Cerezyme® (imiglucerase) Home Infusion:

Risk Minimisation Information for Healthcare Professionals

A Guide for Healthcare Professionals Treating Patients with Gaucher Disease

Essential Non-Promotional Information

Do not discard

Version No. 4: June 2018

Date of Preparation: September 2018 Job No: CERZ-UK-10/10-2255a(1)a(1)

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1. OBJECTIVES AND GOALS

The objective of this document is to provide guidance to healthcare professionals for the management of patients receiving Cerezyme® at home. The process (described in detail below) will start with patient evaluation and selection, and discussion of requirements for home infusion. This is followed by the organisation of home infusion and training.

The goal is to offer home infusion to patients as an alternative to hospital infusion in order to improve quality of life (Hughes, 2007; Milligan, 2006).

Offering home infusion of Cerezyme will make it possible for patients to do the following:

- Receive treatment within his or her own living environment.
- Increase flexibility of infusion 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.

2. PATIENT EVALUATION AND SELECTION

Cerezyme infusions are generally tolerated well (Starzyk, 2007) and patients may prefer to be given their infusions at home (www.gaucher.org.uk). The choice to commence home treatment can be made by the patient and/or caregiver and the treating physician after a period of several months of hospital treatment to ensure satisfactory tolerance (Belmatoug, 2009; Hughes, 2007). It is important to ensure that the patient and/or caregiver understand the nature of the home infusion. Other factors to consider for patient evaluation and selection include:

- Is the home situation safe and adequate?
- Is the patient and/or caregiver able to safely, efficiently, and reliably deliver the Cerezyme infusion?
- Is rapid and reliable communication possible if problems occur?
- Is the patient and/or caregiver aware of the risks of home infusion?

A homecare nurse, with the appropriate training, will assist the patient to ensure optimal treatment.

3. REQUIREMENTS FOR HOME INFUSION

The decision to administer Cerezyme in the home setting is that of the treating physician, in consultation with the patient and/or caregiver. The following information identifies clinical and logistical issues that should be considered prior and subsequent to homecare transition (National Healthcare Protocol for Gaucher Disease, HAS, 2007):

Patient Assessment by Treating Physician

- Patients should be considered medically stable. An evaluation should be completed prior to transition.
- Patients should have received Cerezyme infusions in a controlled setting for several months until there is a documented pattern of well tolerated infusions with no infusion associated reactions (IARs) or mild IARs that have been controlled with pre-medication.
- Patients should have a history of adherence to the prescribed infusion schedule.
- Regular disease monitoring of the home-infused patient is the responsibility of the treating physician.

Home Conditions

- The home environment must be conducive for 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.
- The infusion rate of Cerezyme that was tolerated by the patient in a more controlled setting (e.g., in the hospital or outpatient setting) should not be changed in the home setting unless necessary due to safety considerations.
- Appropriate scheduling and monitoring of the infusion is the responsibility of the treating physician/homecare nurse.
- A resource contact list should be completed and available at home, in the Logbook, (Appendix 11.3) for the patient and/or care giver and the nurse.

Available pre-treatment and emergency treatment

- Appropriate pre-treatment should be provided based on the patient-specific prescription. Treatment administered in the hospital/clinic setting should not be altered in the home setting unless medically warranted.
- Medications must be available to respond to an emergency situation if necessary. Proper education on the use of emergency medications must be provided to the patient and/or caregiver (see Logbook Appendix 11.3).

- In the event the patient experiences an adverse event during the infusion, the patient/caregiver should discontinue the infusion immediately and phone the treating physician or homecare nurse to seek advice. Subsequent infusions may need to occur in a clinical setting.

4. TRAINING IN ADMINISTERING CEREZYME

In principle, the initial instructions will be given in the hospital and the level of support required from the homecare nurse will be discussed and agreed by the treating physician and the patient and/or caregiver.

Should the patient prefer full support when having their infusion at home, the homecare nurse will carry out the entire procedure for the patient.

Should the patient prefer to carry out the procedure him/herself or with the assistance of a caregiver, the patient and/or caregiver will receive training from the homecare nurse while the infusion is being prepared and administered. The homecare nurse will explain and demonstrate the complete infusion procedure to the patient and/or caregiver.

