Package leaflet: Information for the user

Replagal 1 mg/ml
concentrate for solution for infusion
agalsidase alfa

Read all of this leaflet carefully before you start taking 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 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 Replagal is and what it is used for

The active substance in Replagal is agalsidase alfa (1mg/ml). Agalsidase alfa is a form of the human enzyme α-galactosidase. It is produced by switching on the gene for α-galactosidase A in cells. The enzyme is then removed from the cells and made into a sterile concentrate for solution for infusion.

Replagal is used to treat adult patients, as well as adolescents and children from the age of 7, with confirmed diagnosis of Fabry Disease. It is used as long-term enzyme replacement therapy when the level of enzyme in the body is absent or lower than normal as in Fabry Disease.

After 6 months of therapy Replagal significantly reduced pain in patients when compared to placebo (dummy) treated patients. Replagal reduced left ventricle mass in treated patients compared to placebo treated patients. These results suggest the symptoms of the disease are improving or the disease is becoming stable.

2. What you need to know before Replagal is given

You must not be given Replagal

- if you are allergic to agalsidase alfa or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before Replagal is used.

If you notice any of these effects during or after an infusion you should tell your doctor immediately:
- high fever, chills, sweating, fast heart rate.
- vomiting.

- light-headedness.
- hives.
- swelling in your hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in swallowing or breathing.

Your doctor may stop the infusion temporarily (5 – 10 min) until the symptoms go away and then begin the infusion again.

Your doctor may also treat the symptoms with other medicines (antihistamines or corticosteroids).

Most of the time you can still be given Replagal even if these symptoms occur.

If you experience a severe allergic (anaphylactic-type) reaction, the administration of Replagal will be immediately discontinued and an appropriate treatment will have to be initiated by your doctor.

If treatment with Replagal makes your body produce antibodies this will not stop Replagal from working and the antibodies may disappear with time.

If you have advanced renal disease, you may find that your Replagal treatment has a limited effect on your kidneys. Talk to your doctor or pharmacist before using Replagal.

Children

The experience in children 0-6 years old is limited and therefore no dose can be recommended for this age group.

Other medicines and Replagal

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor if you use any medicines containing chloroquine, amiodarone, benoquin or gentamicin. There is a theoretical risk of decreased agalsidase alfa activity.

Pregnancy and breast feeding

Very limited clinical data on pregnancies exposed to Replagal have shown no adverse effects on the mother and newborn child.

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 taking this medicine.

Driving and using machines

You may drive and use machines whilst on Replagal.

Replagal contains sodium

This medicine contains 14.2 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 0.7 % of the recommended maximum daily dietary intake of sodium for an adult.

Keeping a record

In order to improve the traceability of biological medicinal products, the name and batch number of the administered product should be clearly recorded by your healthcare professional. Speak with your healthcare professional if you are not sure.

3. How Replagal is given

This medicine should be applied and supervised by appropriately trained personnel, who will also calculate the dose that you will be given. While remaining under the physician's supervision, Replagal can be self-administered (by you or your caregiver) after appropriate training by the treating physician and/or nurse. Self-administration should occur in the presence of a responsible adult.

The recommended dose is an infusion of 0.2 mg for every kg you weigh. This would be about 14 mg or 4 vials (glass bottles) of Replagal for an average size (70 kg) individual.

Use in children and adolescents

For children and adolescents 7-18 years old a dose of 0.2 mg/kg every other week may be used.

Children and adolescents may be more likely than adults to experience an infusion related reaction. Tell your doctor if you experience any side effects whilst having the infusion.

Method of administration

Replagal has to be diluted in 9 mg/ml (0.9%) sodium chloride solution before use. After dilution Replagal is given in a vein. This will usually be in your arm.

The infusion will be given every two weeks.

Each time you are treated it will take 40 minutes for Replagal to be given to you in a vein. Your treatment will be supervised by a doctor who specialises in the treatment of Fabry Disease.

For self-administration, the dose and rate of infusion given should not be changed without the agreement of the treating physician.

If you use more Replagal than you should

If you believe you have used more Replagal than you should, please contact your doctor.

If you use less Replagal than you should

If you believe you have used less Replagal than you should, please contact your doctor.

If you forget to use Replagal

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

If you stop using Replagal

Do not stop using Replagal without contacting your doctor.

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.

