PACKAGE LEAFLET: INFORMATION FOR THE USER

Aclasta 5 mg solution for infusion
Zoledronic acid

Read all of this leaflet carefully before you are given this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, pharmacist or nurse.

In this leaflet:

1. What Aclasta is and what it is used for
2. Before you are given Aclasta
3. How Aclasta is given
4. Possible side effects
5. How to store Aclasta
6. Further information

1. WHAT ACLASTA IS AND WHAT IT IS USED FOR

Aclasta contains the active substance zoledronic acid. It belongs to a group of medicines called bisphosphonates and is used to treat post-menopausal women and men with osteoporosis or osteoporosis caused by treatment with steroids, and Paget's disease of the bone.

Osteoporosis
Osteoporosis is a disease that involves the thinning and weakening of the bones and is common in women after the menopause, but can also occur in men. At the menopause, a woman's ovaries stop producing the female hormone oestrogen, which helps keep bones healthy. Following the menopause bone loss occurs, bones become weaker and break more easily. Osteoporosis could also occur in men and women because of the long term use of steroids, which can affect the strength of bones. Many patients with osteoporosis have no symptoms but they are still at risk of breaking bones because osteoporosis has made their bones weaker. Decreased circulating levels of sex hormones, mainly oestrogens converted from androgens, also play a role in the more gradual bone loss observed in men. In both women and men, Aclasta strengthens the bone and therefore makes it less likely to break. Aclasta is also used in patients who have recently broken their hip in a minor trauma such as a fall and therefore are at risk of subsequent bone breaks.

Paget's disease of the bone
It is normal that old bone is removed and is replaced with new bone material. This process is called remodelling. In Paget's disease, bone remodelling is too rapid and new bone is formed in a disordered fashion, which makes it weaker than normal. If the disease is not treated, bones may become deformed and painful, and may break. Aclasta works by returning the bone remodelling process to normal, securing formation of normal bone, thus restoring strength to the bone.

2. BEFORE YOU ARE GIVEN ACLASTA

Follow all instructions given to you by your doctor carefully before you are given Aclasta.

You should not be given Aclasta
- if you are allergic (hypersensitive) to zoledronic acid, other bisphosphonates or any of the other ingredients of Aclasta.

- if you have hypocalcaemia (this means that the levels of calcium in your blood are too low).
- if you have severe kidney problems.
- if you are pregnant.
- if you are breast-feeding.

Take special care with Aclasta
Tell your doctor before you are given Aclasta:
- if you are being treated with Zometa, which contains the same active substance as Aclasta.
- if you have a kidney problem, or used to have one.
- if you are unable to take daily calcium supplements.
- if you have had some or all of the parathyroid glands in your neck surgically removed.
- if you have had sections of your intestine removed.

Before you receive treatment with Aclasta, tell your doctor if you have (or have had) pain, swelling or numbness in your gums, jaw or both, if your jaw feels heavy, or if you have lost a tooth. Before you receive dental treatment or undergo dental surgery, tell your dentist you are receiving treatment with Aclasta.

Use in children
Aclasta is not recommended for anyone under 18 years of age. The use of Aclasta in children and adolescents has not been studied.

Taking other medicines
Please tell your doctor, pharmacist or nurse if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

It is especially 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) or diuretics ("waterpills") that may cause dehydration.

Using Aclasta with food and drink
Make sure you drink enough fluids (at least one or two glasses) before and after the treatment with Aclasta, as directed by your doctor. This will help to prevent dehydration. You may eat normally on the day you are treated with Aclasta. This is especially important in patients who take diuretics ("water pills") and in elderly patients.

Pregnancy and breast-feeding
There is no adequate information on the use of zoledronic acid in pregnant women. Studies in animals have shown reproductive toxicological effects. Additionally, there is no information on the use of Aclasta in breast-feeding women. You must not be given Aclasta if you are pregnant or plan to become pregnant.

You must not be given Aclasta if you are breast-feeding.

Ask your doctor, pharmacist or nurse for advice before taking any medicine.