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

While reconstituting and administering Cerezyme, the procedure described in the Summary of Product Characteristics must be closely observed.

A homecare agency, care provider, or hospital will provide equipment required to administer the home infusion.

Genzyme will provide the patient care team with home infusion training and educational material.

5. ORGANISATION OF HOME INFUSION

The following information is intended to provide information and guidance to all persons involved in the procedures for organizing home infusion of Cerezyme.

Patient

General

- The patient and/or caregiver, and/or homecare agency 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.

- The patient and/or caregiver have an understanding of the illness and are able to recognise adverse events and understand the procedure to be followed should these occur. The patient and/or caregiver must agree to the treatment at home.
- The patient and/or caregiver have been adequately trained in the procedures of Cerezyme reconstitution and infusion.
- 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.
- In case the patient carries out the procedure him/herself
    - The patient/caregiver will strictly follow the prescribed method of administration of Cerezyme as stated in the Patient Manual and Reconstitution guide.
    - The patient/caregiver records each administration of Cerezyme in the Logbook.
    - In the event the patient experiences an adverse event effect during the infusion, the patient/caregiver should discontinue the infusion immediately and phone the treating physician or home nurse to seek advice.

Medical

- The patient must be physically and mentally able to undergo the infusions at home. The treating physician is responsible for the recommendation to receive Cerezyme infusions at home.
- The patient has venous access or a central venous access device that allows for adequate infusion.

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. Any changes in Cerezyme administration must be clearly communicated to the patient and described in the Logbook).
- The patient should be regularly monitored for IARs and maintenance of therapeutic goals as per the published guidelines for children (Charrow, 2004) and adults (Weinreb, 2004).

Hospital/Pharmacy

- The hospital/pharmacy arranges the provision of the patient's medication for each prescription

and the equipment/materials required.

Homecare Nurse

- The homecare nurse is qualified to give intravenous (IV) infusions.
- The homecare nurse has been trained on Cerezyme and is aware of the possible adverse events 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 strictly follow the prescribed method of administration of Cerezyme as stated in the Logbook.
- For each patient, the homecare nurse will have a coordinating task vis-à-vis treating physician and patient/care giver in organizing the treatment at home.
- The homecare nurse records each administration of Cerezyme in the Logbook.
- In the event of an IAR, the homecare nurse should discontinue the infusion and phone the treating physician and/or the country-specific national emergency number described in the Logbook.

Third Person/Caregiver

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

The Logbook (Appendix 11.3)

- The Logbook serves as a means of communication for everyone involved in administering Cerezyme in the home setting.
- The Logbook should be kept at the patient's home and will be kept updated by the homecare nurse/patient/caregiver each time Cerezyme is administered.
- The patient/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 treating physician clearly states the dose and the infusion rate, as well as any changes to the dosing regimen.
- The homecare nurse records the findings and actions from the initial interview in the Logbook. The homecare nurse, patient and/or caregiver records all relevant information from subsequent visits in the Logbook.
- In the Logbook, the treating physician clearly states what has to be done and which

medications are to be administered in the event of an IAR.

6. ADMINISTRATION OF CEREZYME

6.1 Prescription

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

6.2 Ancillary Supplies

The medicinal products and equipment required for home treatment include the following:

- Vials of Cerezyme
  - Must be stored at a temperature between +2°C and +8°C.
  - Supplied by the hospital/pharmacy to the patient or to a third party with the appropriate prescription.
- Infusion materials
  - Infusion lines, syringes, needles, compresses, antiseptics, etc. (supplied by the hospital/pharmacy to the patient or delivered by the homecare agency in case of care provided by a homecare nurse).
  - NaCl 0.9% solution and sterile water (supplied by the local pharmacy to the patient or to a third party with the appropriate prescription).

6.3 Preparation of the Cerezyme infusion for intravenous use

Requisites

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

- Vials of Cerezyme (200 U 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 or 1 x 250 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 matter
11. If you notice foreign matter in or discolouration of the liquid, do not use the product and contact the home nurse.

