Cerezyme® (imiglucerase) at Home:

Risk Minimisation Information for Patients

Manual for Patients with Gaucher Disease who Receive Home Infusion of Cerezyme®

Essential Non-Promotional Information

Do not discard.

Version No. 4: June 2018

Read all of this information carefully before you start home infusion.

- Keep this information in an easily accessible place; you may need to read it again.
- If you have further questions, ask your treating physician.
- This medicine has been prescribed for you. Do not pass it on to others even if their symptoms are the same as yours as it may harm them.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the patient information leaflet. You can also report side effects directly via the national reporting system to:
In the UK:
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard
By reporting side effects you can help provide more information on the safety of this medicine. Side effects can also be reported to Sanofi: Tel: 0800 0902314 or via email to uk-drugsafety@sanofi.com

In Ireland:
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: 01 6764971; Fax: 01 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine. Side effects can also be reported to Sanofi: Tel 01 403 5600 or via email to IEPharmacovigilance@sanofi.com

Date of Preparation: September 2018 Job No: CERZ-UK-10/10-2254a(1)a(1)

Table of Contents

Your Disease, Treatment and Home Infusion

Together with your treating physician, you have decided to start home infusion therapy with Cerezyme®. The objective of this document is to provide you with guidance on how to receive Cerezyme at home.

Gaucher disease and treatment

People with Gaucher disease have low levels of an enzyme called acid β-glucosidase. This enzyme helps the body to control the levels of glucosylceramide. Glucosylceramide is a natural substance in the body, made of sugar and fat. In Gaucher disease glucosylceramide levels can get too high inside specific cells called macrophages. When this happens, the cells are called "Gaucher cells". These large cells are mainly present in the bone marrow and organs like the spleen and the liver, and can lead to disrupted function causing low number of blood cells, enlarged liver and spleen, and weaker bones. The presenting symptoms of Gaucher disease include pain in the bones and easy bruising or bleeding. Often the spleen and the liver are enlarged.

Cerezyme is an artificial enzyme called imiglucerase - this can replace the natural enzyme acid β-glucosidase which is lacking or not active enough in patients with Gaucher disease. Cerezyme is used to treat patients who have a confirmed diagnosis of Type 1 or Type 3 Gaucher disease, who show signs of the disease.

Refer to the Package Leaflet of Cerezyme for additional information which is available on the Electronic Medicines Compendium (eMC) website: www.medicines.org.uk/emc in the UK and the medicines.ie website: www.medicines.ie in Ireland.

Home infusion

Currently, in some countries, people suffering from Gaucher disease, and treated with Cerezyme, receive their infusions at home. The decision to receive home treatment should be made by you and your treating physician after several months of hospital treatment to ensure satisfactory tolerance of the infusions.

Home infusion of Cerezyme will make it possible for you to do the following:

- Receive treatment within your own living environment
- Be more flexible on the treatment timing
- Avoid spending time travelling to and from the hospital and being hospitalised
- Follow a normal schooling programme
- Organise social and professional activities more easily
- Facilitate arranging treatment around family and friends

A homecare nurse, with the appropriate training, will train and assist you and/or your caregiver in the beginning to ensure optimal treatment. However, should you prefer full support for your infusion at home, the homecare nurse will carry out the entire procedure.

If you experience side effects with the treatment you must immediately seek the attention of your treating physician or your homecare nurse. Common side effects (occurring in more than 1 in 100 patients) are breathlessness, coughing, hives/ localised swelling of the skin or lining of the mouth or throat, itching, and rash. Some side effects were seen primarily while patients were being given the medicine or shortly after. These have included itching, flushing, hives/localised swelling of the skin or lining of the mouth or throat, chest discomfort, increased heart rate, bluish skin, breathlessness, a sensation of tingling, pricking, burning or numbness of the skin, fall in blood pressure, and backache. If you experience side effects during the infusion, **the infusion should be stopped immediately** and advice should be sought from your treating physician or your homecare nurse. Subsequent infusions may need to occur in a clinical setting.

Note: The dose and rate of the infusion while at home should follow the guidelines provided by your treating physician as noted in the Logbook, and not be changed without the agreement of your treating physician and supervision of the homecare nurse.

