PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

FABRAZYME® 5 mg powder for solution for infusion

FABRAZYME® 35 mg powder for solution for infusion

Agalsidase beta

Contains sugar alcohol (mannitol).

FABRAZYME 5 mg: Each vial contains 30 mg mannitol after reconstitution.

FABRAZYME 35 mg: Each vial contains 210 mg mannitol after reconstitution.

Read all of this this leaflet carefully before you are given FABRAZYME.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- FABRAZYME has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What FABRAZYME is and what it is used for

FABRAZYME contains the active substance agalsidase beta.

FABRAZYME 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.

2. What you need to know before you use FABRAZYME

Do not use FABRAZYME

- If you have experienced an allergic anaphylactic reaction to agalsidase beta or if you are allergic (hypersensitive) to any of the other ingredients of FABRAZYME (listed in section 6 of this leaflet).

Warnings and precautions

Take special care with 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.
- If you have advanced kidney disease.

Children and adolescents

The safety and efficacy of FABRAZYME have not been evaluated in patients younger than 8 years old.

Other medicines and FABRAZYME

Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

FABRAZYME should not be administered with chloroquine, amiodarone, benoquin or gentamicin, due to a risk of decreased agalsidase beta activity.

FABRAZYME with food and drink

Interactions with food and drink are unlikely.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before using FABRAZYME.

Use of FABRAZYME during pregnancy is not recommended. There is no experience with the use of FABRAZYME in pregnant women. FABRAZYME may be excreted into breast milk. Use of FABRAZYME during breastfeeding is not recommended.

Driving or using machines

FABRAZYME may interfere with your ability to drive a vehicle or operate machinery. You should not drive a vehicle or operate machinery until you know how FABRAZYME affects you.

3. How to use FABRAZYME

Do not share medicines prescribed for you with any other person.

Always use FABRAZYME exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

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.

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 providers at the end of this leaflet).

The recommended dose of FABRAZYME is 1 mg/kg body weight, once every 2 weeks. The rate of infusion will be decided by your doctor and may not be changed without the supervision of your doctor.

If you have the impression that the effect of FABRAZYME is too strong or too weak, talk to your doctor or health care provider.

If you receive more FABRAZYME than you should

Your doctor or health care provider will administer FABRAZYME to you and make sure you receive the correct dosage at the correct time.
However, in the event of an overdosage your doctor will manage the overdosage.

If you forget to use FABRAZYME

If you have missed an infusion of FABRAZYME please contact your doctor or health care provider.

4. Possible side effects

FABRAZYME can have side effects.

Not all side effects reported for FABRAZYME are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving FABRAZYME, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop receiving FABRAZYME and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash, hives or itching.
- Fainting.

These are all serious side effects. If you have them, you may have had a serious allergic reaction to FABRAZYME. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent:

- Yellowing of your skin and eyes, also called jaundice.
- Heart palpitations.
- Increased heart rate.
- Shortness of breath.
- Fever and chills.

Less frequent:

- Decreased heart rate.
- Infusion-associated reactions (such as fever, chills, flushing, itching, difficulty breathing, throat tightness, chest discomfort, itchy rash, runny nose, abdominal pain, nausea, vomiting, muscle pain and headache). See section “Warnings and precautions”.

Frequency unknown:

- Serious inflammation of the blood vessels, appearing as purple raised itchy lesions on the skin. Your organs may also be affected and cause symptoms such as fever, muscle aches, joint pain, blood in the urine or stool, abdominal pain, vomiting, cough, numbness and weakness.
- Serious kidney disease which may cause kidney failure, with symptoms such as swelling in the legs and ankles, weight gain, fatigue, poor appetite and urine that looks foamy.
- Lack of oxygen affecting your tissue, causing changes in the colour of your skin, ranging from blue to cherry red.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor as soon as possible if you notice any of the following:

Frequent:

- Nausea, vomiting.
- Headache.
- Abnormal sensations such as tingling anywhere in the body.
- Ringing/buzzing in the ears.
- Motion sickness.
- Increased tear formation.
- Cold symptoms.
- Muscle pain/spasms, pain in the extremities, back pain, joint pain, muscle stiffness.
- Dizziness, drowsiness, reduced sensation to touch, burning sensation, feeling of exhaustion.
- Nasal congestion, cough, wheezing.
- Redness of the skin.
- Flushing, increase/decrease in blood pressure, pale skin colour.

Less frequent:

- Swelling or pain of the ear area.
- Reddening of the eyes.
- Indigestion, difficulty swallowing.

- Influenza-like symptoms.
- Stuffy nose.
- Increased sensitivity to stimulation.
- Pain in the throat and airways.
- Purplish discolouration of the skin.
- Skin discomfort.
- Infusion site pain.
- Blood clotting at injection site.

