Package leaflet: Information for the user

Aldurazyme 100 U/ml concentrate for solution for infusion
Laronidase

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Aldurazyme is and what it is used for

Aldurazyme is used to treat patients with MPS I disease (Mucopolysaccharidosis I). It is given to treat the non-neurological manifestations of the disease.

People with MPS I disease have either a low level or no level of an enzyme called α-L-iduronidase, which breaks down specific substances (glycosaminoglycans) in the body. As a result, these substances do not get broken down and processed by the body as they should. They accumulate in many tissues in the body, which causes the symptoms of MPS I.

Aldurazyme is an artificial enzyme called laronidase. This can replace the natural enzyme which is lacking in MPS I disease.

2. What you need to know before you are given Aldurazyme

You should not be given Aldurazyme
If you are allergic (hypersensitive) to laronidase or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before using Aldurazyme. If you are treated with Aldurazyme, you may develop infusion-associated reactions. An infusion-associated reaction is any side effect occurring during the infusion or until the end of the infusion day (see section 4 “Possible Side Effects”). Some of these reactions may be severe. When you experience such a reaction, **you should immediately contact your doctor**.

If these reactions occur, the Aldurazyme infusion should be stopped immediately and appropriate treatment will be started by your doctor.
These reactions may be particularly severe if you have a pre-existing MPS I-related upper airway obstruction.
You may be given additional medication such as antihistamines and paracetamol to help prevent allergic-type reactions.

Other medicines and Aldurazyme
Inform your doctor if you are using medicines containing chloroquine or procaine, due to a possible risk of decreasing the action of Aldurazyme.

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

Pregnancy, breast-feeding and fertility
There is not enough experience of the use of Aldurazyme in pregnant women. You should not be given Aldurazyme during pregnancy unless clearly necessary.
It is not known whether Aldurazyme appears in breast milk. It is recommended to stop breast-feeding during treatment with Aldurazyme.
No information is available on the effects of Aldurazyme on fertility.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines
The effects on the ability to drive and to use machines have not been studied.

Aldurazyme contains sodium
This medicinal product contains 1.29 mmol sodium per vial. To be taken into consideration by patients on a controlled sodium diet.

3. How Aldurazyme is given

Instruction for use - dilution and administration
The concentrate for solution for infusion has to be diluted before administration and is for intravenous use (see information for health care professionals).
Administration of Aldurazyme should be carried out in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available.

Dosage
The recommended dosage regimen of Aldurazyme is 100 U/kg body weight given once every week as an intravenous infusion. The initial infusion rate of 2 U/kg/h may be gradually increased every fifteen minutes, if tolerated, to a maximum of 43 U/kg/h. The total volume of the administration should be delivered in approximately 3-4 hours.

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

If you miss an infusion of Aldurazyme
If you have missed an Aldurazyme infusion, please contact your doctor.

If you are given more Aldurazyme than needed
No case of overdose of Aldurazyme has been reported.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects were mainly seen while patients were being given the medicine or shortly after (infusion-associated reactions). If you experience any reaction like this, you should **contact your doctor immediately.** The number of these reactions decreased the longer that patients were on Aldurazyme. The majority of these reactions were mild or moderate in intensity. However, severe systemic allergic reaction (anaphylactic reaction) has been observed in patients during or up to 3 hours after Aldurazyme infusions. Some of the symptoms of such a severe allergic reaction were life-threatening and included extreme difficulty breathing, swelling of the throat, low blood pressure, and low oxygen level in the body. A few patients who had a prior history of severe MPS I related upper airway and pulmonary involvement, experienced severe reactions including bronchospasm (airway constriction), respiratory arrest, and swelling of the face. The frequency of bronchospasm and respiratory arrest is unknown. The frequency of severe allergic reaction (anaphylactic reaction) and swelling of the face is considered common and may affect up to 1 in 10 people.

Very common symptoms (may affect more than 1 in 10 people) which were not serious include headache, nausea, abdominal pain, rash, joint disease, joint pain, back pain, pain in arms or legs, flushing, fever, chills, increased heart rate, increased blood pressure, and reaction at the infusion site.

Other side effects include the following:

Common (may affect up to 1 in 10 people)
- increased body temperature
- tingling
- dizziness
- cough
- difficulty in breathing
- vomiting
- diarrhoea
- swelling of the neck
- hives
- itching
- hair loss
- cold sweat, heavy sweating
- muscle pain
- paleness
- cold hands or feet
- feeling hot, feeling cold
- fatigue
- influenza like illness
- restlessness

Not known (frequency cannot be estimated from the available data)
- bluish color of the skin (due to lower levels of oxygen in the blood)
- fast breathing
- redness of the skin
- leakage of the drug into the surrounding tissue at the site of injection, which may cause swelling or redness
- swelling of arms and/or legs

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aldurazyme

Keep this medicine out of the sight and reach of children.

You should not be given this medicine after the expiry date which is stated on the label after the letters EXP. The expiry date refers to the last day of that month.

Unopened vials:
Store in a refrigerator (2°C – 8°C).

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aldurazyme contains
- The active substance is laronidase. One ml of the solution in the vial contains 100 U of laronidase. Each vial of 5 ml contains 500 U of laronidase.
- The other ingredients are sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, polysorbate 80, water for injections.

What Aldurazyme looks like and contents of the pack
Aldurazyme is supplied as a concentrate for solution for infusion. It is a solution that is clear to slightly opalescent, and colourless to pale yellow.

Pack size: 1, 10 and 25 vials per carton. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Genzyme Europe B.V., Gooimeer 10, NL-1411 DD, Naarden, The Netherlands.

Manufacturer
Genzyme Ltd., 37 Hollands Road, Haverhill, Suffolk CB9 8PU, United Kingdom.
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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Each vial of Aldurazyme is intended for single use only. The concentrate for solution for infusion has to be diluted with sodium chloride 9 mg/ml (0.9%) solution for infusion using aseptic technique. It is recommended that the diluted Aldurazyme solution be administered to patients using an infusion set equipped with an 0.2 μm in-line filter.

From a microbiological safety point of view, the product should be used immediately. If not used immediately, in-use storage should not be longer than 24 hours at 2°C - 8°C provided that dilution has taken place under controlled and validated aseptic conditions.

Aldurazyme should not be mixed with other medicinal products in the same infusion.

Preparation of the Aldurazyme Infusion (Use Aseptic Technique)
- Determine the number of vials to be diluted based on the individual patient's weight. Remove the required vials from the refrigerator approximately 20 minutes in advance in order to allow them to reach room temperature (below 30˚C).
- Before dilution, visually inspect each vial for particulate matter and discoloration. The clear to slightly opalescent and colourless to pale yellow solution should be free of visible particles. Do not use vials exhibiting particles or discoloration.
- Determine the total volume of infusion based on the individual patient's weight, either 100 ml (if bodyweight is less or equal than 20 kg) or 250 ml (if bodyweight is more than 20 kg) of 0.9% sodium chloride intravenous solution.
- Withdraw and discard a volume of sodium chloride 9 mg/ml (0.9%) solution for infusion from the infusion bag equal to the total volume of Aldurazyme to be added.
- Withdraw the required volume from the Aldurazyme vials and combine the withdrawn volumes.
- Add the combined volumes of Aldurazyme to the sodium chloride 9 mg/ml (0.9%) solution for infusion.
- Mix the solution for infusion gently.
- Prior to use visually inspect the solution for particulate matter. Only clear and colourless solutions without visible particles should be used.

Any unused product or waste material should be disposed of in accordance with local requirements.