Package leaflet: Information for the user

Fabrazyme 35 mg

powder for concentrate for solution for infusion
Agalsidase beta

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 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 Fabrazyme is and what it is used for

Fabrazyme contains the active substance agalsidase beta and is used as enzyme replacement therapy in Fabry disease, where the level of α-galactosidase enzyme activity is absent or lower than normal. If you suffer from Fabry disease a fat substance, called globotriaosylceramide (GL-3), is not removed from the cells of your body and starts to accumulate in the walls of the blood vessels of your organs.

Fabrazyme is indicated for use as long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease.

Fabrazyme is indicated in adults, children and adolescents aged 8 years and older.

2. What you need to know before you use Fabrazyme

Do not use Fabrazyme
- if you are allergic to agalsidase beta or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before using Fabrazyme.

If you are treated with Fabrazyme, 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). If you experience a reaction like this, you should **tell your doctor immediately**. You may need to be given additional medicines to prevent such reactions from occurring.

Children and adolescents
No clinical studies have been performed in children 0-4 years old. The risks and benefits of Fabrazyme in children aged 5 to 7 years have not yet been established and therefore no dose can be recommended for this age group.

Other medicines and Fabrazyme
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 beta activity.

Pregnancy, breast-feeding and fertility
Use of Fabrazyme during pregnancy is not recommended. There is no experience with the use of Fabrazyme in pregnant women. Fabrazyme may get into breast milk. Use of Fabrazyme during breast-feeding is not recommended. Studies have not been performed to examine the effects of Fabrazyme 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 taking this medicine.

Driving and using machines
Do not drive or use machines if you experience dizziness, sleepiness, vertigo or fainting during or shortly after administration of Fabrazyme (see section 4). Talk to your doctor first.

Fabrazyme contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.

3. How to use Fabrazyme

Fabrazyme is given through a drip into a vein (by intravenous infusion). It is supplied as a powder which will be mixed with sterile water before it is given (see information for Health Care Professionals at the end of this leaflet).
Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Fabrazyme is only used under the supervision of a doctor who is knowledgeable in the treatment of Fabry disease. Your doctor may advise that you can be treated at home provided you meet certain criteria. Please contact your doctor if you would like to be treated at home.

The recommended dose of Fabrazyme for adults is 1 mg/kg body weight, once every 2 weeks. No changes in dose are necessary for patients with kidney disease.

Use in children and adolescents
The recommended dose of Fabrazyme for children and adolescents 8 – 16 years is 1 mg/kg body weight, once every 2 weeks. No changes in dose are necessary for patients with kidney disease.

If you use more Fabrazyme than you should
Doses up to 3 mg/kg body weight have shown to be safe.

If you forget to use Fabrazyme
If you have missed an infusion of Fabrazyme, please contact your doctor.

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

4. Possible side effects

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

In clinical studies side effects were mainly seen while patients were being given the medicine or shortly after ("infusion related reactions"). Severe life-threatening allergic reactions ("anaphylactoid reactions") have been reported in some patients. If you experience any serious side effect, you should **contact your doctor immediately**.

Very common symptoms (may affect more than 1 in 10 people) include chills, fever, feeling cold, nausea, vomiting, headache and abnormal feelings in the skin such as burning or tingling. Your doctor may decide to lower the infusion rate or give you additional medicines to prevent such reactions from occurring.

List of other side effects:

Common (may affect up to 1 in 10 people):
- chest pain
- difficulty in breathing
- pallor
- itching
- abnormal tear secretion
- feeling weak
- tinnitus
- nasal congestion
- diarrhoea
- redness
- muscle pain
- increased blood pressure
- sudden swelling of the face or throat
- oedema in extremities
- vertigo
- stomach discomfort
- muscle spasms
- sleepiness
- increased heart beat
- abdominal pain
- back pain
- rash
- low heart rate
- lethargy
- syncope
- cough
- abdominal discomfort
- swelling face
- joint pain
- decreased blood pressure
- chest discomfort
- face oedema
- exacerbated difficulty in breathing
- muscle tightness
- fatigue
- flushing
- pain
- throat tightness
- dizziness
- palpitations
- decreased sensitivity to pain
- burning sensation
- wheezing
- urticaria
- pain at the extremities
- nasopharyngitis
- hot flush
- feeling hot
- hyperthermia
- decreased mouth sensitivity
- musculoskeletal stiffness

Uncommon (may affect up to 1 in 100 people):
- tremor
- red eyes
- ear pain
- throat pain
- fast breathing
- itchy rash
- feeling hot and cold
- difficulty swallowing
- infusion site pain
- infusion site reaction
- itching eyes
- ear swelling
- bronchospasm
- runny nose
- heart burn
- skin discomfort
- musculoskeletal pain
- rhinitis
- influenza-like illness
- malaise
- low heart rate due to conduction disturbances
- increased sensitivity to pain
- upper respiratory tract congestion
- red rash
- (mottled purplish) skin discoloration
- coldness of the extremities
- injection site blood clotting
- skin discoloration
- oedema

The following information is intended for healthcare professionals only:

Instructions for use – reconstitution, dilution and administration

The powder for concentrate for solution for infusion has to be reconstituted with water for injections, diluted with 0.9% sodium chloride intravenous solution and then administered by intravenous infusion.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage and conditions are the responsibility of the user. The reconstituted solution cannot be stored and should be promptly diluted; only the diluted solution can be held for up to 24 hours at 2ºC -8ºC.