Dilution

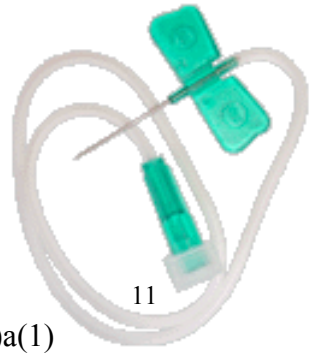
1. Disinfect the cap/opening of 1 or 2 bags of NaCl 0.9% solution using chlorhexidine and allow to air dry.
2. Calculate the quantity of reconstituted Cerezyme solution present in the vials and draw the same quantity from the bag of NaCl 0.9% solution, thus creating enough space to add the reconstituted 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 and 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. Have the patient 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.
8. Attach the prepared infusion bag to the drip stand and open the valve.

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 if stored up to 24 hours 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.

6.4 Preparation of the Cerezyme infusion in case of venous access device

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

Proper home care of a venous access device involves regular irrigation with heparin to prevent clotting and attention to a sterile technique to keep the device free of infectious agents. The patient and/or caregiver will be informed of the following necessary steps:

- 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.

7. CEREZYME SAFETY INFORMATION

Approximately 15% of patients treated with Cerezyme develop immunoglobulin G (IgG) antibodies to imiglucerase during the first year of therapy. Patients who develop IgG antibody are most likely to do so within 6 months of treatment and will rarely develop antibodies to Cerezyme after 12 months of therapy. Patients with antibody to imiglucerase have a higher risk of hypersensitivity reactions. Conversely, not all patients with symptoms of hypersensitivity have detectable IgG antibody. If a patient experiences a reaction suggestive of hypersensitivity, subsequent testing for imiglucerase antibodies is advised.

Treatment with Cerezyme should be approached with caution in patients who have exhibited symptoms of hypersensitivity to the product. Symptoms suggestive of hypersensitivity occurring during, or shortly after, infusions included pruritis, flushing, urticaria, angioedema, chest discomfort, tachycardia, cyanosis, respiratory symptoms, paraesthesia, backache and hypotension. **The infusion should be discontinued immediately if these symptoms occur.** Most patients have successfully continued therapy after a reduction in rate of infusion and pre-treatment with antihistamines and/or corticosteroids.

Adverse drug reactions are listed by system organ class and frequency (common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and rare (≥1/10,000 to <1/1,000)) in Table 5-1 below. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness.

Table 5-1: Common and Uncommon Adverse Events

Nervous system disorders	Uncommon:	Dizziness, headache, paraesthesia*
Cardiac disorders	Uncommon:	Tachycardia*, cyanosis*
Vascular disorders	Uncommon:	Flushing*, hypotension*
Respiratory, thoracic and mediastinal disorders	Common:	Dyspnoea*, coughing*
Gastrointestinal disorders	Uncommon:	Vomiting, nausea, abdominal cramping, diarrhoea
Immune system disorders	Common:	Hypersensitivity reactions
	Rare :	Anaphylactoid reactions
Skin and subcutaneous tissue disorders	Common:	Urticaria/angioedema*, pruritus*, rash*
Musculoskeletal and connective tissue disorders	Uncommon:	Arthralgia, backache*
General disorders and administration site conditions	Uncommon:	Infusion site discomfort, infusion site burning, infusion site swelling, injection site sterile abscess, chest discomfort*, fever, rigors, fatigue

* Symptoms suggestive of hypersensitivity
Source: Summary of Product Characteristics (SmPC), July 2016

8. SAFETY REPORTING

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the appropriate national reporting system and contactSanofi. Contact details below;

In the UK: Yellow Card Scheme

www.mhra.gov.uk/yellowcard.

Suspected adverse reactions should also be reported to Sanofi: Tel: 0800 0902314.
Alternatively, please complete an Adverse Event Form (Appendix 11.2) and send via E-mail 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.
Suspected adverse reactions should also be reported to Sanofi: Tel: 01 403 5600.
Alternatively, please complete an Adverse Event Form (Appendix 11.2) and send via E-mail to (IEPharmacovigilance@sanofi.com).