Organisation

Patient

- You and/or your caregiver must agree to receive the treatment at home.
- The home environment should be conducive to the provision of the home infusion therapy including a clean environment with electricity, water, telephone access, refrigeration, and physical space to support storage of Cerezyme and other infusion supplies.
- You must be physically and mentally able to undergo the infusions at home. The treating physician is responsible for the indication to receive Cerezyme infusions at home.
- You have accessible blood veins that allow an infusion needle to be inserted. When you have a central venous access device you should be able to insert the infusion needle into the septum.
- You and/or your caregiver have been informed by the treating physician about the treatment to be provided at home, the associated risks, the possible complications, and the provision of medical assistance at home.
- You and/or your caregiver have an understanding of Gaucher disease, and are able to recognise side effects and understand the procedures to be followed should they occur.
- You and/or your caregiver have been adequately trained in the procedures of Cerezyme reconstitution and infusion.

Homecare Nurse (to be added depending on the country)

- The homecare nurse is qualified to give intravenous (IV) infusions.
- The homecare nurse has been trained in administering Cerezyme and is aware of the possible side effects and the actions to be taken should they occur.
- The homecare nurse will establish with the patient and/or caregiver the level of support necessary.
- The homecare nurse will have a coordinating task together with the treating physician and you and/or your caregiver in organizing the treatment at home.
- The homecare nurse will strictly follow the prescribed dose and rate of administration of Cerezyme as stated in the Logbook.
- The homecare nurse will record each administration of Cerezyme in the Logbook.
- In the event of a side effect occurring during or shortly after the infusion (i.e., infusion

associated reaction), the homecare nurse/patient/caregiver should discontinue the infusion and phone the treating physician and/or the country-specific national emergency number provided in the Logbook.

Treating physician

- The treating physician is responsible for the initiation of all necessary administrative actions, allowing other stakeholders (pharmacy, nurse, patient, caregiver) to proceed.
- The treating physician is responsible for the dose and the infusion rate, to be described in the Logbook. Any changes must be clearly communicated to the patient and described in the Logbook.

Third Person / Caregiver

It is preferable for a caregiver/third party to be present during home infusion.

The Logbook (Appendix 1.2)

- The Logbook serves as a means of communication for everyone involved in administering Cerezyme at home.
- The Logbook should be kept at your home and will be kept up to date by you, your caregiver or the homecare nurse.
- In the Logbook, the treating physician clearly states the dose and the infusion rate, as well as any changes.
- The homecare nurse records the finding and actions from the initial interview and you, your caregiver or the homecare nurse notes all relevant information from subsequent visits in the Logbook.
- You and/or your caregiver and/or homecare nurse will strictly follow the prescribed dose and rate of infusion of Cerezyme as stated in the Logbook.
- You and/or your caregiver and/or homecare nurse will record each administration of Cerezyme in the Logbook.
- You and/or your caregiver must take the Logbook along to the hospital at each appointment for a check-up and bring it home afterwards.
- In the Logbook, the patient/caregiver/homecare nurse clearly describes what actions have been taken for the infusion side effect based on the advice of the treating physician or the homecare nurse.

Pharmacy and infusion equipment

Treatment and all necessary equipment will be provided dependent on local arrangements and regulations.

Training in Administration of Cerezyme

In principle, the initial instructions will be given in the hospital. The level of support required from the homecare nurse will be discussed and agreed by you and/or your care giver and your treating physician.

Should you prefer full support to receive your infusion at home, the homecare nurse will carry out the entire procedure for you.

Should you prefer to carry out the procedure yourself, or with the assistance of your caregiver, you and/or your caregiver will receive training from the homecare nurse while the infusion is being prepared. The homecare nurse will explain and demonstrate the complete infusion procedure to you and/or your caregiver.

At subsequent visits, the homecare nurse will be present to assist if required, but you and/or your caregiver will gradually transition to performing more of the administration under the homecare nurse's supervision until you feel confident with the entire infusion procedure.

While reconstituting and administering Cerezyme, the procedure described in the Patient Information Leaflet must be closely followed.

How do I prepare and administer Cerezyme?

