Package leaflet: Information for the user

Myozyme® 50 mg powder for concentrate for solution for infusion

Alglucosidase alfa

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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4

What is in this leaflet

1. What Myozyme is and what it is used for

Myozyme is used to treat adults, children and adolescents of all ages who have a confirmed diagnosis of Pompe disease.

People with Pompe disease have low levels of an enzyme called alpha-glucosidase. This enzyme helps the body control levels of glycogen (a type of carbohydrate). Glycogen provides the body with energy, but in Pompe disease the levels of glycogen can get too high.

Myozyme contains an artificial enzyme called alglucosidase alfa – this can replace the natural enzyme which is lacking in Pompe disease.

2. What you need to know before you are given Myozyme

Do not use Myozyme:
If you have experienced life-threatening allergic (hypersensitive) reactions to alglucosidase alfa or any of the other ingredients of this medicine (listed in section 6) and re-administration of the medicine was not successful. Symptoms of life-threatening allergic reactions include, but are not limited to, low blood pressure, very fast heart rate, difficulty breathing, vomiting, facial swelling, hives or rash.

Warnings and Precautions
If you are treated with Myozyme, you may experience an infusion-associated reaction while you are being given the medicine or during the hours following the infusion. Such a reaction comprises different symptoms like low blood pressure, chest discomfort, throat tightness, face, lips or tongue swelling (angioedema), hives (urticaria), dizziness, rash, itchy skin, nausea, vomiting, cough and bronchospasm (see section 4 for an overview of all infusion-associated reactions). An infusion-associated reaction can sometimes be very severe. If you experience a reaction like this, you should **tell your doctor immediately**. You may need to be given pre-treatment medicines to prevent an allergic reaction (e.g. antihistamines and/or corticosteroids) or to reduce fever (antipyretics).

In studies doctors have used medicines to suppress the immune system to reduce the production of antibodies. Because you have Pompe disease, there is a risk that you get a severe infection of your airways or lungs. Using these medicines to suppress the immune system may further increase this risk.

If you experience severe ulcerative lesions of your skin, please inform your doctor. If you experience swelling of your lower limbs or generalized swelling, please inform your doctor. Your doctor should consider discontinuation of the administration of Myozyme and initiate appropriate medical treatment. Your doctor should consider the risks and benefits of re-administering Myozyme.

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Other medicines and Myozyme
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding and fertility
There is limited experience of the use of Myozyme in pregnant women. You should not be using Myozyme during pregnancy unless clearly necessary. Tell your doctor if you are breastfeeding. There is limited experience suggesting that Myozyme passes into human breast milk in very small amounts. No effects on the breastfeed infant is expected. Therefore breastfeeding during the treatment may be considered. However, you can discuss with your doctor whether to interrupt breastfeeding as a precautionary measure for the first 24 hours after each dose of Myozyme. 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
Take care when driving or using any tools or machines shortly after infusion of Myozyme, since you may experience dizziness, sleepiness, shaking, and/or low blood pressure.

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

3. How Myozyme is given

Myozyme will be given to you under the supervision of a doctor who is experienced in the treatment of Pompe disease.

The dose you receive is based on your body weight. The recommended dosage of Myozyme is 20 mg per kg of body weight. It will be given to you once every 2 weeks.

Home infusion
Your doctor may consider that you can have home infusion of Myozyme if it is safe and convenient to do so. If you get any side effects during an infusion of Myozyme, your home infusion staff member may stop the infusion and start appropriate medical treatment.

Use in children and adolescents
The recommended dosage of Myozyme in children and adolescents is the same as in adults.

Instructions for proper use
Myozyme 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.

If you are given more Myozyme than you should
If you are given Myozyme at a higher dose or infusion rate than recommended, you may experience infusion associated reactions. Such a reaction may include symptoms like :

- skin and lips turning blue because of a lack of oxygen in body tissues, increased heart rate, palpitations
- difficulty in breathing, cough
- dizziness, headache, taste disturbance
- high blood pressure, hot flush
- tongue swelling, vomiting, diarrhoea, feeling sick (nausea)
- chest pain, chest discomfort, throat tightness, fever, chills, feeling cold, redness at the infusion site
- muscle pain
- reddening of the skin

If you experience a reaction like this, you should tell your doctor immediately (see section 2). The rate of your infusion will be reduced or the infusion will be interrupted, and, as appropriate, you may receive a corrective treatment.

