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

The medicine is dispensed with a doctor's prescription only

ACLASTA®

Zoledronic acid 5 mg/100 ml
Solution for intravenous infusion (I.V.)

Each bottle with 100 ml of solution contains 5 mg zoledronic acid (anhydrous).

Inactive and allergenic ingredients in the preparation - see section 6 "Further Information".
Injection instructions are at the end of this leaflet and in the leaflet for the physician.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. Keep this leaflet; you may need to read it again.
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.
This medicine is not intended for children and adolescents under 18 years of age. The use of Aclasta in children and adolescents has not been studied.

1. WHAT IS THE MEDICINE INTENDED FOR?

Aclasta is used for:
- Treatment of Paget's disease of the bone.
- Treatment of osteoporosis:
  - in postmenopausal women
  - in men

  at increased risk of fracture, including those with a recent low-trauma hip fracture.
- Treatment and prevention of glucocorticoid-induced osteoporosis (a type of steroids).
- Prevention of postmenopausal osteoporosis in women for whom bisphosphonate therapy is indicated.

Therapeutic group: bisphosphonates.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- you are sensitive (allergic) to the active ingredient, zoledronic acid, other bisphosphonates or any of the other ingredients of the medicine (listed in section 6).
- you have hypocalcaemia (this means that the levels of calcium in your blood are too low).
- you have severe kidney problems.
- you are pregnant.
- you are breastfeeding.

Special warnings regarding use of the medicine

Before treatment with Aclasta, tell the doctor if:
- you are being treated with any medicine containing zoledronic acid, which is also the active substance of Aclasta.
- you have kidney problems, or had in the past.
- you are unable to take daily calcium and vitamin D supplements.
- some or all of the parathyroid glands in your neck were surgically removed.
- sections of your intestine have been removed.

There have been post-marketing reports of a side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) in patients receiving Aclasta (zoledronic acid) for osteoporosis. ONJ can also occur after stopping treatment.
It is important to try and prevent development of ONJ as it is a painful condition that can be difficult to treat. In order to reduce the risk of developing ONJ, there are some precautions you should take.

Before receiving Aclasta treatment, tell your doctor, pharmacist or nurse if:
- you have any problems with your mouth or teeth such as poor dental health, gum disease, or a planned tooth extraction;
- you do not receive routine dental care or have not had a dental check-up for a long time;
- you are a smoker (as this may increase the risk of dental problems);
- you have previously been treated with a bisphosphonate (used to treat or prevent bone disorders);
- you are taking medicines called corticosteroids (such as prednisolone or dexamethasone);
- you have cancer.

Your doctor may ask you to undergo a dental examination before you start treatment with Aclasta.
While being treated with Aclasta, you should maintain good oral hygiene (including regular teeth brushing) and have routine dental check-ups. If you wear dentures, you should make sure these fit properly. If you are under dental treatment or are due to undergo dental surgery (e.g. tooth extraction), inform your doctor about your dental treatment and tell your dentist that you are being treated with Aclasta. Contact your doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, or sores that are not healing or are discharging, as these could be signs of ONJ.

If you are taking, or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. It is important for your doctor to know all the medicines you are taking, especially if you are taking any medicines known to be harmful to your kidneys (e.g. aminoglycosides [a type of antibiotic use to treat certain infections]) or diuretics (several types of medicines used to treat different states of fluid retention in the body, hypertension and others), that may cause dehydration.

Use of the medicine and food
You can eat as usual on the day you are treated with Aclasta.

Pregnancy and breastfeeding
You must not be given Aclasta if you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby. Ask your doctor, pharmacist or nurse for advice before taking this medicine.

Driving and using machines
If you feel dizzy while taking Aclasta, do not drive or use machines until you feel better.

Important information regarding some of the ingredients of the medicine
Aclasta contains 7.04 mg sodium in each 100 ml vial.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.
The dosage and treatment regimen will be determined by the doctor only.

Osteoporosis:
The usual dosage is generally 5 mg given as one infusion per year into the vein by your doctor or nurse. The infusion will take at least 15 minutes.
In case you recently broke your hip, it is recommended to administer Aclasta two or more weeks after your hip repair surgery.
It is important to take calcium and vitamin D supplements (for example tablets) as directed by your doctor.
For osteoporosis, Aclasta works for one year. The doctor will let you know when to return for your next dose.