An adverse event (AE) is defined as any untoward medical occurrence in a patient administered a medicinal product which does not necessarily have to have a causal relationship with this treatment. A serious adverse event (SAE) involves an occurrence defined as having at least one of the following outcomes or characteristics:

- Results in death
- Is life-threatening (any event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Required inpatient hospitalisation or prolongation of an existing hospitalisation
- Results in persistent or significant disability/incapacity (any adverse event that resulted in a substantial disruption of a person's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect
- Is an important medical event (any event that, based upon appropriate medical judgement, may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above)

9. FURTHER INFORMATION

Please refer to the Summary of Product Characteristic for complete indication statements and further information about the approved use of Cerezyme (imiglucerase). The SmPC is available on the Electronic Medicines Compendium (eMC) website: www.medicines.org.uk/emc in the UK and on the medicines.ie website: www.medicines.ie in Ireland. Other detailed information on Cerezyme is available at the European Medicines Agency (EMA) website (see http://www.ema.europa.eu).

10. REFERENCES

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11. APPENDICES

11.1 HEALTHCARE PROFESSIONAL RECONSTITUTION GUIDE

11.2 ADVERSE EVENT FORM

11.3 LOGBOOK

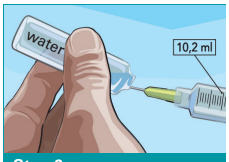
11.1 Healthcare Professional Reconstitution Guide

Health Care Professional Reconstitution guide for Cerezyme® (1)

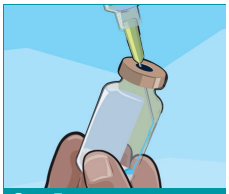
–Treatment for Gaucher Disease –

Step 2: preparation of the equipment

Step 4: observe aseptic technique



Step 6: drawing of sterile water



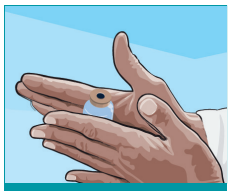
Step 7: injection of sterile water

Preparation

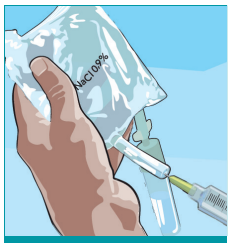
1. The vials should be stored in a refrigerator at a temperature between 2°C and 8°C.
2. Prepare the equipment:
   - The number of vials of Cerezyme required is determined based on the patient's weight. Each vial contains 200 or 400 units of imiglucerase. Approximately 30 minutes before preparation, 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

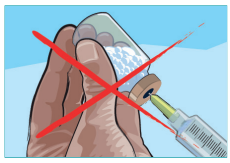
3. Remove the flip-off cap from the Cerezyme vial.
4. Disinfect the rubber stopper of the Cerezyme vial with chlorhexidine and allow to air dry.
5. Open the sterile water for injections.
6. Draw the required number of ml of sterile water for injections into the syringe: 5.1 ml for 200 U vials or 10.2 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).

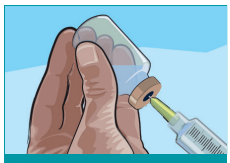


Step 8: carefully swirl the vial using a circular movement of the hands



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





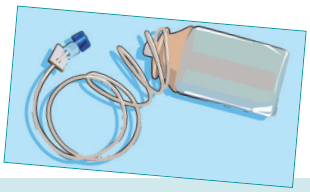
Step 13: at the time of drawing, the reconstituted product should not contain any foam

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.

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genzyme

Date of Preparation: September 2018 Job No: CERZ-UK-10/10-2255a(1)a(1)

11.2 Adverse Event Form

SANOFI GENZYME

Enzyme Replacement Therapies* Adverse Event Reporting Form

GENZYME ERT Adverse Event Report Form - (*Cerezyme, Fabrazyme, Aldurazyme, Myozyme, Lumizyme)

Report Date: DD-MMM-YYY	Report Type: ☐Initial ☐Follow-up	Registry ID (if applicable):	Patient Initials:	Drug/Biologic: (select ONE) ☐Cerezyme ☐Fabrazyme ☐Aldurazyme ☐Myozyme ☐Lumizyme ☐NONE Reason: ___________________	Lot Number & Expiration Date:
Reporter Name, Institution, Address:		Age:	Gender: [ ] Male [ ] Female	Indication: Gaucher Phenotype: ☐Type 1 ☐Type 2 ☐ Type 3 Pompe Phenotype: ☐ Infantile-onset ☐ Late-onset	
		Country:		Dose: Units: Frequency:	
		Date of Birth: DD-MMM-YYYY		Administration schedule (including rate ramp schedule):	
Reporter's Telephone Number:		Height: ☐ cm ☐ in	Weight: ☐ kg ☐ lb	Route: ☐ I.V. ☐ Other _______________	
Reporter's Fax Number:		Pregnant? ☐ Yes ☐ No ☐ NA If yes, please complete pregnancy forms		Therapy Start Date: DD-MMM-YYYY	
Please provide the patient's medical history.				Date of Last Dose (prior to event): DD-MMM-YYYY	
				Therapy Stop Date: DD-MMM-YYYY ☐ continuing	

