Myozyme® (alglucosidase alfa) Home Infusion Guide for Healthcare Professionals

This educational material is part of the marketing authorisation and has been approved by the Health Products Regulatory Authority (HPRA)

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This guide is not intended to suggest or recommend home infusion therapy for any patient. The decision to use home infusion therapy is made by the prescribing Healthcare Professional (HCP), who knows the patient's current clinical status and previous infusion history, in consultation with the patient and/or his/her caregiver. This guide is solely intended to support HCPs in the management of patients receiving alglucosidase alfa via home infusion therapy.

This document does not replace the Safety Information Package (SIP), which is a separate educational material intended for healthcare professionals on the medical management of the risks associated with the administration of alglucosidase alfa.

PURPOSE OF THIS DOCUMENT

This document aims to provide guidance to healthcare professionals for the management of patients receiving alglucosidase alfa at home, to mitigate the important risks "medication errors in the home infusion setting" and "infusion-associated reactions including hypersensitivity and anaphylactic reactions with or without development of IgG and IgE antibodies".

The decision to transfer alglucosidase alfa infusion to the patient's home setting is made by the prescribing HCP and should consider patient and/or caregiver preferences and medical status.

The home infusion will take place under the responsibility of the prescribing HCP and should be supervised by a healthcare professional who should always be available during the home infusion and for a specified time after infusion. Distribution of the educational material should only be executed if the prescribing HCP decides that the patient is eligible for home infusion treatment.

It is the responsibility of the prescribing HCP to ensure a safe administration to avoid the risk of medication errors in the home infusion setting and mitigate the risk of infusion-associated reactions (IARs), in particular hypersensitivity reactions. This should be checked and documented by the prescribing HCP.

The processes presented in this document serve as overall guidance but are subject to local medical practice and national rules and regulations.

Information for HCPs prescribing alglucosidase alfa

Criteria to determine eligibility for Home infusion

Before making any arrangements for setting up alglucosidase alfa infusion at home, the prescribing HCP should consider the following:

- The prescribing HCP is responsible for the decision to administer alglucosidase alfa infusions at home after evaluation of the patient's condition.
- The patient's underlying co-morbidities and ability to adhere to the home infusion requirements must be taken into account when evaluating the patient for eligibility to receive home infusion.
- The patient has been tolerating the infusion well in a hospital or outpatient setting and has no history of moderate to severe IARs for the past few months.
- The patient must adhere to regular disease monitoring as agreed with the prescribing HCP.
- The patient has reasonably uncomplicated venous access or may have a central venous access device placed that allows adequate infusion.
- Home infusion infrastructure, resources, and procedures, including training, must be established and available to the healthcare professional.
- 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 alglucosidase alfa and other infusion supplies.
- Appropriate information should be given by the prescriber and/or nurse to the patient and/or caregiver prior to initiation of home infusion.
- The patient and/or caregiver(s) must have been informed by the prescribing HCP about the treatment to be provided at home, the associated risks, and the provision of medical assistance at home for situations such as hypersensitivity reactions or medication errors, and should agree to the treatment at home.
- The patient and/or caregiver(s) must understand the illness and be able to recognise adverse events, and must understand the procedure to be followed should these occur.
- The HCP supervising the infusion should be available at all times during the home infusion and for a specified time after the infusion.
- Distribution of the educational material should only be executed if the prescribing HCP decides that the patient is eligible for home infusion treatment. The patient must be given the patient/caregiver guide, which includes information about the signs and symptoms of IARs and the recommended actions for their management. In addition, an Infusion Diary should be given to the patient/caregiver to record the infusion details and document any adverse events and IARs, including allergic-type hypersensitivity reactions before, during or after the infusion. In this diary, some contact details must be filled in by the prescribing HCP. This guide should be completed by the patient/caregiver and/or the infusion HCP, kept by the patient at home and shown to the prescribing HCP during regular follow-up visits.

