PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

CEREZYME® 400 powder for concentrate for solution for infusion

Imiglucerase

Contains sugar alcohol: each reconstituted vial contains 320 mg mannitol per 10 mL.

Read all of this leaflet carefully before you start receiving CEREZYME.

- 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.
- CEREZYME 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 CEREZYME is and what it is used for
2. What you need to know before you receive CEREZYME
3. How CEREZYME is administered
4. Possible side effects
5. How to store CEREZYME
6. Contents of the pack and other information.

1. What CEREZYME is and what it is used for

CEREZYME is indicated for long-term enzyme replacement therapy for paediatric and adult patients with a confirmed diagnosis of Type I or Type 3 Gaucher disease that results in one or more of the following conditions:

a. anaemia (low number of red blood cells) after exclusion of other causes such as iron deficiency,

b. thrombocytopenia (a tendency to bleed easily due to low numbers of platelets – a type of blood cell),

c. bone disease after exclusion of other causes such as vitamin D deficiency, and

d. hepatomegaly or splenomegaly (spleen or liver enlargement).

People with Gaucher disease have low levels of an enzyme called β-glucocerebrosidase. This enzyme helps the body control levels of glucocerebroside. Glucocerebroside is a natural substance in the body, made of sugar and fat. In Gaucher disease, glucocerebroside levels can get too high.

CEREZYME is an artificial enzyme called imiglucerase. This can replace the natural enzyme acid β-glucocerebrosidase, which is lacking or not active enough in patients with Gaucher disease.

2. What you need to know before you receive CEREZYME

Do not receive CEREZYME

If you are allergic (hypersensitive) to imiglucerase or any of the other ingredients of CEREZYME (listed in section 6).

Warnings and precautions

Take special care with CEREZYME:

- If you are treated with CEREZYME, you may experience an allergic reaction while you are receiving CEREZYME or shortly thereafter (see section 4 for the symptoms of an allergic

reaction). If you experience a reaction like this, you should tell your doctor immediately. Your doctor may perform a test, to determine if you have an allergic reaction to CEREZYME.

- If you experience high blood pressure in the lungs (pulmonary hypertension) while having Gaucher disease. The cause can be unknown, or it can be due to heart, lung or liver problems. It can occur whether the patient is treated with CEREZYME or not. However, if you suffer from any shortness of breath, you should contact your doctor immediately.

Other medicines and CEREZYME

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

CEREZYME with food and drink

CEREZYME may be given with or without food.

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 receiving CEREZYME.

It is not known whether CEREZYME is excreted in human milk.

Driving and using machines

Do not drive a vehicle or operate any machinery requiring your attention, until you know how you will react to CEREZYME.

CEREZYME contains sodium chloride

CEREZYME contains approximately 34 mg sodium per reconstituted vial (i.e. 3,4 mg/mL), equivalent to 1,7 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. Additionally,

CEREZYME is administered in 0,9 % sodium chloride intravenous solution (see section 6.6). To be taken into consideration by patients on a sodium-controlled diet.

3. How CEREZYME is administered

Do not share medicines prescribed for you with any other person.
Always use CEREZYME exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are not sure.
Your doctor will tell you how long your treatment with CEREZYME will last. If you have the impression that the effect of CEREZYME is too strong or too weak, talk to your doctor or pharmacist.

Each vial of CEREZYME is for single use only.
CEREZYME is administered through a drip into a vein (intravenous infusion) over 1 – 2 hours.
At initial infusions, CEREZYME should be administered at a rate not exceeding 0,5 units/kg/min. At subsequent administrations, infusion rate may be increased, but should not exceed 1 unit/kg/min. Infusion rate increases should occur under the supervision of your doctor.

Your dose will be specific to you. Your doctor will calculate your dose, based on how severe your symptoms are, and other factors. The recommended dose of CEREZYME is 60 units/kilogram body weight, given once every 2 weeks.

Your doctor will closely monitor your response to your treatment, and may adjust your dose (up or down) until he/she finds the best dose to control your symptoms. Once this dose is found, your doctor will still monitor your responses to make sure you are using the right dose. This might be every 6 to 12 months.

Instructions for reconstitution and dilution

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

Determine the number of vials to be reconstituted, based on your individual dosage regimen and take the vials from the refrigerator.

Occasionally, small dosage adjustments may be made to avoid discarding partially used vials. Dosages may be rounded to the nearest full vial, as long as the monthly administered dosage remains substantially the same.

Use aseptic techniques.