	Event #1	Event #2	Event #3	Event #4
Event term(s): (List one term per column) Provide Diagnosis, if known				
	Event Start Date & Time: DD-MMM-YYYY	Event Start Date & Time: DD-MMM-YYYY	Event Start Date & Time: DD-MMM-YYYY	Event Start Date & Time: DD-MMM-YYYY
	Event Stop Date & Time: DD-MMM-YYYY ☐ Ongoing	Event Stop Date & Time: DD-MMM-YYYY ☐ Ongoing	Event Stop Date & Time: DD-MMM-YYYY ☐ Ongoing	Event Stop Date & Time: DD-MMM-YYYY ☐ Ongoing
Event Serious:	☐ YES ☐ NO	☐ YES ☐ NO	☐ YES ☐ NO	☐ YES ☐ NO
Infusion Associated Reaction?: If yes, please include time to onset	☐ YES ☐ NO Time to onset: ____________________	☐ YES ☐ NO Time to onset: ____________________	☐ YES ☐ NO Time to onset: ____________________	☐ YES ☐ NO Time to onset: ____________________
Severity:	☐ Mild ☐ Moderate ☐ Severe	☐ Mild ☐ Moderate ☐ Severe	☐ Mild ☐ Moderate ☐ Severe	☐ Mild ☐ Moderate ☐ Severe
Outcome of the Event:	☐ Recovered ☐ Recovered with sequelae Specify:_______________ ☐ Recovering ☐ Not recovered ☐ Fatal Cause of death: ___________ ☐ Not applicable ☐ Unknown	☐ Recovered ☐ Recovered with sequelae Specify: ____________ ☐ Recovering ☐ Not recovered ☐ Fatal Cause of death: ____________ ☐ Not applicable ☐ Unknown	☐ Recovered ☐ Recovered with sequelae Specify: ____________ ☐ Recovering ☐ Not recovered ☐ Fatal Cause of death: ______________ ☐ Not applicable ☐ Unknown	☐ Recovered ☐ Recovered with sequelae Specify: ______________ ☐ Recovering ☐ Not recovered ☐ Fatal Cause of death:__________ ☐ Not applicable ☐ Unknown
Serious Criteria:	☐ Not applicable (non-serious) ☐ Life-threatening ☐ Fatal ☐ Inpatient/prolonged hospitalization ☐ Persistent or significant disability/incapacity ☐ Important medical event ☐ Congenital anomaly/birth defect	☐ Not applicable (non-serious) ☐ Life-threatening ☐ Fatal ☐ Inpatient/prolonged hospitalization ☐ Persistent or significant disability/incapacity ☐ Important medical event ☐ Congenital anomaly/birth defect	☐ Not applicable (non-serious) ☐ Life-threatening ☐ Fatal ☐ Inpatient/prolonged hospitalization ☐ Persistent or significant disability/incapacity ☐ Important medical event ☐ Congenital anomaly/birth defect	☐ Not applicable (non-serious) ☐ Life-threatening ☐ Fatal ☐ Inpatient/prolonged hospitalization ☐ Persistent or significant disability/incapacity ☐ Important medical event ☐ Congenital anomaly/birth defect
Action Taken with Suspect Drug:	☐ Discontinued ☐ Dose changed Specify: ________________________ ☐ None Did event abate after drug was stopped or dose changed? ☐ Yes ☐ No ☐ Unknown Date Stopped: DD-MMM-YYYY Did event reoccur after drug was restarted? ☐ Yes ☐ No ☐ NA ☐ Unknown Date Re-started: DD-MMM-YYYY	☐ Discontinued ☐ Dose changed Specify: ________________________ ☐ None Did event abate after drug was stopped or dose changed? ☐ Yes ☐ No ☐ Unknown Date Stopped: DD-MMM-YYYY Did event reoccur after drug was restarted? ☐ Yes ☐ No ☐ NA ☐ Unknown Date Re-started: DD-MMM-YYYY	☐ Discontinued ☐ Dose changed Specify: ________________________ ☐ None Did event abate after drug was stopped or dose changed? ☐ Yes ☐ No ☐ Unknown Date Stopped: DD-MMM-YYYY Did event reoccur after drug was restarted? ☐ Yes ☐ No ☐ NA ☐ Unknown Date Re-started: DD-MMM-YYYY	☐ Discontinued ☐ Dose changed Specify: _______________ ☐ None Did event abate after drug was stopped or dose changed? ☐ Yes ☐ No ☐ Unknown Date Stopped: DD-MMM-YYYY Did event reoccur after drug was restarted? ☐ Yes ☐ No ☐ NA ☐ Unknown Date Re-started: DD-MMM-YYYY