Requirements and organisation of home infusion

- The home infusion will take place under the accountability of the prescribing HCP.
- The prescribing HCP is responsible for prescribing the medication, including all necessary equipment, for administration of alglucosidase alfa at home.
- The prescribing HCP is also responsible for the organisation of the home infusion and needs to agree upon the home infusion procedure. The infusion HCP will carry out the entire procedure for the infusion and supervise the infusion at the patient's home.
- The prescribing HCP is responsible for selecting the infusion rate and dose. The infusion rate of alglucosidase alfa that was previously tolerated by the patient in a hospital or outpatient setting must not be changed in the home setting, unless necessary due to safety considerations.
- Pre-infusion treatment (e.g., antihistamines, paracetamol, ibuprofen, corticosteroids), if administered in the hospital or another appropriate setting of outpatient care, must be provided based on the patient-specific prescription. This treatment must not be altered in the home setting, unless medically warranted at the discretion of the prescribing HCP.
- Once the patient has been deemed eligible for home infusion based on the primary criteria stated above, a set of requirements must be considered to ensure that alglucosidase alfa infusions can be safely, efficiently, and reliably delivered at the patient's home.
- Dose and infusion rate should remain constant while at home and must not be changed by the infusion HCP without consulting the prescribing HCP.
- Appropriate scheduling and monitoring of the infusions are the responsibility of the prescribing HCP and the infusion HCP. In addition, the prescribing HCP must establish an infusion protocol to be documented by the infusion HCP.
- In principle, the initial instructions and training of the infusion HCP will be provided by Sanofi. The level of support required from the infusion HCP in the home setting will be discussed and agreed by the prescribing HCP and the patient and/or caregiver(s).
- If the patient experiences adverse reactions during the home infusion, the infusion process should be stopped immediately, and appropriate medical treatment should be initiated. The infusion HCP should immediately inform the prescribing HCP if an IAR or hypersensitivity occurs. Events can occur during the infusion or up to several hours after the infusion has ended. If the patient experiences adverse reactions during the home infusion, subsequent infusions may need to occur in a hospital or in an appropriate setting of outpatient care until no such adverse reactions occur and the prescribing HCP determines that it is acceptable to return to home infusions.
- Emergency treatment must be available and provided based on the patient-specific prescription in case of IARs. Instructions and a documented emergency plan must be provided within the Infusion Diary and given to the infusion HCP prior to setting up home infusion. In addition, cardiopulmonary resuscitation equipment should be readily available during the infusion at home. The prescribing HCP must ensure that a rapid and reliable line of communication is available for the infusion HCP to expedite an emergency response in case immediate medical attention is required.

Information for HCPs administering alglucosidase alfa

Administration of alglucosidase alfa

Instructions for use relating to the reconstitution, dilution and administration can be found in the Summary of Product Characteristics (SmPC) of alglucosidase alfa[1]. A detailed description is provided in this section.

Roles and responsibilities – Infusion HCP

- The infusion HCP will have a coordinating role in organising the treatment at home and will establish, with the prescribing HCP and the patient and/or caregiver(s), the level of support necessary at home.
- The infusion HCP must be qualified to give intravenous infusions and be appropriately trained on Pompe disease and the administration of alglucosidase alfa. In addition, they must be trained in recognising the IARs likely to occur (including serious adverse events such as anaphylactic reactions) and in the actions to be implemented to manage adverse events. (See section 'RECOGNITION AND HANDLING OF INFUSION ASSOCIATED REACTIONS (IARs)').
- The infusion HCP must document each alglucosidase alfa infusion in an Infusion Diary and share these with the prescribing HCP on a regular basis as agreed with the prescribing HCP.
- Appropriate scheduling and monitoring of the infusions are the responsibility of the prescribing HCP and the infusion HCP, in agreement with the patient or patient's caregiver.
- In case of occurrence of an adverse event, such as hypersensitivity reactions, medication errors in the home infusion setting, or IARs during or after the infusion, the infusion HCP must follow the patient-specific emergency measures provided by the prescribing HCP in an emergency plan. This can include temporarily stopping or discontinuing the infusion.
- In case of adverse events, including medication errors in the home infusion setting, the infusion HCP must immediately contact the prescribing HCP and/or call the national emergency number. See 'REPORTING OF ADVERSE EVENTS' for reporting details.

Prescription

The alglucosidase alfa dose, required reconstituted volume, infusion volume, infusion rate, premedication, emergency medication, as well as any changes, will be determined by the prescribing HCP. Any changes of the prescription (dose or infusion rate) must be documented.

The infusion HCP must strictly follow the procedure for preparation and administration of alglucosidase alfa and must monitor the infusion as prescribed by the prescribing HCP. The infusion HCP must verify the presence of the prescribed premedication, emergency medication and equipment.

The infusion HCP must not change the dose of alglucosidase alfa or the infusion protocol (rate, duration, and steps of infusion) of alglucosidase alfa prescribed by the prescribing HCP, unless necessary due to safety considerations.

As alglucosidase alfa is prescribed in a body weight-dependent dosage, it is important to monitor the patient's weight regularly to ensure correct dosing of the medication. The prescribing HCP determines how to proceed in case of body weight changes. To mitigate the risk of medication errors in the home infusion setting, the correct determination of infusion volume is of high importance and must be defined by the prescribing HCP.

Pharmacy and Infusion Equipment

Pharmacy and all necessary Infusion Equipment will be provided according to local arrangements and regulations.

Supplies

The medication and following supplies will be provided by appropriate prescription from the prescribing HCP.

- Vials with alglucosidase alfa powder for concentrate for solution for infusion (50 mg per vial); must be stored in a clean refrigerator at a temperature between +2°C and +8°C (consider the number of vials needed based on the body weight of the patient).
- Sterile water for injection to reconstitute alglucosidase alfa (10.3 ml per vial)
- 0.9% NaCl solution for intravenous administration

- 0.9% NaCl solution to flush infusion line
- Chlorhexidine 0.5% in alcohol 70% (antiseptic solution)
- Appropriate number of syringes depending on the dose of alglucosidase alfa
- Sterile hypodermic needles (calibre Gauge 20G or 21G), plan 2 needles per 4 vials
- In-line low protein-binding 0.2 µm filter
- Supplies for the installation of a peripheral venous path or central venous path according to local guidelines
- Supplies needed for intravenous infusion according to local guidelines and material required to comply with hygienic and aseptic conditions as well as waste disposal rules according to local guidelines.
- Pre-infusion treatment medication (if applicable)
- Emergency medication

Preparation

NOTE: The instructions for use (dilution and administration) can be found in the alglucosidase alfa SmPC.[1] A detailed description is provided in this section.