Reconstitution:

Reconstitute each vial with 10,2 mL sterile water for injection. Avoid forceful impact of water for injections on the powder and, by mixing gently, avoid foaming of the solution. The reconstituted volume is 10,6 mL. The pH of the reconstituted solution is approximately 6,1.

The final concentration and administration volume are provided in the following table:

	400 unit vial
Sterile water for reconstitution	10,2 mL
Final volume of reconstituted product	10,6 mL
Concentration after reconstitution	40 units/mL
Withdrawal volume	10,0 mL
Units of enzyme within final volume	400 units

After reconstitution, the solution is a clear, colourless liquid, free from foreign matter. The reconstituted solution should be further diluted. Before further dilution, visually inspect the reconstituted solution in each vial for foreign particles and discolouration. Do not use vials exhibiting foreign particles or discolouration. Since CEREZYME does not contain any preservatives, vials should be promptly diluted after reconstitution and not be stored for subsequent use.

For in-use storage time after reconstitution, see section 5.

Dilution:

The reconstituted solution contains 40 units imiglucerase per mL. The reconstituted volume allows accurate withdrawal of 10,0 mL (equal to 400 units) from each vial. Withdraw 10,0 mL reconstituted solution from each vial and combine the withdrawn volumes. The appropriate amount of CEREZYME for each patient is diluted with 0,9 % sodium chloride injection, to a final volume of 100 – 200 mL.

Administration:

Because CEREZYME is a protein solution, slight flocculation (described as thin translucent fibres) occurs occasionally after dilution. The diluted solution may be filtered through an in-line low protein-binding 0,2 µm filter during administration in order to remove any protein particles. This will not lead to any loss of imiglucerase activity. It is recommended that the diluted solution be administered within 3 hours. The product diluted in 0,9 % sodium chloride intravenous solution will retain chemical stability if stored up to 24 hours at 2 °C to 8 °C under protection from light; microbiological safety will depend on the reconstitution and dilution having been performed aseptically.

For in-use storage time after dilution, refer to section 5.

Home infusion

If you have tolerated your infusions well for several months, infusion of CEREZYME at home may be considered.

Your doctor may recommend that you can be treated at home, provided you meet certain criteria.

Infusion of CEREZYME by yourself or your caregiver at home, requires training by a health care professional in a clinical setting. You or your caregiver will be instructed in infusion technique and the keeping of a treatment diary.

If you experience any adverse events during the infusion, you should stop the infusion process and contact your doctor immediately.

Subsequent infusions may need to occur in a clinical setting.

Your dose and infusion rate should remain constant while at home, and not be changed without supervision of your doctor.

If you receive more CEREZYME than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre immediately. Take this leaflet with you so your doctor will know what you have used.

If a dose of CEREZYME was missed

If you have missed an infusion, please contact your doctor.

4. Possible side effects

CEREZYME can have side effects.

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

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

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

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to CEREZYME. 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:

Common (occurring in more than 1 in 100 patients)

- Fever.
- Blue tinge to the nails, lips or face due to insufficient oxygen in the blood.
- Abnormal fast heart rate.
- Chest discomfort.

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:

Common (occurring in more than 1 in 100 patients):

- Dizziness, headache.
- Flushing, low blood pressure.
- Coughing.
- Nausea, stomach pain, vomiting, diarrhoea.
- Backache.
- Unusual weakness or tiredness.
- Chills (feelings of coldness, accompanied by shivering).

Uncommon (occurring in more than 1 in 1 000 patients)

- Burning, swelling, sterile abscess at injection site.

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 CEREZYME.

5. How to store CEREZYME

Store at 2 °C to 8 °C (in a refrigerator).

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

CEREZYME, after reconstitution, has been shown to be stable for up to 12 hours when stored at room temperature (25 °C) and at 2 – 8 °C. CEREZYME, when diluted, has been shown to be stable for up to 24 hours when stored at 2 – 8 °C, protected from light. Microbiological safety will depend on the reconstitution and dilution having been performed aseptically.

Do not use CEREZYME after the expiration date on the vial.

Discard any unused portion of the solution. Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What CEREZYME contains

CEREZYME contains imiglucerase.

Each reconstituted vial contains 400 units imiglucerase per 10 mL (40 units per 1 mL).

The other ingredients are trisodium citrate, disodium hydrogen citrate, mannitol, and polysorbate 80.

What CEREZYME looks like and contents of the pack

CEREZYME is supplied as a sterile, non-pyrogenic, white to off-white lyophilised cake of powder.

The reconstituted powder is a clear, colourless liquid, free from foreign matter.

The sterile lyophilised powder is packed into 20 mL clear glass vials, each packed into a unit carton.

Pack size: 1 vial.

Holder of certificate of registration

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