If you experience a severe allergic (anaphylactic-type) reaction, the administration of Replagal will be immediately discontinued and an appropriate treatment will have to be initiated by your doctor.

Most side effects are mild to moderate. More than 1 in 10 people (frequency "very common") may have a reaction during or following an infusion of Replagal (infusion related reaction). These effects include chills, headache, nausea, fever, tiredness, unsteadiness, difficulty breathing, shaking, cough and vomiting. However, some effects may be serious and may need treatment. Infusion related reactions involving the heart including heart muscle ischemia and heart failure, may occur in patients with Fabry disease involving the heart structures (frequency "not known" (cannot be estimated from the available data)). Your doctor may stop the infusion temporarily (5 - 10 min) until the symptoms go away and then begin the infusion again. Your doctor may also treat the symptoms with other medicines (antihistamines or corticosteroids). Most of the time you can still be given Replagal even if these symptoms occur.

List of other side effects:

Very common: may affect more than 1 in 10 people
- swelling in the tissue (e.g., legs, arm)
- tingling or numbness or pain in fingers or toes
- ear ringing
- palpitations
- sore throat
- abdominal pain, diarrhoea
- rash
- back or limb pain, muscle pain, joint pain
- chest pain, cold symptoms, fever, feeling sick

Common: may affect up to 1 in 10 people:
- change in the taste of food, prolonged sleep
- eyes tearing
- increased ear ringing
- increased heart rate, heart rhythm problems
- increased blood pressure, low blood pressure, facial flushing (redness)
- hoarseness, or tight throat, runny nose
- abdominal discomfort
- acne, red or itchy or mottled skin, excessive sweating
- muscle and bone discomfort, swelling of the extremities or joints
- hypersensitivity
- chest tightness, increased feeling lack of energy, feeling cold or hot, flu-like symptoms, discomfort

Uncommon: may affect up to 1 in 100 people:
- severe allergic (anaphylactic-type) reaction
- blink reflex abnormal
- increased heart rate
- low level of oxygen in your blood and sticky throat secretions
- sense of smell is different
- collection of fluid under the skin may lead to swelling of body parts, lace-like discoloration of the skin e.g., in the leg
- sensation of heaviness
  injection site rash

Children and adolescents

Side effects reported in children were, in general, similar to those reported in adults. However, infusion related reactions (fever, difficulty breathing, chest pain) and pain aggravated occurred more frequently.

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 Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Replagal

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 label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).

Do not use Replagal if you notice that there is discolouration or other foreign particles present.

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 to protect the environment.

6. Contents of the pack and other information

What Replagal contains

- The active substance is agalsidase alfa. Each ml of Replagal contains 1 mg of agalsidase alfa.
- The other ingredients are: Sodium phosphate monobasic, monohydrate
  Polysorbate 20
  Sodium chloride
  Sodium hydroxide
  Water for injections

Replagal contains sodium. See section 2.

What Replagal looks like and contents of the pack

Replagal is a concentrate for solution for infusion. Your medicine is available in vials containing 3.5 mg/ 3.5 ml of agalsidase alfa. Pack sizes of 1, 4 or 10 vials are available.
Not all pack sizes may be marketed.

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This leaflet was last revised in February 2023.

The following information is intended for medical or healthcare professionals only:

Instructions for use, handling and disposal

Replagal treatment should be supervised by a physician experienced in the management of patients with Fabry Disease or other inherited metabolic diseases.

Replagal is administered at a dose of 0.2 mg/kg body weight every other week by intravenous infusion over 40 minutes.

1. Calculate the dose and number of Replagal vials needed.

2. Dilute the total volume of Replagal concentrate required in 100 ml 9 mg/ml sodium chloride solution for infusion (0.9%w/v). Care must be taken to ensure the sterility of the prepared solutions since Replagal does not contain any preservative or bacteriostatic agent; aseptic technique must be observed. Once diluted, the solution should be mixed gently but not shaken.

3. The solution should be inspected visually for particulate matter and discolouration prior to administration.

4. Administer the infusion solution over a period of 40 minutes using an intravenous line with an integral filter. Since no preservative is present, it is recommended that administration is started as soon as possible. However, the chemical and physical stability of the diluted solution has been demonstrated for 24 hours at 25°C.

5. Do not infuse Replagal concomitantly in the same intravenous line with other agents.

6. For single use only. Any unused product or waste material should be disposed of in accordance with local requirements.