Requisites

Supplied by the hospital/pharmacy to you or to a third party with the appropriate prescription.

- Vials of Cerezyme (200 or 400 U per vial); must be stored at a temperature of between +2°C and +8°C.
- Sterile water for injections to reconstitute Cerezyme
- 0.9% sodium chloride (NaCl) intravenous solution, 2 x 100 ml for IV administration
- 0.9% sodium chloride (NaCl) intravenous solution, 2 x 50 ml to flush infusion line pre- and post-infusion
- Chlorhexidine 0.5% in Alcohol 70% (antiseptic solution)
- Appropriate number of 10 ml and 50 ml syringes depending upon dose of Cerezyme
- 3 x sterile hypodermic needles (1.1 x 40 mm)
- 1 x butterfly needle
- In line low protein-binding 0.2 micron filter
- Hypodermic needle tray
- Micropore tape
- Mediswabs
- Sharps bin
- Hand wash
- Additional requisites if using a venous access device
    - Heparin
    - Needles for heparin
    - Dressing pack
    - Sterile gloves
- Emergency medication (antihistamines and/or corticosteroids)

Preparations

1. Prepare a clean work area and lay out the requisites.
2. The vials with Cerezyme should be removed from the refrigerator to reach room temperature approximately 30 minutes before preparation
3. Check the expiry date printed on the bottom of the vial pack (do not use Cerezyme after the expiry date).
4. Verify if the number of vials received is correct.
5. Prepare only the number of vials required for 1 infusion
   (*Note:* Cerezyme may not be stored in reconstituted or diluted form for later use).

Reconstituting Cerezyme

1. Remove the flip-off cap from the Cerezyme vial.
2. Disinfect the rubber stopper of the Cerezyme vial with chlorhexidine and allow to air dry.
3. Open the sterile water for injections.
4. Draw the required number of ml of sterile water into the syringe.
   - For 200 U vials, reconstitute each vial with 5.1 ml water for injections; the reconstituted volume is 5.3 ml.
   - For 400 U vials, reconstitute each vial with 10.2 ml water for injections; the reconstituted volume is 10.6 ml.
5. Inject the water gently into a vial of Cerezyme.
6. Repeat the process for more Cerezyme vials if required.
7. Carefully swirl the vial(s) to mix the solution (avoid forceful shaking during the reconstitution process to avoid foaming of the solution).
8. Small bubbles may appear after the mixing.
9. Let the solution settle for a few minutes to allow any bubbles present to disappear and to ensure that the powder is properly reconstituted.
10. After reconstitution, Cerezyme should be inspected visually before use. Because this is a protein solution, slight flocculation (described as thin translucent fibres) occurs occasionally

after dilution. The reconstituted solution must be a clear, colourless liquid, free from foreign matters.

11. If you notice foreign matters or discolouration of the liquid, do not use the product and contact the homecare nurse.

Dilution

1. Disinfect the cap/opening of 1 or 2 bags of NaCl 0.9% solution using chlorhexidine and allow to air dry.
2. Calculate the quantity of reconstituted Cerezyme solution present in the vials and draw the same quantity from the bag of NaCl 0.9% solution, thus creating enough space to add the reconstituted Cerezyme solution.
   For instance, if the prescribed quantity is 3 vials of Cerezyme of 400 units each, remove 30 ml (=3 x 10 ml) of NaCl solution from the bag of NaCl solution. Never remove more than half the content of the bag of NaCl to ensure that at least half the diluted solution consists of NaCl.
3. Using one or more 50 ml syringes, draw 5 ml from each of several reconstituted 200 U vials or 10 ml for the 400 U vials so as to minimise the number of operations. At the point when these quantities are drawn, the reconstituted product should not contain any foam.
4. Then gently inject the total volume of the reconstituted Cerezyme solution into the bag of NaCl 0.9% solution.
5. Carefully mix this Cerezyme solution.
6. The diluted solution should be filtered through an in-line low protein-binding 0.2 micron filter during administration.