Frequency unknown:

- Blood test results showing lower blood oxygen levels.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256-3700 (tel), or
- 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 FABRAZYME.

5. How to store FABRAZYME

Unopened vials:

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

Reconstituted and diluted solutions:

FABRAZYME contains no preservatives. From a microbiological point of view, FABRAZYME should be used immediately. If not used immediately, in-use storage and conditions prior to use are the responsibility of the user. The reconstituted solution cannot be stored and should be promptly diluted. Only the diluted solution can be stored for up to 24 hours at 2 °C to 8 °C.

- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the label or carton.
- 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 FABRAZYME contains

The active ingredient is agalsidase beta.

FABRAZYME 5 mg:

Each vial of FABRAZYME 5 mg contains a nominal value of 5 mg of agalsidase beta. After reconstitution each vial contains 5 mg/mL of agalsidase beta. The reconstituted solution must be further diluted.

FABRAZYME 35 mg:

Each vial of FABRAZYME 35 mg contains a nominal value of 35 mg of agalsidase beta. After reconstitution each vial contains 5 mg/mL (35 mg/7 mL) of agalsidase beta. The reconstituted solution must be further diluted.

For information on reconstitution and dilution of FABRAZYME, see information for health care providers at the end of this leaflet.

The other ingredients are mannitol and sodium phosphate.

What FABRAZYME looks like and the contents of the pack

FABRAZYME is a sterile, non-pyrogenic, white to off-white lyophilised cake or powder.

The reconstituted product is a clear solution, free from foreign matter.

FABRAZYME 5 mg is supplied in a single-use, clear type I glass 5 mL vial (5 mg). The closure consists of a grey siliconised butyl stopper and an aluminium seal with a grey plastic flip-off cap.

Pack size: 1 vial per carton.

FABRAZYME 35 mg is supplied in a single-use, clear type I glass 20 mL vial (35 mg). The closure consists of a grey siliconised butyl stopper and an aluminium seal with a purple plastic flip-off cap.

Pack size: 1 vial per carton.

Holder of the certificate of registration

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Registration numbers

FABRAZYME 5 mg: 46/31/0583

FABRAZYME 35 mg: 46/31/0584

Date of registration: 12 December 2017

The following information is intended for health care providers only.

Instructions for use – reconstitution, dilution and administration:

The powder concentrate for solution for infusion must be reconstituted with sterile water for injection, diluted with 0,9 % sodium chloride intravenous solution and then administered by intravenous infusion.

FABRAZYME contains no preservatives. From a microbiological point of view, FABRAZYME 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 stored for up to 24 hours at 2 °C – 8 °C.

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 **FABRAZYME 5 mg** vial by slowly injecting 1,1 mL of sterile water for injection. Avoid forceful impact of the water for injection on the powder and avoid foaming. This is done by slow dropwise addition of sterile water for injection down the inside wall of the vial and not directly onto the lyophilised cake. Roll and tilt each vial gently. Do not invert, swirl or shake the vial. Each vial will yield a 5,0 mg/mL clear, colourless solution (total extractable dose per vial is 5 mg, 1,0 mL).
Reconstitute each **FABRAZYME 35 mg** vial by slowly injecting 7,2 mL of sterile water for injection. Avoid forceful impact of the sterile water for injection on the powder and avoid foaming. This is done by slow dropwise addition of sterile water for injection down the inside wall of the vial and not directly

onto the lyophilised cake. Roll and tilt each vial gently. Do not invert, swirl or shake the vial. Each vial will yield a 5,0 mg/mL clear, colourless solution (total extractable dose per vial is 35 mg, 7,0 mL).

3. The reconstituted solution contains 5 mg agalsidase beta per mL. FABRAZYME 5 mg's total extractable dose per vial is 5 mg, 1,0 mL. FABRAZYME 35 mg's total extractable dose per vial is 35 mg, 7,0 mL.

4. The reconstituted solution appears as a clear, colourless solution. Before further dilution, visually inspect the reconstituted solution in each vial for particulate matter and discolouration. Do not use the solution if foreign particles are observed or if the solution is discoloured.

5. After reconstitution it is recommended to promptly dilute the vials, to minimise protein particle formation over time (see section "Dilution").

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

Dilution:

7. 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.

8. Remove the airspace within the infusion bag to minimise the air/liquid interface.

9. Slowly, withdraw 1,0 mL (equal to 5 mg) or 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.

10. Then slowly inject the reconstituted solution directly into the 0,9 % sodium chloride intravenous solution (not into any remaining airspace) to a final concentration between 0,05 mg/mL and 0,7 mg/mL. Determine the total volume of 0,9 % sodium chloride 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. Do not shake or excessively agitate the infusion bag.

Administration:

11. 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.

Pharmaceutical incompatibilities:

FABRAZYME must not be mixed with other medicines in the same infusion.