Scheduling Status:

S4

REPLAGAL 1 mg/ml concentrate for solution for infusion

agalsidase alfa

Sugar free

Read all of this leaflet before you are given REPLAGAL.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor pharmacist, nurse or other health care provider.

What is in this leaflet

1. What REPLAGAL is and what it is used for

2. What you need to know before you take REPLAGAL

3. How to take REPLAGAL

4. Possible side effects

5. How to store REPLAGAL

6. Contents of the pack and other information

1. What REPLAGAL is and what it is used for

Active ingredient: agalsidase alfa

Inactive ingredients: Sodium phosphate monobasic, monohydrate; Polysorbate 20; Sodium chloride; Sodium hydroxide and Water for injections.

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.

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. What you need to know before you use REPLAGAL

REPLAGAL should not be administered to you:

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

Warnings and Precautions

Tell your doctor or health care provider before being given the infusion:

If you notice any of the effects below during or after an infusion you should tell your doctor immediately:

- high fever, chills, fast heart rate;
- vomiting;
- light-headedness;
- hives
- swelling of 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 working and the antibodies may disappear with time.

Children and Adolescents

REPLAGAL has not yet been studied in children less than 6 years old and there is only 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.

Other medicines and REPLAGAL:

Always tell your healthcare provider if you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of REPLAGAL with these medicines may cause undesirable interactions. Tell your doctor or pharmacist if you are taking any other medicines, including any you have bought at your pharmacy, supermarket or health food shop. Please consult your doctor, pharmacist or other healthcare professional for advice.

REPLAGAL with food and drink:

Interactions with food or drink are unlikely.

Pregnancy and breastfeeding:

If you are pregnant or breast-feeding your baby while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

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

Driving and using machinery:

You may drive and operate machinery whilst on REPLAGAL.

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 medicines, 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 to use REPLAGAL

Always take REPLAGAL exactly as your doctor has told you. You should check with your doctor if you are unsure.

While remaining under the medical doctors supervision, Replagal can be self-administered (by you or your caregiver) after appropriate training by the treating medical doctor and/or nurse.
Self-administration should occur in the presence of a responsible adult.

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.

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

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.

If you have the impression that the effect of REPLAGAL is too strong or too weak, talk to your doctor or pharmacist.

If you take more REPLAGAL than you should:

Since a health care provider will administer REPLAGAL, he/she will control the dosage. However, in the event of overdosage, your doctor will manage the overdosage

If you forget to have REPLAGAL:

Since a health care provider will administer REPLAGAL, it is unlikely that the dose will be missed. If, however, you have missed a REPLAGAL infusion, please contact your doctor

4. Possible side effects

REPLAGAL can have side effects. Not all side effects reported for REPLAGAL are included in this leaflet.

Most side effects of REPLAGAL are mild to moderate. More than 1 in 10 people (frequency “very common”) may have a reaction during or following an infusion of REPLAGAL. 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 (eg legs, arm)
- tingling or numbness or pain in fingers or toes
- ear ringing
- palpitations
- Sore throat
- abdominal pain, diarrhoea
- rash at the infusion site
- 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 eg in the leg
- sensation of heaviness
- injection site rash

Should your general health worsen while taking REPLAGAL, or 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.

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 side effects, talk to your doctor. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of REPLAGAL

5. How to store REPLAGAL

- Store in a refrigerator (2 °C – 8 °C).
- Do not freeze.
- STORE ALL MEDICINES OUT OF REACH 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.
- Do not use REPLAGAL if you notice that there is discolouration or other foreign particles present.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets)

6 Contents of the pack and other information

What REPLAGAL contains

The active substance is agalsidase alfa.

The other ingredients are:

Sodium phosphate monobasic

Monohydrate

Polysorbate 20

Sodium chloride

Sodium hydroxide

Water for injection.

What REPLAGAL looks like and contents of the pack

Your medicine is available in clear, transparent 5 ml glass vials containing 3,5 mg/ 3,5 ml of agalsidase alfa. The vials are closed with a grey rubber stopper and sealed with a one-piece aluminium seal and white flip-off cap. Pack sizes of 1, 4 or 10 vials are available.

REPLAGAL is a clear and colourless solution and essentially free of particles. Finished product may develop a minute amount of fine particulate matter during storage.

Holder of Certificate of Registration

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

Instructions for use, handling and disposal

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.