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

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Side effects were mainly seen while patients were being given the medicine or shortly after ("infusion related effects"). Some of these infusion related side effects were serious or life-threatening. Life threatening reactions, including very severe generalised allergic reactions and anaphylactic shock, have been reported in some patients. Symptoms of such reactions include low blood pressure, very fast heart rate, difficulty breathing, vomiting, facial, lip or tongue swelling, hives or rash. Some patients have experienced infusion related side effects in the form of flu-like symptoms, which lasted for a few days after completion of the infusion.

Should you experience any reaction like this, please **tell your doctor immediately.** You may need to be given pre-treatment medicines to prevent an allergic reaction (e.g. antihistamines and/or corticosteroids) or to reduce fever (antipyretics).

Very common: may affect more than 1 in 10 people
- Hives
- Rash
- Increased heart rate
- (Facial) flushing
- Fever or increased body temperature
- Cough
- Increased breathing rate
- Vomiting
- Low level of oxygen in the blood

Common: may affect up to 1 in 10 people
- Paleness
- Increased or high blood pressure
- Bluish discolouration of the skin
- Chills
- Agitation
- Tremor
- Headache
- Tingling
- Pain or local reaction at the site of the drip
- Dizziness
- Irritability
- Itchy skin
- Retching
- Swelling of the face, swelling of the throat or severe combined swelling of the face, throat and tongue due to a severe allergic reaction
- Swelling of the arms and legs
- Nausea
- Chest discomfort
- Throat tightness
- Diarrhoea
- Tiredness
- Muscle pain
- Muscle spasms
- Severe ulcerative lesions of the skin
- Redness of the skin

Not known: frequency cannot be estimated from the available data
- Swelling around the eyes
- Asthma
- Abnormal breathing sounds, including a whistling sound
- Difficulty in breathing (including shortness of breath)
- Cold extremities (e.g. hands, feet)
- Decreased or low blood pressure
- Narrowing of the blood vessels causing blood flow to be decreased
- Sudden constriction of bronchi restricting air going in and out the lungs (bronchospasm)

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The following information is intended for healthcare professionals only:

Instructions for use – reconstitution, dilution and administration

Myozyme has to be reconstituted with water for injections, then diluted with sodium chloride 9 mg/ml (0.9%) solution for injection and then administered by intravenous infusion. Reconstitution and dilution should be performed in accordance with good practice rules, particularly for the respect of asepsis.

Due to the proteinaceous nature of the product, particle formation may occur in the reconstituted solution and final infusion bags. Therefore, a 0.2 micron low protein binding in-line filter should be used for administration.
It was demonstrated that the use of a 0.2 micron in-line filter removes visible particles and does not result in an apparent loss of protein or activity.

Determine the number of vials to be reconstituted based on the individual patient's dose regimen (mg/kg) and remove the required vials from the refrigerator in order to allow them to reach room temperature (approximately 30 minutes). Each vial of Myozyme is for single use only.

Use aseptic technique

- **Reconstitution**

Reconstitute each 50 mg vial of Myozyme with 10.3 ml water for injections using a syringe with a needle diameter not larger than 20 gauge. Add the water for injections by slow drop-wise addition down the side of the vial and not directly onto the lyophilised cake. Tilt and roll each vial gently. Do not invert, swirl or shake the vial. The reconstituted volume is 10.5 ml containing 5 mg enzyme/ ml, and appears as a clear, colourless to pale yellow solution which may contain particles in the form of thin white strands or translucent fibres. Perform an immediate inspection of the reconstituted vials for particulate matter and discoloration. If upon immediate inspection foreign particles other than those described above are observed, or if the solution is discoloured, do not use. The pH of the reconstituted solution is approximately 6.2.