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

3. HOW ACLASTA IS GIVEN

Follow carefully all instructions given to you by your doctor or nurse. You should check with your doctor or nurse if you are not sure.

Your doctor should do a blood test to check your kidney functions (levels of creatinine) before each dose of Aclasta. It is important for you to drink at least one or two glasses of fluid (such as water), within a few hours before receiving Aclasta, as directed by your doctor or nurse.

Osteoporosis
The usual dose is 5 mg given as one infusion per year into a vein by your doctor or nurse. The infusion will take at least 15 minutes.

In case you recently broke your hip, it is recommended that Aclasta is administered 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. Your doctor will let you know when to return for your next dose.

Paget's disease
The usual dose is 5 mg, given to you as one initial infusion into a vein 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 being given 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.

If a dose of Aclasta is missed
Contact your doctor or hospital as soon as possible to re-schedule your appointment.

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.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Aclasta can cause side effects, although not everybody gets them. In most cases, no specific treatment is required.

Side effects may occur with certain frequencies, which are defined as follows:

Very common:	affects more than 1 user in 10
Common:	affects 1 to 10 users in 100
Uncommon:	affects 1 to 10 users in 1,000
Rare:	affects 1 to 10 users in 10,000
Very rare:	affects less than 1 user in 10,000
Not known:	frequency cannot be estimated from the available data.

Side effects related to the first infusion are very common (occurring in more than 30% of patients) 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 headache, 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.

Very common side effects
Fever

Common side effects
Headache, dizziness, sickness, vomiting, diarrhoea, 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 muscle pain), chills, feeling of tiredness and lack of interest, weakness, pain, feeling unwell, skin reactions such as redness, swelling and/or pain at the infusion site.

In patients with Paget's disease: symptoms due to low blood calcium, such as muscle spasms, or numbness, or a tingling sensation especially in the area around the mouth.

Irregular heart rhythm (atrial fibrillation) has been seen in patients receiving Aclasta for post-menopausal osteoporosis. It is currently unclear whether Aclasta causes this irregular heart rhythm but you should report it to your doctor if you experience such symptoms after you have received Aclasta.

Uncommon side effects
Flu, upper respiratory tract infections, decreased red 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, eye sensitivity to light, spinning sensation, increased blood pressure, flushing, cough, shortness of breath, upset stomach, abdominal pain, constipation, dry mouth, heartburn, 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 test results, abnormal frequent urination, swelling of hands, ankles or feet, thirst, toothache, taste disturbances.

Additional side effects which have been reported (frequency not known): severe allergic reactions including dizziness and difficulty breathing, swelling mainly of the face and throat, decreased blood pressure, pain in the mouth, teeth and jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth, kidney disorder (e.g. decreased urine output), dehydration secondary to post-dose symptoms such as fever, vomiting and diarrhoea.

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.

If you notice any of these side effects, tell your doctor.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, pharmacist or nurse.

5. HOW TO STORE ACLASTA

Your doctor, pharmacist or nurse knows how to store Aclasta properly.

- Keep out of the reach and sight of children.
- Do not use Aclasta after the expiry date which is stated on the carton and bottle after EXP.
- The unopened bottle does not require any special storage conditions.
- 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.

6. FURTHER INFORMATION

What Aclasta contains
- The active substance is zoledronic acid. Each bottle with 100 ml of solution contains 5 mg zoledronic acid anhydrous (as monohydrate).
  One ml solution contains 0.05 mg zoledronic acid (as monohydrate).
- The other ingredients are mannitol, sodium citrate and water for injections.

What Aclasta looks like and contents of the pack
Aclasta is a clear and colourless solution. It comes in 100 ml plastic bottles as a ready-to-use solution for infusion. It is supplied in packs containing one bottle as unit pack or in multi-packs comprising 5 packs, each containing 1 bottle. Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

The following information is intended for medical or healthcare professionals only (see section 3):

How to prepare and administer Aclasta

- Aclasta 5 mg solution for infusion 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 out of the reach and sight of children.
- Do not use Aclasta after the expiry date which is stated on the carton and bottle.
- The unopened bottle does not require any special storage conditions.
- 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.