Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Fabrazyme 35 mg
Powder for concentrate for solution for infusion

Active ingredient:
Each vial contains agalsidase beta 35 mg
After reconstitution each vial contains 5 mg of agalsidase beta per ml.

Inactive ingredients and allergens: see section 2 'Important information about some of this medicine's ingredients' and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

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

Therapeutic group: other alimentary tract and metabolism products – enzymes.

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 in your organs.

2. Before using this medicine

Do not use this medicine if:

You are sensitive (allergic) to agalsidase beta or to any of the other ingredients in this medicine (see section 6).

Special warnings about using this medicine
Talk to your doctor or pharmacist before using Fabrazyme.
If you are treated with Fabrazyme, you may develop infusion related reactions. An infusion related reaction is any side effect occurring during the infusion or until the end of the infusion day (see section 4). If you experience such a reaction, you should **tell your doctor immediately**. You may need to receive additional medicines to prevent such reactions from occurring.

Children and adolescents
No clinical studies have been performed in children aged 0 to 4 years. 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.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist.
Particularly if you are taking:
Chloroquine (to treat malaria), amiodarone (to treat arrhythmia), benoquin or gentamicin (to treat bacterial infections). There is a theoretical risk of decreased agalsidase beta activity.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine.
Use of Fabrazyme during pregnancy is not recommended. There is no experience with the use of Fabrazyme in pregnant women.
Fabrazyme may penetrate into breast milk. Use of Fabrazyme during breastfeeding is not recommended.
No studies have been performed to examine the effects of Fabrazyme on fertility.

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.

Important information about some of this medicine's ingredients
This medicine contains less than 1 mmol (23 mg) sodium per vial, that is to say essentially 'sodium free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually:
1 mg/kg body weight, once every 2 weeks. No changes in dosage are necessary for patients with kidney disease.

Do not exceed the recommended dose.

Mode of administration
Fabrazyme is given by infusion into a vein (by intravenous infusion). It is supplied as a powder which will be mixed with sterile water prior to administration.

If you use more Fabrazyme than you should
Dosages 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.
Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Fabrazyme may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

In clinical studies, side effects were observed mainly during administration of the medicine to patients or shortly after administration ("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 side effects (may affect more than one in ten users):
chills, fever, feeling cold, nausea, vomiting, headache and abnormal sensations 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.

Additional side effects
Common side effects - affect 1-10 in 100 users:

- 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
- loss of consciousness (syncope)
- cough
- abdominal discomfort
- swelling of the face
- joint pain
- decreased blood pressure
- chest discomfort
- facial 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 flushes
- feeling hot
- high fever (hyperthermia)
- decreased mouth sensitivity
- musculoskeletal stiffness

Uncommon side effects - affect 1-10 in 1,000 users:

- tremor
- eye redness
- ear pain
- throat pain
- fast breathing
- itchy rash
- feeling hot and cold
- difficulty in swallowing
- infusion site pain
- infusion site reaction
- itching eyes
- ear swelling
- bronchospasm
- runny nose
- heartburn
- 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
- skin discolouration (purplish spots)
- coldness of the extremities
- blood clot formation at the injection site
- skin discolouration
- oedema

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- lower blood oxygen levels
- serious inflammation of the blood 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.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions
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 the medicine via wastewater or household waste. Ask the pharmacist how to throw away the medicine (medicines you no longer use). This will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
Mannitol, sodium phosphate dibasic heptahydrate, sodium phosphate monobasic monohydrate.

What the medicine looks like and contents of the pack:
White to off-white powder.

After reconstitution, the medicine 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.

Registration holder and importer's name and address: Sanofi-Aventis Israel Ltd., 10 Beni Gaon St., P.O.B. 8090, Netanya.

Revised in October 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 124-94-30313

DOR-Fab-PIL-0423-03

הוראות שימוש לצוות הרפואי
تعليمات الاستعمال للطاقم الطبي
Instructions for Use by Medical Staff

Fabrazyme 35 mg

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

The number of vials should be determined to be reconstituted based on the individual patient's weight and the required vials should be removed 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
Each vial of Fabrazyme 35 mg has to be reconstituted with 7.2 ml water for injections. Forceful impact of water for injection on the powder and foaming should be avoided. This is done by slow drop-wise addition of the water for injection down the inside of the vial and not directly onto the lyophilisate. Each vial should be rolled and tilted gently. The vial should not be inverted, swirled or shaken.

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, the reconstituted solution in each vial should be visually inspected for particulate matter and discolouration. The solution should not be used if foreign particles are observed or if the solution is discoloured.

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

Dilution
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 solution for injection from the infusion bag.

The airspace within the infusion bag should be removed to minimise the air/liquid interface.
7.0 ml (equal to 35 mg) of the reconstituted solution from each vial up to the total volume required should be slowly withdrawn for the patient dose. Filter needles should not be used and foaming should be avoided.

The reconstituted solution should slowly be injected directly into the 0.9% sodium chloride solution for injection (not in any remaining airspace) to a final concentration between 0.05 mg/ml and 0.7 mg/ml. The total volume of sodium chloride 0.9% solution for infusion should be determined (between 50 and 500 ml) based on the individual dose. For doses lower than 35 mg a minimum of 50 ml should be used, 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. The infusion bag should be gently inverted or lightly massaged to mix the diluted solution. The infusion bag should not be shaken or excessively agitated.

Administration
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.

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