Enzyme Replacement Therapies* Adverse Event Reporting Form continued Page 2

(*Cerezyme, Fabrazyme, Aldurazyme, Myozyme, Lumizyme)

Was Treatment Administered? If yes, please specify.:	Event #1	Event #2	Event #3	Event #4
	☐ YES Specify: _____ ☐ NO	☐ YES Specify: _____ ☐ NO	☐ YES Specify: _____ ☐ NO	☐ YES Specify: _____ ☐ NO

If Fatal, date of death: DD-MMM-YYYY **Autopsy:** ☐ **Yes** ☐ **No** **If Yes, please attach**
Cause of Death:

Was a 0.2 micron inline filter used during the administration? ☐ Yes ☐ No

HOME INFUSION INFORMATION

Did the patient receive the infusion associated with this event in a home setting? ☐ Yes ☐ No ☐ Unknown

Who administered the home infusion associated with this event? _____

On what date did the patient begin home infusions? DD-MMM-YYYY

Please approximate the number of home infusions the patient has received to date: _____

Has the patient reported similar events during infusion that occurred in a hospital setting? ☐ Yes ☐ No ☐ Unknown

Did you notice a medication error that may explain the occurrence of the event(s)? ☐ Yes ☐ No If yes, please explain:_____

If the patient experienced an IAR, were samples for immunology testing obtained? If so, please provide date and timing of sample draw as well as test type.

Type Sample date	IgE ☐ Yes ☐ No DD-MMM-YYYY	Complement ☐Yes ☐No DD-MMM-YYY	Tryptase ☐ Yes ☐ No DD-MMM-YYYY	Other: DD-MMM-YYYY

PRE-TREATMENT MEDICATIONS

Medication	Dose, Schedule or Total Daily Dose (units)	Start Date	Stop Date	Indication
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	

CONCOMITANT MEDICATIONS

Medication	Dose, Schedule or Total Daily Dose (units)	Start Date	Stop Date	Indication
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	
		DD-MMM-YYYY	DD-MMM-YYYY ☐ continuing	

PREVIOUS USE OF OTHER ENZYME REPLACEMENT THERAPY-

If no previous Enzyme Replacement Therapy, please select **NA ☐**

Medication	Dose, Schedule or Total Daily Dose (units)	Start Date	Stop Date	Reason for stopping previous ERT - please describe in medical history section page 1
		DD-MMM-YYYY	**DD-MMM-YYYY**	Development of antibodies YES ☐ NO ☐ Serious Adverse Reaction YES ☐ NO ☐
		DD-MMM-YYYY	DD-MMM-YYYY	Development of antibodies YES ☐ NO ☐ Serious Adverse Reaction YES ☐ NO ☐
		DD-MMM-YYYY	**DD-MMM-YYYY**	Development of antibodies YES ☐ NO ☐ Serious Adverse Reaction YES ☐ NO ☐

Adverse Event Description: Diagnosis (if known). Also describe signs, symptoms, severity, time course, relevant medical history, and relevant laboratory data.

Include results of confirmatory procedures if any. Indicate any medication required to treat the event.

Physician (Printed Name) _____ Physician Signature (Signed Name) _____ DD-MMM-YYYY Date _____

11.3 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)	