After reconstitution it is recommended to promptly dilute the vials (see below).

- **Dilution**

When reconstituted as above, the reconstituted solution in the vial contains 5 mg alglucosidase alfa per ml. The reconstituted volume allows accurate withdrawal of 10.0 ml (equal to 50 mg) from each vial. This should then be further diluted as follows: Slowly withdraw the reconstituted solution from each vial until the volume for the patient's dose is obtained using a syringe with a needle diameter not larger than 20 gauge. The recommended final concentration of alglucosidase in the infusion bags ranges from 0.5 mg/ml to 4 mg/ml. Remove airspace within the infusion bag. Also remove an equal volume of sodium chloride 9 mg/ml (0.9%) solution for injection, that will be replaced with reconstituted Myozyme. Slowly inject the reconstituted Myozyme directly into the sodium chloride 9 mg/ml (0.9%) solution for injection. Gently invert or massage the infusion bag to mix the diluted solution. Do not shake or excessively agitate the infusion bag.

- Feeling hot
- Feeling cold
- Feeling generally unwell (malaise)
- Feeling weak
- Sleepiness
- Fainting
- Burning sensation
- Increased sweating
- Eyes tearing
- Mottled skin
- Restlessness
- Wheezing
- Throat irritation
- Lack of oxygen in body tissues
- Decreased heart rate
- Heart stopping
- A forceful heartbeat that may be rapid or irregular (palpitations)
- Chest pain (not in the heart)
- Inflammation of membrane that covers eyeball and eyelid
- Abdominal pain
- Indigestion
- Difficulty in swallowing
- Joint pain
- Temporary suspension or sudden cessation of breathing
- Protein loss in urine
- Nephrotic Syndrome: swelling of lower limbs, generalized swelling and protein loss in urine
- Swelling and thickening of the skin at infusion site in case of leakage of the product outside blood vessels
- Redness of the palms
- Transient skin discoloration
- Redness at the infusion site
- Hives (rash) at the infusion site
- Itching at the infusion site
- Blister

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the contact details listed below. By reporting side effects you can help provide more information on the safety of this medicine.

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

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

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

5. How to store Myozyme
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.

Store in a refrigerator (2°C – 8°C).

After dilution, an immediate use is recommended. However, chemical and physical in-use stability has been demonstrated for 24 hours at 2 to 8°C when stored under protection from light.

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.

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The final infusion solution should be administered as close to preparation time as possible.

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

- **Administration**

It is recommended to start the administration of the diluted solution within three hours. The total time between reconstitution and completion of the infusion should not exceed 24 hours.

The recommended dose regimen of Myozyme is 20 mg/kg of body weight administered once every 2 weeks as an intravenous infusion.

Infusions should be administered incrementally. It is recommended that the infusion begin at an initial rate of 1 mg/kg/h and be gradually increased by 2 mg/kg/h every 30 minutes if there are no signs of IARs (Infusion Associated Reactions) until a maximum rate of 7 mg/kg/h is reached.

6. Contents of the pack and other information
What Myozyme contains
- The active substance is alglucosidase alfa. One vial contains 50 mg of alglucosidase alfa. After reconstitution, the solution contains 5 mg of alglucosidase alfa per ml and after dilution the concentration varies from 0.5 mg to 4 mg/ml.
- The other ingredients are
  - mannitol (E421),
  - sodium dihydrogen phosphate monohydrate (E339)
  - disodium phosphate heptahydrate (E339)
  - polysorbate 80 (E433).

What Myozyme looks like and contents of the pack
Myozyme is a powder for concentrate for solution for infusion in a vial (50 mg/vial). Each pack contains 1, 10 or 25 vials. Not all pack sizes may be marketed.

The powder is white to off-white. After reconstitution it is a clear, colourless to pale yellow solution, which may contain particles. The reconstituted solution must be further diluted.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder
Sanofi 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:

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

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

United Kingdom (Northern Ireland)
sanofi-aventis Ireland Ltd. T/A SANOFI
Tel: +44 (0) 800 035 2525

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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.