Paget's disease:
For the treatment of Paget's disease, Aclasta must only be prescribed by a doctor with experience in the treatment of Paget's disease of the bone.
The usual dosage is 5 mg, given to you as one initial intravenous infusion by your doctor or nurse. The infusion will take at least 15 minutes. Aclasta may work for longer than one year, and your doctor will let you know if you need to be treated again.
Your doctor may advise you to take calcium and vitamin D supplements (e.g. tablets) for at least the first ten days after treatment with Aclasta. It is important that you follow this advice carefully so that the level of calcium in your blood does not become too low in the period after the infusion. Your doctor will inform you regarding the symptoms associated with hypocalcaemia.

Do not exceed the recommended dose.

Be sure that you drink enough fluids (at least one or two glasses) before and after treatment with Aclasta, as directed by your doctor. This will help to prevent dehydration. This is particularly important in patients taking diuretics and in elderly patients (age 65 and older).

Tests and follow up
- For patients with Paget's disease - it is recommended to measure blood calcium levels before infusion of Aclasta.
- Your doctor may ask you to undergo a dental examination before you start treatment with Aclasta (see "Special warnings regarding use of the medicine").
- Your doctor should do a blood test to check your kidney function (levels of creatinine) before each dose of Aclasta. It is important for you to drink at least 2 glasses of fluid (such as water), a few hours before receiving treatment with Aclasta, as directed by your healthcare provider.

If you forgot to take the medicine
Contact your doctor or hospital as soon as possible to reschedule your appointment.

Adhere to the treatment regimen as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with this medicine without consulting the doctor.

Before stopping Aclasta therapy
If you are considering stopping Aclasta treatment, please go to your next appointment and discuss this with your doctor. Your doctor will advise you and decide how long you should be treated with Aclasta.

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

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

4. SIDE EFFECTS

As with any medicine, use of Aclasta may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
Side effects related to the first infusion are very common, but are less common following subsequent infusions.
The majority of the side effects, such as fever and chills, pain in the muscles or joints, and headaches, occur within the first three days following the dose of Aclasta. The symptoms are usually mild to moderate and go away within three days. Your doctor can recommend a mild pain reliever such as ibuprofen or paracetamol to reduce these side effects. The chance of experiencing these side effects decreases with subsequent doses of Aclasta.

Some side effects could be serious

Common side effects (effects that occur in 1-10 in 100 users)
There have been reports of heart rhythm disorders (atrial fibrillation) in postmenopausal female patients receiving Aclasta for the treatment of osteoporosis. It is not known whether Aclasta causes heart rhythm disorders, but you must report to your doctor if you experience symptoms of heart rhythm disorders after receiving Aclasta.

Uncommon side effects (effects that occur in 1-10 in 1,000 users)
Swelling, redness, pain and itching in the eyes or eye sensitivity to light.

Very rare side effects (effects that 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.

Side effects of unknown frequency
- Pain in the mouth and/or jaw, swelling or non-healing sores in the mouth or jaw, discharge, numbness or a feeling of heaviness in the jaw, or loosening of a tooth; these could be signs of bone damage in the jaw (osteonecrosis). Tell your doctor or dentist immediately if you experience such symptoms while being treated with Aclasta or after stopping treatment.
- Kidney disorders (e.g. decreased urine output) may occur. Your doctor should do a blood test to check your kidney function before each dose of Aclasta. It is important for you to drink at least 2 glasses of fluid (such as water), within a few hours before receiving Aclasta, as directed by your healthcare provider.

If you experience any of these side effects, contact your doctor immediately.

Aclasta may also cause other side effects

Additional side effects observed for the indications: treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture, including those who recently experienced a low-trauma hip fracture; treatment and prevention of glucocorticoid-induced osteoporosis; treatment of Paget's disease of the bone

Very common side effects (effects that occur in more than 1 in 10 users)
Fever.

Common side effects (effects that occur in 1-10 in 100 users)
Headache; dizziness; nausea; vomiting; diarrhea; pain in the muscles; pain in the bones and/or joints; pain in the back, arms or legs; flu-like symptoms (e.g. tiredness, chills, joint and/or muscle pain); chills; feeling of tiredness and lack of interest; weakness; pain; general unwell feeling, pain and swelling at the injection site.
In patients with Paget's disease of the bone, cases of symptoms due to low blood calcium (hypocalcemia) such as muscle spasms, or numbness, or tingling especially around the mouth, have been reported.

