of a fracture, the doctor will weigh continuation of treatment. Some cases of poor healing have been reported. See section 2 "Before using the medicine" for "Special warnings regarding use of the medicine" for further information on bone fractures.
If any of the side effects worsen, or if you are suffering from a side effect not mentioned in this leaflet, consult the doctor.

5) HOW SHOULD THE MEDICINE BE STORED?
Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
Storage: Do not store above 25°C.
Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

6) FURTHER INFORMATION
In addition to the active ingredient, the medicine also contains:
Silicified microcrystalline cellulose (consisting of microcrystalline cellulose and colloidal anhydrous silica), croscarmellose sodium, stearic acid, magnesium stearate, opadry II white (consisting of polyvinyl alcohol, macrogol 3350, titanium dioxide, talc).

What does the medicine look like and what are the contents of the package:
Bonefos 800 mg is marketed in tablet form. The tablets are white, film-coated, oval, with a score line, and labeled with L134 on one side.
Bonefos 800 mg is marketed in a package which contains 30 tablets.

Registration holder and address: Bayer Israel Ltd., 36 Hacharash St., Hod Hasharon 45240.

Manufacturer and address: Bayer OY, Turku, Finland.

This leaflet was checked and approved by the Ministry of Health in June 2013.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 127 59 30006 00