Use Aseptic Technique

1. Determine the number of vials to be reconstituted based on the individual patient's weight and remove the required vials from the refrigerator in order to allow them to reach room temperature (in approximately 30 minutes). Each vial of Fabrazyme is intended for single use only.

Reconstitution

2. Reconstitute each vial of Fabrazyme 35 mg with 7.2 ml water for injections. Avoid forceful impact of the water for injections on the powder and avoid foaming. This is done by slow drop-wise addition of the water for injection down the inside of the vial and not directly onto the lyophilized cake. Roll and tilt each vial gently. Do not invert, swirl or shake the vial.

3. The reconstituted solution contains 5 mg agalsidase beta per ml, and appears as a clear colourless solution. The pH of the reconstituted solution is approximately 7.0. Before further dilution, visually inspect the reconstituted solution in each vial for particulate matter and discoloration. Do not use the solution if foreign particles are observed or if the solution is discoloured.

4. After reconstitution it is recommended to promptly dilute the vials, to minimise protein particle formation over time.

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

Dilution

6. Prior to adding the reconstituted volume of Fabrazyme required for the patient dose, it is recommended to remove an equal volume of 0.9% sodium chloride intravenous solution, from the infusion bag.

7. Remove the airspace within the infusion bag to minimize the air/liquid interface.

8. Slowly, withdraw 7.0 ml (equal to 35 mg) of the reconstituted solution from each vial up to the total volume required for the patient dose. Do not use filter needles and avoid foaming.

9. Then slowly inject the reconstituted solution directly into the 0.9% sodium chloride intravenous solution (not in any remaining airspace) to a final concentration between 0.05 mg/ml and 0.7 mg/ml. Determine the total volume of sodium chloride 0.9% solution for infusion (between 50 and 500 ml) based on the individual dose. For doses lower than 35 mg use a minimum of 50 ml, for doses 35 to 70 mg use a minimum of 100 ml, for doses 70 to 100 mg use a minimum of 250 ml and for doses greater than 100 mg use only 500 ml. Gently invert or lightly massage the infusion bag to mix the diluted solution.

Not known (frequency cannot be estimated from the available data):

- lower blood oxygen levels
- serious inflammation of the vessels

In some patients initially treated at the recommended dose, and whose dose was later reduced for an extended period, some symptoms of Fabry disease were reported 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 national reporting system listed below. By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace 4
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
www.medicinesauthority.gov.mt/adrportal

5. How to store Fabrazyme

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 after 'EXP'. The expiry date refers to the last day of that month.

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

Reconstituted and diluted solutions
The reconstituted solution cannot be stored and should be promptly diluted. The diluted solution can be held for up to 24 hours at 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 Fabrazyme contains
- The active substance is agalsidase beta, one vial contains 35 mg.
- The other ingredients are:
  - Mannitol
  - Sodium phosphate monobasic, monohydrate
  - Sodium phosphate dibasic, heptahydrate.

What Fabrazyme looks like and contents of the pack
Fabrazyme is supplied as a white to off-white powder. After reconstitution it is a clear, colourless liquid, free from foreign matter. The reconstituted solution must be further diluted. Package sizes: 1, 5 and 10 vials per carton. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing authorisation holder
Genzyme Europe B.V., Paasheuvelweg 25,
1105 BP Amsterdam, The Netherlands
Manufacturer
Genzyme Ireland Limited, IDA Industrial Park,
Old Kilmeaden Road, Waterford, Ireland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Malta
Sanofi S.r.l.
Tel: +39 02 39394275

Ireland
sanofi-aventis Ireland Ltd. T/A SANOFI
Tel: +353 (0) 1 403 56 00

United Kingdom
Sanofi
Tel +44 (0)845 372 7101

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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.

Do not shake or excessively agitate the infusion bag.

Administration

10. It is recommended to administer the diluted solution through an in-line low protein-binding 0.2 µm filter to remove any protein particles which will not lead to any loss of agalsidase beta activity. The initial infusion rate should be no more than 0.25 mg/min (15 mg/hour) to minimise the potential occurrence of infusion-associated reactions. After patient tolerance is established, the infusion rate may be increased gradually with subsequent infusions.