Filling the Infusion Line

1. Remove the infusion system from the package and close it using the roller clamp.
2. Connect the spike in the NaCl 0.9% bag and fill the infusion system by holding the drip chamber upside down and opening the clamp.
3. Fill the entire system, remove any air bubbles that may be present and close the roller clamp.
4. Connect the infusion bag containing Cerezyme to the y-system.

Inserting the Needle in the Vein

1. Ensure that some strips of sticking plaster are hanging ready for use and that the start of the infusion system is within reach. Place the chlorhexidine close by, along with some gauzes.
2. Remove the butterfly needle from the packaging.
3. Sit down and rest one arm on the table (preferably on the clean cloth).
4. Apply the tourniquet and disinfect the area where the needle is to be inserted and allow it to dry.
5. Pull the skin tight and insert the needle (with its eye facing upward) at a slight angle through the skin and into the vein. When the needle has entered the vein, a 'flash' of blood will be visible at the start of the tubing.
6. Insert the needle approximately 0.5 cm in the vein to ensure that it does not immediately pop out again. Tape the butterfly needle into place using a plaster.
7. Loosen the tourniquet and remove the cap from the tube. The tube will now fill up with blood. If this does not happen, the needle is not positioned correctly in the vein. The process must then be repeated using a new needle.
8. Attach the prepared infusion bag to the drip stand and open the valve. Sit down and relax while the infusion takes place.

Administration

The reconstituted solution must be administered as prescribed within 3 hours of having been prepared. The product diluted in NaCl 0.9% solution will retain chemical stability up to 24 hours at a temperature if stored at a temperature between 2°C and 8°C away from light.

The Cerezyme dose, infusion rate as well as any changes will be determined by the treating physician.

After the Cerezyme infusion has been completed, the system is flushed with NaCl 0.9% solution at the same rate and the needle removed.

In case of a central venous access device

When you have a venous access device for the delivery of Cerezyme, you and/or your caregiver will be shown how to care for the device.

Proper homecare of a venous access device involves regular irrigation with a drug called heparin to prevent clotting and attention to a sterile technique to keep the device free of infectious agents. The following steps are necessary:

- When in use, cover site with transparent occlusive dressing. No dressing required when not in use.
- Flush with 5 mL saline before and after each use.
- Flush with 5 mL heparin (100 U/mL) after each use.

Safety Assessments

Should side effects occur during the infusion, or if you feel unwell when taking the treatment or after the treatment, contact the homecare nurse or the treating physician promptly. Common side effects (occurring in more than 1 in 100 patients) are breathlessness, coughing, hives/ localised swelling of the skin or lining of the mouth or throat, itching, and rash. Some side effects were seen primarily while patients were being given the medicine or shortly after. These have included itching, flushing, hives/localised swelling of the skin or lining of the mouth or throat, chest discomfort, increased heart rate, bluish skin, breathlessness, a sensation of tingling, pricking, burning or numbness of the skin, fall in blood pressure, and backache. If you experience side effects during the infusion, **the infusion should be stopped immediately** and advice should be sought from your treating physician or your homecare nurse. Any side effects should also be recorded in the Logbook.

In case severe side effects occur during or shortly after the infusion that require immediate attention/intervention, call the local emergency medical service (see Logbook Appendix 1.2).

Preparation/administration mistake

If you become aware that a mistake was made while preparing and/or administering of the drug please contact the homecare nurse or the treating physician.

Appendices

1.1 Patient Reconstitution Guide

1.2 Logbook

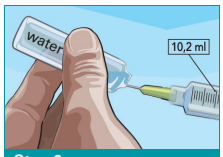
1.1 Patient Reconstitution Guide

Patient Reconstitution guide for Cerezyme® (1)

