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EPAR summary for the public

Aclasta

zoledronic acid

This document is a summary of the European Public Assessment Report (EPAR) for Aclasta. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Aclasta.

What is Aclasta?

Aclasta is a solution for infusion (drip) into a vein that contains the active substance zoledronic acid.

What is Aclasta used for?

Aclasta is used to treat osteoporosis (a disease that makes bones fragile) in women who have been through the menopause and in men. It is used in patients who are at risk of fractures (broken bones) including those who have recently broken their hip in a minor trauma such as a fall, and in patients whose osteoporosis is linked to long-term treatment with glucocorticoids (a type of steroid).

Aclasta is also used to treat Paget's disease of the bone in adults. This is a disease where the normal process of bone growth is changed.

The medicine can only be obtained with a prescription.

How is Aclasta used?

Aclasta is given as an infusion lasting at least 15 minutes. This can be repeated once a year in patients being treated for osteoporosis. Patients who have broken their hip should not receive Aclasta any earlier than two weeks after the operation to repair the fracture. For Paget's disease, only one infusion of Aclasta is usually given, but additional infusions can be considered if the patient's disease comes back. The effect of each infusion lasts for a year or more.

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Patients must have adequate fluids before and after treatment, and should receive adequate supplements of vitamin D and calcium. Using paracetamol or ibuprofen (anti-inflammatory medicines) shortly after Aclasta can reduce symptoms such as fever, muscle pain, influenza (flu)-like symptoms, joint pain and headache in the three days following the infusion. In the treatment of Paget's disease of the bone, Aclasta must only be used by a doctor who has experience in the treatment of the disease. Aclasta should not be used in patients with severe kidney problems.

How does Aclasta work?

Osteoporosis happens when not enough new bone grows to replace the bone that is naturally broken down. Gradually, the bones become thin and fragile, and more likely to fracture. In women, osteoporosis is more common after the menopause, when the levels of the female hormone oestrogen fall. Osteoporosis can also occur in both sexes as a side effect of glucocorticoid treatment. In Paget's disease, the bone breaks down more quickly, and when it grows back, it is weaker than normal.

The active substance in Aclasta, zoledronic acid, is a bisphosphonate. It stops the action of the osteoclasts, the cells in the body that are involved in breaking down the bone tissue. This leads to less bone loss in osteoporosis and less disease activity in Paget's disease. Zoledronic acid has also been authorised in the European Union (EU) as Zometa since March 2001 for the prevention of bone complications in patients with cancer that is affecting the bone, and for the treatment of hypercalcaemia (high blood calcium levels) caused by tumours.

How has Aclasta been studied?

Because zoledronic acid has been authorised in the EU as Zometa for a number of years, the company presented the results of some studies carried out with Zometa, which were taken into account when assessing Aclasta.

For osteoporosis, Aclasta has been studied in three main studies. The first compared Aclasta with placebo (a dummy treatment) in almost 8,000 elderly women with osteoporosis, looking at the number of fractures in the spine and the hip over three years. The second study compared Aclasta with placebo in 2,127 men and women with osteoporosis who had recently broken their hip, and looked at the number of fractures over up to five years. The third compared one infusion of Aclasta with daily treatment with risedronate (another bisphosphonate) in 833 men and women with osteoporosis caused by glucocorticoids, and looked at the change in the density of the bones in the spine over a year. In these studies, the patients could take other medicines for osteoporosis, but not other bisphosphonates.

For Paget's disease, Aclasta has been compared with risedronate in a total of 357 adults in two studies lasting six months. The patients received one infusion of Aclasta or they took risedronate once a day for two months. The main measure of effectiveness was the number of patients who responded to treatment, defined as blood levels of serum alkaline phosphatase (an enzyme involved in the breakdown of bone) returning to normal or falling at least three-quarters of the way back to normal.

What benefit has Aclasta shown during the studies?

In osteoporosis, Aclasta was more effective than the comparator medicines. In the study of elderly women, the risk of fractures in the spine was reduced by 70% in patients taking Aclasta (without any other medicines for osteoporosis) over three years when compared with those taking placebo. There was a 41% risk reduction in hip fractures, when comparing all women taking Aclasta (with or without other osteoporosis medicines) with those taking placebo. In the study of men and women who had broken their hip, 9% of the patients receiving Aclasta had a fracture (92 out of 1,065), compared with

13% of the patients receiving placebo (139 out of 1,062). Finally, Aclasta was more effective than risedronate at increasing spine bone density over a year's treatment in patients taking glucocorticoids.

In Paget's disease, Aclasta was more effective than risedronate. After six months, around 96% of patients had responded to treatment in the two studies, compared with around 74% of the patients who received risedronate.

What is the risk associated with Aclasta?

Most side effects with Aclasta tend to occur within the first three days after infusion, becoming less common with repeated infusions. The most common side effect with Aclasta (seen in more than 1 patient in 10) is fever. Osteonecrosis of the jaw (damage to the bones of the jaw, which could lead to pain, sores in the mouth or loosening of teeth) has been reported rarely (seen in between 1 and 10 patients in 10,000). For the full list of all side effects reported with Aclasta, see the package leaflet.

Aclasta must not be used in people who are hypersensitive (allergic) to zoledronic acid, to other bisphosphonates or to any of the other ingredients. Aclasta must not be used in patients with severe kidney problems, hypocalcaemia (low blood calcium levels), or in pregnant or breastfeeding women.

Why has Aclasta been approved?

The CHMP decided that Aclasta's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Aclasta?

A risk management plan has been developed to ensure that Aclasta is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Aclasta, including the appropriate precautions to be followed by healthcare professionals and patients.

The company that makes Aclasta will provide educational packs in each Member State for doctors who prescribe Aclasta for osteoporosis, reminding them how the medicine should be used. It will also provide an information pack for patients to explain the medicine's side effects, remind them of the need for adequate calcium and vitamin D supplementation, and when patients should contact their doctor. Patients will also be provided with a reminder card on the risk of osteonecrosis of the jaw, instructing patients to contact their doctor if they experience symptoms.

Other information about Aclasta:

The European Commission granted a marketing authorisation valid throughout the EU for Aclasta on 15 April 2005.

The full EPAR for Aclasta can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Aclasta, read the Package Leaflet (also part of the EPAR).

This summary was last updated in 04-2015.