

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Clasteon 800 mg, film-coated tablets

Active ingredient and its quantity in each film-coated tablet:
800 mg disodium clodronate (as tetrahydrate)

For the list of inactive ingredients and allergens, please see section 2 sub-section "Important information about some of this medicine's ingredients" and section 6.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

The medicine is intended for adults above the age of 18.

1. What is this medicine intended for?

- For treatment of bone lysis or destruction (osteolysis) in patients suffering from enhanced bone breakdown as a result of tumors.
- For treatment of hypercalcemia (excess calcium in blood) in case of malignancy (cancer).

Therapeutic group: bisphosphonates.

2. Before using this medicine:

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient (sodium clodronate), similar medicines or any of the other ingredients contained in the medicine (listed in section 6)
- you have severe kidney dysfunction
- you are taking other medicines of the bisphosphonates group

Special warnings about using this medicine:

Before treatment with Clasteon 800 mg, tell your doctor if:

- you have kidney problems
- you have or have previously had pain, swelling or numbness of the jaw or a heavy jaw feeling or loosening of a tooth.

If you are undergoing **dental treatment** or are expected to undergo **dental surgery**, tell your dentist that you are being treated with a bisphosphonate. Certain dental treatments are not recommended while taking bisphosphonates.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist.

Particularly if you are taking:

- non-steroidal anti-inflammatory drugs for pain relief, such as ibuprofen or diclofenac
- antibiotics
- antacids
- mineral supplements
- estamustine used to treat prostate cancer

Do not take any other medicines by mouth for 2 hours before and up to 1 hour after taking each dose of Clasteon 800 mg.

Using this medicine and food:

It is important to take the tablets on an empty stomach (otherwise your body will not absorb the medicine properly). Except for drinking plain water, do not eat or drink for 2 hours before and 1 hour after each dose intake.

It is particularly important to avoid drinking milk during this period.

You can drink water whenever you like.

Pregnancy and breastfeeding:

Generally, Clasteon 800 mg is not given to women during pregnancy. If you are pregnant, think that you are pregnant or if you are planning to become pregnant, consult your doctor or pharmacist before taking the medicine.

Do not breastfeed during treatment with Clasteon 800 mg.

Driving and using machines:

Clasteon 800 mg has no known effect on the ability to drive or operate machines.

Important information about some of this medicine's ingredients:

This medicine contains 128.24 mg sodium per tablet. This should be taken into consideration by patients on a low sodium diet.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Make sure to drink plenty of fluids (such as water) before, during and after the treatment.

Clasteon 800 mg tablets are intended for use in adults only.

Only your doctor will determine your dose and how you should take this medicine. The recommended dosage is usually:

The daily dosage varies. In most cases, the dose is between 1600 mg (2 tablets) per day and 3200 mg (4 tablets) per day. If you have kidney problems, the dose may be reduced.

Do not exceed the recommended dose.

- Swallow the tablets with plain water. The Clasteon 800 mg tablet may be divided into two halves to ease swallowing, but the two halves must be taken at the same time
- Do not crush or dissolve the tablets prior to intake. Never take them with milk because it reduces the amount of medicine that your body can absorb.
- If you have been prescribed a **single daily dose** of Clasteon 800 mg, the tablets should be taken (preferably in the morning) on an empty stomach with a glass of plain water. After taking the Clasteon 800 mg tablets, **you should not eat, drink (other than plain water) or take any other medicines by mouth for 1 hour.**
- If you have been ordered to divide the Clasteon 800 mg **dose** to be taken **twice daily**, the first dose should be taken as recommended in the previous section. The second dose should be taken between meals, **more than 2 hours after and 1 hour before eating, drinking (other than plain water); during this period, avoid milk and/or taking any other medicines by mouth.**
- Take the tablets even if you are not eating at present.

If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, **immediately** see a doctor or go to a hospital emergency room and bring the medicine package with you. **Drink plenty of water.** Your doctor may check your blood calcium level and how well your kidneys and liver are functioning.

Symptoms of an overdose may be nausea or vomiting.