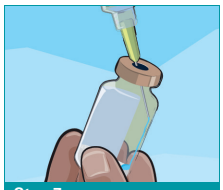
–Treatment for Gaucher Disease –

Step 2: preparation of the equipment

Step 4: observe aseptic technique



Step 6: drawing of sterile water



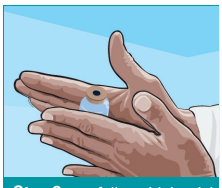
Step 7: injection of sterile water

Preparation

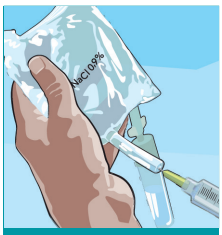
1. The vials should be stored in a refrigerator at a temperature between 2°C and 8°C.
2. Prepare the equipment:
   - The number of vials of Cerezyme required is determined based on the patient's weight. Each vial contains 200 or 400 units of imiglucerase. Approximately 30 minutes before preparation, the vials should be removed from the refrigerator to reach room temperature. Check the expiry date printed on the bottom of the vial pack (do not use Cerezyme after the expiry date).
   - Sterile water for injections to reconstitute Cerezyme
   - NaCl 0.9% solution, 2 x 100 ml for IV administration
   - NaCl 0.9% solution, 2 x 50 ml to flush infusion line pre- and post-infusion
   - Chlorhexidine 0.5% in alcohol 70% (antiseptic solution)
   - Appropriate number of 10 ml and 50 ml syringes depending upon dose of Cerezyme
   - 3 x sterile hypodermic needles (1.1 x 40mm); 1 x butterfly needle
   - In-line low protein-binding 0.2 micron filter
   - Hypodermic needle tray; Micropore tape; Mediswabs; Sharps bin; Handwash

Reconstitution using sterile water

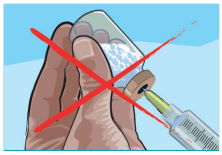
3. Remove the flip-off cap from the Cerezyme vial.
4. Disinfect the rubber stopper of the Cerezyme vial with chlorhexidine and allow to air dry.
5. Open the sterile water for injections.
6. Draw the required number of ml of sterile water for injections into the syringe: 5.1 ml for 200 U vials or 10.2 ml for 400 U vials.
7. Inject the sterile water gently down the glass side of each vial.
8. Carefully swirl the vial(s) to mix the solution (avoid forceful shaking during the reconstitution process to avoid foaming of the solution).
9. Small bubbles may appear after the mixing.
10. Let the solution settle for a few minutes to allow any bubbles present to disappear and to ensure that the powder is properly reconstituted (check that there are no foreign particles or discolouration).

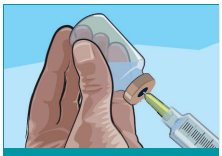


Step 8: carefully swirl the vial using a circular movement of the hands



Step 12: withdraw and discard 5 ml (200 U vial) or 10 ml (400 U vial) from the bag for each vial used





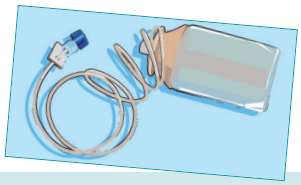
Step 13: at the time of drawing, the reconstituted product should not contain any foam

Dilution in 0.9% NaCl

11. Disinfect the cap/opening of 1 or 2 bags of NaCl 0.9% solution using chlorhexidine and allow to air dry.
12. Calculate the quantity of reconstituted Cerezyme solution present in the vials and draw the same quantity from the bag of NaCl solution, thus creating enough space to add the reconstituted Cerezyme solution.
    For instance, if the prescribed quantity is 3 vials of Cerezyme of 400 units each, remove 30 ml (=3 x 10 ml) of NaCl solution from the bag of NaCl solution. Never remove more than half the content of the bag of NaCl to ensure that at least half the diluted solution consists of NaCl.
13. Using one or more 50 ml syringes, draw 5 ml (200 U vial) or 10 ml (400 U vial) from the reconstituted vials. When these quantities are drawn, the reconstituted product should not contain any foam. Gently inject the total volume of the reconstituted Cerezyme solution into the bag of NaCl 0.9% solution.
14. Carefully mix this Cerezyme solution.
15. The diluted solution should be filtered through an in-line low protein-binding 0.2 micron filter during administration.

Administration

16. The Cerezyme dose and infusion rate will be determined by the treating physician.
17. Cerezyme must be administered by intravenous infusion.
18. The solution must be administered within three hours of reconstitution.
19. At the end of the infusion, to ensure that the total treatment dose is administered, rinse the tubing using a 50 ml bag of 0.9% NaCl, without increasing the infusion rate.
20. In light of microbiological safety, the preparation should be used immediately. If the preparation cannot be used immediately, it may be kept in a refrigerator between 2°C and 8°C, away from light, for a maximum period of 24 hours.