Uncommon side effects (effects that occur in 1-10 in 1,000 users)
Flu; upper respiratory tract infection; decreased red blood cell count; loss of appetite; sleeplessness; sleepiness which may include reduced alertness and awareness; tingling sensation or numbness; extreme tiredness; trembling; temporary loss of consciousness; eye infection or irritation or inflammation with pain and redness; spinning sensation; increased blood pressure; flushing; cough; shortness of breath; upset stomach; abdominal pain; constipation; heartburn; dry mouth; skin rash; excessive sweating; itching; skin reddening; neck pain; stiffness in muscles, bones and/or joints; joint swelling; muscle spasms; shoulder pain; pain in your chest muscles and rib cage; joint inflammation; muscular weakness; abnormal kidney function test results; abnormally frequent urination; swelling of hands, ankles or feet; thirst, toothache, taste disturbances; acute reaction (e.g. fever, increased heart rate, tiredness, loss of appetite); non-cardiac chest pain.

Rare side effects (effects that occur in 1-10 in 10,000 users)
Unusual fracture of the thigh bone particularly in patients on long-term treatment for osteoporosis may occur rarely. Contact your doctor if you experience pain, weakness or discomfort in your thigh, hip or groin as this may be an early indication of a possible fracture of the thigh bone.

Side effects of unknown frequency
Severe allergic reaction including dizziness and difficulty breathing, swelling mainly of the face and throat, difficulty breathing with wheezing or cough, itchy rash; decreased blood pressure; dehydration secondary to side effects such as fever, vomiting and diarrhea.

Additional side effects observed for the indication: prevention of osteoporosis in postmenopausal women who require bisphosphonate therapy

Very common side effects (effects that occur in more than one in ten users)
Headache; nausea; muscle pain; pain; chills.

Common side effects (effects that occur in 1-10 in 100 users)
Loss of appetite; trembling; sleepiness which may include reduced alertness and awareness; eye infection or irritation or inflammation with pain and redness; abdominal pain; constipation; night sweats; pain in your muscles; pain in your bones and/or joints; muscle spasms; pain in your chest muscles and rib cage; pain in jaw; neck pain; swelling of your hands, ankles or feet; non-cardiac chest pain.

Uncommon side effects (effects that occur in 1-10 in 1,000 users)
Anxiety; decreased skin sensitivity; disturbed sense of taste; blurred vision; flank pain.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the carton package and vial. The expiry date refers to the last day of that month.
- Store below 30°C.
- After opening, the solution is chemically and physically stable for at least 24 hours at a temperature of 2°C to 8°C. For further instructions, see: **INFORMATION FOR THE HEALTHCARE PROFESSIONAL**.
- Do not use this medicine if you notice that the package is damaged.
- Discard the remains of the solution that have not been used.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Mannitol, sodium citrate, water for injection
- Aclasta contains 7.04 mg sodium in each 100 ml vial.
- What the medicine looks like and what are the contents of the package: **The solution:** clear and colorless. **The vial:** plastic, colorless 100 ml vial, with a grey rubber stopper and an aluminium cap that opens.
  The package contains 1, 3 or 6 vials. Not all package sizes may be marketed.
- Registration holder and address - Novartis Israel Ltd., 36 Shacham St., Petach-Tikva.
- Manufacturer and address - Novartis Pharma Stein AG, Stein, Switzerland
  Or: Fresenius Kabi Austria GmbH, Graz, Austria
  for Novartis Pharma AG, Basel, Switzerland.
- This leaflet was checked and approved by the Ministry of Health on: July 31, 2016.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  135 99 31323

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

Patients treated with Aclasta should be given the package leaflet following administration.
The following information is intended for healthcare professionals only:

How to prepare and administer Aclasta
Aclasta solution for infusion (Zoledronic acid 5 mg/100 ml) is ready for use.
For single use only. Any unused solution should be discarded. Only clear solution free from particles and discoloration should be used. Aclasta must not be mixed or given intravenously with any other medicinal product and must be given through a separate vented infusion line at a constant infusion rate. The infusion time must not be less than 15 minutes. Aclasta must not be allowed to come into contact with any calcium-containing solutions. If refrigerated, allow the refrigerated solution to reach room temperature before administration. Aseptic techniques must be followed during preparation of the infusion. The infusion must be conducted according to standard medical practice.

How to store Aclasta
- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and bottle after EXP.
- The unopened bottle should be stored below 30°C.
- After opening the bottle, the product should be used immediately in order to avoid microbial contamination. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C. Allow the refrigerated solution to reach room temperature before administration.

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