Cerezyme® (imiglucerase) Home Infusion: A Guide for Healthcare Professionals Treating Patients with Gaucher Disease

Version: 5

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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 imiglucerase 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 imiglucerase 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

Imiglucerase 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, 2007; 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 imiglucerase 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 imiglucerase 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 imiglucerase 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 imiglucerase and other infusion supplies.
- The infusion rate of imiglucerase 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 are the responsibility of the treating physician/homecare nurse.
- A resource contact list should be completed and available at home, in the Logbook, (Appendix 11.1) for the patient and/or caregiver 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 if necessary. Proper education on the use of emergency medications must be provided to the patient and/or caregiver (see Logbook, Appendix 11.1).

- 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 IMIGLUCERASE

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 imiglucerase, the procedure described in the Summary of Product Characteristics (SmPC) must be closely observed. **Error! Reference source not found.**

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

Sanofi 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 imiglucerase.

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 knowledge 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 imiglucerase 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 imiglucerase and other infusion supplies.
- In case the patient carries out the procedure him/herself, they should refer to the home infusion Patient manual
    - The patient/caregiver will strictly follow the prescribed method of administration of imiglucerase as stated in the Patient Manual.
    - The patient/caregiver records each administration of imiglucerase 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 imiglucerase 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 imiglucerase 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 imiglucerase 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 imiglucerase 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 imiglucerase in the Logbook.
- In the event of an IAR, the homecare nurse should discontinue the infusion and phone the treating physician and/or the emergency services number described in the Logbook.

Third Person/Caregiver

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

The Logbook (Appendix 11.1)

- The Logbook serves as a means of communication for everyone involved in administering imiglucerase 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 imiglucerase 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 IMIGLUCERASE

6.1 Prescription

The imiglucerase 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 imiglucerase
  - Must be stored at a temperature of 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 imiglucerase infusion for intravenous use

Preparation

1. Prepare a clean work area and lay out the requisites.

2. The vials should be stored in a refrigerator at a temperature between +2°C and +8°C

3. Prepare the equipment:

- Prepare only the number of vials required for 1 infusion (Note: imiglucerase may not be stored in reconstituted or diluted form for later use)

- The number of vials of imiglucerase required is determined based on the patient's weight and dose. Each vial contains 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 vial pack (do not use imiglucerase after the expiry date).
- Sterile water for injections to reconstitute imiglucerase.
- 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 imiglucerase.
- 3 x sterile hypodermic needles (1.1 x 40 mm); 1 x butterfly needle.
- In-line low protein-binding 0.2 µm filter is recommended.
- Hypodermic needle tray; Micropore tape; Mediswabs; Sharps bin; Handwash.
- Other equipment to be supplied for IV infusion according to local guidelines. Materials required to comply with hygienic and aseptic conditions as well as waste disposal rules.
- Additional requisites if using a venous access device
    - Heparin
    - Needles for heparin
    - Dressing pack
    - Sterile gloves
- Emergency medication (antihistamines and/or corticosteroids.

Reconstitution using sterile water.

4. Remove the flip-off cap from the imiglucerase vial.

5. Disinfect the rubber stopper of the imiglucerase vial with chlorhexidine and allow to air dry.

6. Open the sterile water for injections.

7. Draw 10.2 ml of sterile water for injections into the syringe.

8. Inject the sterile water gently down the glass side of each vial.

9. Carefully swirl the vial(s) to mix the solution (avoid forceful shaking during the reconstitution process to avoid foaming of the solution).

10. Small bubbles may appear after the mixing.

11. 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). In case of foreign particles or discolouration, do not use the product and contact the home nurse.

Dilution in 0.9% NaCl

12. Disinfect the cap/opening of 1 or 2 bags of NaCl 0.9% solution using chlorhexidine and allow to air dry.

13. Calculate the quantity of reconstituted imiglucerase solution present in the vials and draw the same quantity from the bag of NaCl solution, thus creating enough space to add the reconstituted imiglucerase solution.

For instance, if the prescribed quantity is 3 vials of imiglucerase 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.

14. Using one or more 50 ml syringes, 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 imiglucerase solution into the bag of NaCl 0.9% solution.

15. Carefully mix this imiglucerase solution.

16. The diluted solution should be filtered through an in-line low protein-binding 0.2 µm filter during administration.

Filling the Infusion Line

17. Remove the infusion system from the package and close it using the roller clamp.

18. 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.

19. Fill the entire system, remove any air bubbles that may be present and close the roller clamp.

20. Connect the infusion bag containing imiglucerase to the y-system.

Inserting the Needle in the Vein

21. 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.

22. Remove the butterfly needle from the packaging.

23. Have the patient sit down and rest one arm on the table (preferably on the clean cloth).

24. Apply the tourniquet and disinfect the area where the needle is to be inserted and allow it to dry.

25. 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.

26. 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.

27. 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.

28. Attach the prepared infusion bag to the drip stand and open the valve.

Administration

29. The imiglucerase dose and infusion rate will be determined by the treating physician.

30. Imiglucerase must be administered by intravenous infusion.

31. Prior to infusion start, fill the infusion system with the mixed solution; fill the entire system to remove any air bubbles that may be present.

32. 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 and +8°C under protection from light; but microbiological safety will depend on the reconstitution and dilution having been performed aseptically.

Preparation of the imiglucerase infusion in case of venous access device

When the patient has a venous access device for the delivery of imiglucerase, 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. IMIGLUCERASE SAFETY INFORMATION

Approximately 15% of patients treated with imiglucerase 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 imiglucerase 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 imiglucerase 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 include rash, pruritis, flushing, urticaria, angioedema, chest discomfort, tachycardia, cyanosis, dyspnea, coughing, paraesthesia, backache, and hypotension.

The infusion should be discontinued immediately if these symptoms occur, and the patients should contact their physician. Most patients have successfully continued therapy after a reduction in rate of infusion and pre-treatment with antihistamines and/or corticosteroids. Please refer to the SmPC available at www.medicines.ie for full safety information and adverse drug reactions.

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 contacting HPRA Pharmacovigilance, website: www.hpra.ie. Side effects should also be reported to Sanofi: Tel: 01 403 5600 e-mail: IEPharmacovigilance@sanofi.com.

9. FURTHER INFORMATION

Please refer to the SmPC for complete indication statements and further information about the approved use of imiglucerase available at www.medicines.ie.

10. REFERENCES

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11. APPENDICES

11.1 Logbook

Logbook for 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:	
Emergency services number	Telephone:	

Administration details (to be completed by treating physician)

imiglucerase administered since	Date (dd-mmm-yyyy):
First infusion at home	Date (dd-mmm-yyyy):
Reasons for imiglucerase infusion at home	
Please indicate support to be provided by nurse	
imiglucerase 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 emergency services _____
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 of infusion	
Batch number / Number of vials used.	
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 of infusion	
Batch number / Number of vials used.	
Duration of administration	
Rate of administration	
Problems/Remarks (related to infusion, e.g., side effects)	

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