Undesirable effects

- In a small number of patients undesirable effects have been reported which are related to the route of administration: discomfort, pruritus, burning, swelling or sterile abscess at the site of venipuncture.
- Symptoms suggestive of hypersensitivity have been noted in approximately 3% of the patients. Onset of such symptoms has occurred during or shortly after infusions; these have included pruritus, flushing, urticaria/angioedema, chest discomfort, tachycardia, cyanosis, respiratory symptoms, paraesthesia, and backache. Hypotension associated with hypersensitivity has also been reported rarely. These symptoms generally respond to treatment with antihistamines and/or corticosteroids. Patients should be advised to discontinue infusion of the product and contact their physician if these symptoms occur.

Home treatment

- The home environment must be conducive to home infusion therapy including a clean environment with electricity, water, telephone access, refrigeration, and physical space to support storage of Cerezyme and other infusion supplies.
- It is preferable for a caregiver/third party to be present with the patient.
- The patient and/or caregiver have been adequately trained in the procedures of Cerezyme reconstitution and infusion.
- A portable infusion system like a portable diffuser may be used (positive pressure infusion system).

[1]The use of Cerezyme® (imiglucerase) is indicated for use as a long-term enzyme replacement therapy in patients with a confirmed diagnosis of non-neuronopathic (Type 1) or chronic neuronopathic (Type 3) Gaucher disease who exhibit clinically significant non-neurological manifestations of the disease.

The non-neurological manifestations of Gaucher disease include one or more of the following conditions: anaemia, after exclusion of all other causes such as iron deficiency; thrombocytopenia; bone disease, after exclusion of all other causes such as Vitamin D deficiency; hepatomegaly or splenomegaly.

DO NOT DISPLAY IN VIEW OF THE PUBLIC - LEGAL INFORMATION OVERLEAF

genzyme

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1.2 Logbook

Logbook for Cerezyme® Home Infusion

General data

Patient	Name:	
	Address:	
	City:	
	Telephone:	
Nurse	Name:	
	Organisation:	
	Telephone:	
Treating physician	Name:	
	Hospital:	
	Address:	
	City:	
	Telephone:	
Pharmacy	Name:	
	Address:	
	City:	
	Telephone:	
National emergency number	Telephone:	

Administration details (to be completed by treating physician)

Cerezyme administered since	Date (dd-mmm-yyyy):
First infusion at home	Date (dd-mmm-yyyy):
Reasons for Cerezyme infusion at home	
Please indicate support to be provided by nurse	
Cerezyme dosing regimen (dose, frequency, and rate of infusion)	

Emergency treatment details (to be completed by treating physician)

Necessary actions in the event of a serious infusion associated reaction:

1. Stop the infusion
2. Call the national emergency number 999
3. Call the physician

Infusion data (to be completed by homecare nurse and/or patient and/or caregiver)

Date of infusion	Date (dd-mmm-yyyy):
Patient's general health condition: specific problems/ remarks	
Dose/rate of infusion	
Number of vials used	200 U vials: …… 400 U vials: ……
Duration of administration	
Rate of administration	
Problems/Remarks (related to infusion, e.g. side effects)	

Date of infusion	Date (dd-mmm-yyyy):
Patient's general health condition: specific problems/ remarks	
Dose/rate of infusion	
Number of vials used	200 U vials: …… 400 U vials: ……
Duration of administration	
Rate of administration	
Problems/Remarks (related to infusion, e.g. side effects)	

Date of infusion	Date (dd-mmm-yyyy):
Patient's general health condition: specific problems/ remarks	
Dose/rate of infusion	
Number of vials used	200 U vials: …… 400 U vials: ……
Duration of administration	
Rate of administration	
Problems/Remarks (related to infusion, e.g. side effects)	

Date of infusion	Date (dd-mmm-yyyy):
Patient's general health condition: specific problems/ remarks	
Dose/rate of infusion	
Number of vials used	200 U vials: …… 400 U vials: ……
Duration of administration	
Rate of administration	
Problems/Remarks (related to infusion, e.g. side effects)	