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REPLAGAL™ 1 mg/ml

Concentrate for solution for infusion

Agalsidase alfa

Shire
Human Genetic Therapies

Read all of this leaflet carefully before you start taking this medicine.
- 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. 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 or pharmacist.

In this leaflet:

1. WHAT REPLAGAL IS AND WHAT IT IS USED FOR

The active substance in Replagal is agalsidase alfa (1 mg/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 Fabry Disease. It is used as enzyme replacement therapy when the level of enzyme in the body is lower than normal as in Fabry Disease.

2. BEFORE YOU TAKE REPLAGAL

Do not take Replagal

If you are allergic (hypersensitive) to agalsidase alfa or any of the other ingredients of Replagal.

Take special care with Replagal

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, itching or rash;
- swelling in your hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in swallowing or breathing;
- pain or tenderness in chest, muscles or joints.

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 working and the antibodies may disappear with time.

Use in Children

There is limited clinical data in children 7-18 years old. No unexpected safety issues were encountered in the studies with Replagal in children 7-18 years of age. Following treatment with Replagal 0.2mg/kg every other week, changes in the clinical parameters of Fabry disease in children were similar to those seen in earlier adult Fabry patient studies.

Using other medicines

There is no known interaction of Replagal with other medicines.

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

Taking Replagal with food and drink

Interactions with food or drink are unlikely.

Pregnancy and breast feeding

Very limited clinical data on pregnancies exposed to Replagal (n=4) have shown no adverse effects on the mother and newborn child.

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

Driving and using machines

You may drive and operate machinery whilst on Replagal.

3. HOW TO TAKE REPLAGAL

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 usual 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. 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 is specialized in the treatment of Fabry Disease.

If you forget to have Replagal

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

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Replagal can cause side effects, although not everybody gets them. Most side effects are mild to moderate. About 1 out of 7 patients may have a reaction during or following an infusion of Replagal. These effects include chills, headache, nausea, fever, facial flushing (redness) and tiredness. Low blood pressure may also occur. However some effects may be serious and may need treatment.

Very common side effects (occurring in more than 1 in 10 treated patients) include the following:
- headache
- flushing (redness)
- nausea
- chills, fever
- general pain or discomfort, tiredness.

Common side effects (occurring in less than 1 in 10 treated patients) include the following:
- tingling or numbness or pain in fingers or toes, change in the taste of food, eyes tearing, ears ringing, shakes, unsteadiness, prolonged sleep
- palpitations, increased heart rate, increased blood pressure
- cough, chest pain or tightness, hoarseness, sore or tight throat, sticky throat secretions, runny nose
- vomiting, abdominal pain or discomfort, diarrhoea
- acne, red or itchy or mottled skin, rash at the infusion site
- back or limb pain, swelling of the extremities or joints
- feeling cold or hot, flu-like symptoms, malaise

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

5. HOW TO STORE REPLAGAL

Keep out of the reach and sight of children.

Do not use Replagal 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.

Store in a refrigerator (2°C to 8°C).

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

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Replagal contains

- The active substance is agalsidase alfa (1 mg/1 ml)
- The other ingredients are: Sodium phosphate monobasic, monohydrate
  Polysorbate 20
  Sodium chloride
  Sodium hydroxide
  Water for injections

What Replagal looks like and contents of the pack

Replagal is a concentrate for solution for infusion. A clear and colourless solution.
Your medicine is available in vials (Type I glass) containing 1 mg/1 ml of agalsidase alfa.
Pack sizes of 1, 4 or 10 vials are available.
Not all pack sizes may be marketed.

Marketing Authorization Holder:

Shire Human Genetic Therapies AB, Svärdvägen 11 D, 182 33 Danderyd, Sweden

Manufacturers:

There are three alternative sites responsible for the manufacture of the drug product:

Vetter Pharma-Fertigung GmbH & Co. KG
Eisenbahnstrasse 2-4
88085 Langenargen, Germany

Cangene bioPharma, Inc. (CBI)
1111 South Paca Street
Baltimore, MD 21230, USA

Baxter Pharmaceutical Solutions LLC
927 South Curry Pike
Bloomington, IN 47402, USA

For any information about this medicine or to report any side effects in Lebanon and all MENA countries, please contact the local representative of the Marketing Authorisation Holder:

Biologix FZ Co., Dubai Free Zone, Road WB 21, Warehouse C17, PO Box 54405, Al Tawar, Dubai, United Arab Emirates.
Telephone no.: 00971 4 2997171
Email address: Pharmacovigilance@blgx.net

This leaflet was last approved in 12/2011; version number 3.

To report any side effect(s):

• Lebanon and All MENA countries:

Biologix FZ Co.
Fax: + 961 9 222141
Email: Pharmacovigilance@blgx.net
Website: www.algorithm-lb.com

• Saudi Arabia:

- National Pharmacovigilance and Drug Safety Center (NPC)
  Call NPC at +966-11-2038222,
  Exts: 2317-2356-2353-2354-2334-2340
  • Fax: +966-11-205-7662
  • Toll-free: 8002490000
  • Email: npc.drug@sfda.gov.sa
  • Website: www. sfda.gov.sa/npc

• Other GCC States

Also contact the relevant competent authority.

This is a medicinal product
- A medicinal product is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicinal product.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicines out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists

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 and within 3 hours of dilution. 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.