If you forget to take the medicine at the scheduled time, do not take the forgotten dose. Take the next dose at the usual time.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects:

Like with any medicine, using Clasteon 800 mg may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them. Stop taking the tablets and contact your doctor immediately if any of the following occur:

- Wheezing or difficulty breathing
- Swelling of the face, tongue or throat
- Allergic skin reactions, such as rash, redness or itching

If you experience any of the following serious side effects, seek immediate medical attention:

- Numbness and tingling sensations around the mouth and/or in the fingers and toes, muscle cramps or spasms (in the back, hands and/or feet) or seizures.
- Kidney problems - may be manifested as feeling generally unwell, reduced appetite and you may observe foamy urine.
- Severe kidney damage - may include symptoms such as weakness or tiredness, change in frequency of urination and swelling of the face, arms, legs and abdomen. These problems are more common when patients are taking certain types of anti-inflammatory drugs (usually diclofenac) together with Clasteon 800 mg.
- Pain, swelling or numbness of the jaw, a heavy jaw feeling or loosening of a tooth, especially if you have been treated in the past with bisphosphonates, such as zoledronate and pamidronate.
- Severe bone, joint and/or muscle pain - can appear several days to several months after starting treatment with Clasteon 800 mg.
- Contact your doctor if you have ear pain, discharge from the ear, and/or an ear infection. These could be signs of damage in the ear bone (osteonecrosis of the external auditory canal) (very rare).
- Unusual fracture of the thigh bone (rare), mainly in patients receiving long-term treatment for osteoporosis. Contact your doctor if you experience pain, weakness or discomfort in the thigh, hip or groin, as these may be an initial sign of a possible fracture of the thigh bone.

Additional side effects:

Common side effects (occur in less than 1-10 in 100 users):

- Low blood calcium levels without any symptoms (asymptomatic hypocalcaemia) or a small increase in the levels of liver enzymes, which can be detected in blood tests
- Diarrhoea
- Nausea or vomiting

Rare side effects (occur in 1-10 in 10,000 users)

- Low blood calcium levels with symptoms (symptomatic hypocalcaemia) such as numbness and tingling sensation around the mouth and/or in the fingers and toes, muscle cramps or spasms (in the back, hands and/or feet), seizures, at lower frequency
- Increase in blood levels of a hormone (parathyroid hormone) or certain enzymes (alkaline phosphatase), which can be detected in blood tests
- Allergic skin reaction, such as rash, redness or itching
- Difficulty breathing (bronchospasm) – if you experience any difficulty breathing, contact your doctor immediately
- Unusual fracture of the thigh bone (mainly in patients receiving long-term treatment for osteoporosis) - contact your doctor if you experience pain, weakness or discomfort in the thigh, hip or groin, as these may be an early indication of a possible fracture of the thigh bone.

Very rare side effects (occur in less than 1 in 10,000 users):

- Talk to your doctor if you have ear pain, discharge from the ear, and/or an ear infection. These could be signs of bone damage in the ear.

Other side effects (of unknown frequency):

- Breathing problems in aspirin sensitive asthma patients
- Allergic reaction causing difficulty breathing - if you experience any difficulty breathing, contact your doctor immediately
- Kidney problems which may include severe kidney damage, and in rare cases life threatening kidney failure, have been reported. These problems are more common when patients are taking certain types of anti-inflammatory drugs (usually diclofenac) together with Clasteon 800 mg.
- Death of tissue in the jaw bones (osteonecrosis) occurring mainly in patients treated in the past with bisphosphonates such as zoledronate and pamidronate. Symptoms include pain, swelling or numbness of the jaw, a heavy jaw feeling or loosening of a tooth
- Severe bone, joint and/or muscle pain - can appear several days to several months after starting treatment with Clasteon 800 mg. However, these symptoms may be related to the reason due to which you are taking Clasteon 800 mg.
- Swelling and irritation of the uvea (the layer beneath the sclera) – has been observed during treatment with Clasteon 800 mg.
- Swelling, infection or inflammation of the conjunctiva

Your doctor may perform blood tests from time to time, to check that Clasteon 800 mg tablets are working properly.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store below 30°C. Store in the original package.
- Do not throw away any medicine via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information:

In addition to the active ingredient, this medicine also contains:

Starch pregelatinised, microcrystalline cellulose, colloidal silica anhydrous, sodium starch glycolate (type A), magnesium stearate, talc, polyvinyl alcohol, titanium dioxide (E171) and macrogol (E1521)

What the medicine looks like and contents of the pack:

Clasteon 800 mg tablets are white, oval, convex film-coated tablets with a score line. The score line is intended for tablet breaking to ease swallowing and not to divide into equal doses.

Each pack contains 10, 30 or 60 tablets arranged in blisters. Not all pack sizes may be marketed.

Registration holder's name and address:

BioAvenir Ltd., 1 David Hamelech St., Herzliya Pituach 4666101

Manufacturer's name and address:

Abiogen Pharma S.p.A., Pisa, Italy

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 158-03-34600-00

This leaflet was revised in 12.21 according to the Ministry of Health guidelines