Before the infusion, the infusion HCP must evaluate the patient to assess their general condition and check for any condition that could interfere with the infusion. Any abnormalities should be noted in the infusion diary. If the patient has any acute illnesses, the prescribing HCP should be consulted before proceeding with the infusion.

Also, before starting the preparation of alglucosidase alfa, the infusion HCP must evaluate the patient's medical status, including vital signs and signs of fever or infection. Patients with an acute underlying illness at the time of alglucosidase alfa infusion, including a respiratory infection that may prompt respiratory distress, appear to be at greater risk for IARs. In such cases, the infusion must not be performed, and treatment should be resumed when the patient has fully recovered, at the discretion of the prescribing HCP.

Before reconstitution, it is also recommended to install the venous pathway (peripheral venous catheter), or to connect the patient's central venous pathway, according to local protocols, to ensure alglucosidase alfa can be administered immediately after its reconstitution.

The infusion HCP must also:

- ensure the vials reach room temperature prior to preparing the solution for infusion, which can be done while placing the intravenous line. Vials should be removed from the refrigerator and set aside for approximately 30 minutes to allow them to reach room temperature.
- Check if the number of vials is appropriate based on the individual patient's dose regimen (mg/kg).
- Check the vials for discolorations, foreign particles, and expiry date. Do not use vials after the labelled expiry date.

Reconstitution

Please note aseptic technique should be used during reconstitution!

- Remove the flip-off cap from the alglucosidase alfa vial.
- Disinfect the rubber stopper of the alglucosidase alfa vial with chlorhexidine and allow to air dry.
- Open the sterile water for injection.
- Draw the required amount (ml) of sterile water into the syringe.
    - Each vial should be reconstituted by slowly injecting 10.3 ml of water for injections to each vial. Each vial will yield 50 mg/10 ml (5 mg/ml).
- Avoid forceful impact of the water on the powder and foaming. This is performed by slow drop-wise addition of the water down the inside of the vial and not directly onto the lyophilized powder.

- Each vial should be tilted and rolled gently to dissolve the lyophilized powder. It should not be inverted, swirled, or shaken.
- Small bubbles may appear after mixing. Let the solution settle for 10-20 minutes to allow any bubbles present to disappear and to ensure that the powder is properly reconstituted.
- Repeat the process for all alglucosidase alfa vials.
- Immediate visual inspection should be performed on the reconstituted vials for particulate matter and discolouration. The reconstituted concentrate should appear as a clear, colourless to pale yellow solution which may contain particles in the form of thin white strands or translucent fibres. If upon immediate inspection foreign particles other than those described above are observed, or if the solution is discoloured, do not use.
- It is recommended to dilute alglucosidase alfa immediately upon reconstitution.

Dilution

The reconstituted solution should be diluted in 0.9% NaCl in water to a final concentration of 0.5 mg/ml to 4 mg/ml.

- Disinfect the cap/opening of one bag of 0.9% NaCl solution using chlorhexidine and allow to air dry.
- Insert the needle in the cap of the infusion bag and withdraw a volume of 0.9% NaCl solution, equivalent to the volume of the reconstituted alglucosidase alfa solution to be added. This corresponds to 1 ml for 5 mg of prescribed alglucosidase alfa.
    - *For example, if the prescribed dose is 1200 mg for a 60 kg patient, the volume of* alglucosidase alfa *to be diluted is 1200 mg / 5 mg/ml = 240 ml. Therefore, 240 ml should be removed from the bag of 0.9% NaCl solution.*
- Remove any air from the infusion bag.
- Draw 10 ml (corresponding to 50 mg) from each vial of reconstituted alglucosidase alfa solution slowly into a syringe.
- The reconstituted solution should be added slowly and directly into the 0.9% NaCl solution. Foaming or agitation of the infusion bag should be avoided. Introduction of air into the infusion bag should be avoided.
    - *In the above-described example, 240 ml of reconstituted* alglucosidase alfa *will be added to the infusion bag.*
- Mix the infusion bag solution by gently inverting or massaging the infusion bag. It should not be shaken.
- Protect the infusion bag from any heat or vibration and administer immediately upon dilution.
- After dilution, immediate use is recommended. However, chemical and physical in-use stability has been demonstrated for 24 hours at +2 to +8°C when stored under protection from light.

Administration

- Once alglucosidase alfa has been diluted, attach the tubing to the infusion bag and remove any air.
- Connect a low protein binding 0.2 µm in line filter to the infusion bag. This step avoids administration of inadvertently introduced particles during preparation.
- Prime the infusion line with the diluted alglucosidase alfa via gravity and connect the infusion line to the patient's vein path.
- Before starting the infusion, check the patient's pulse, blood pressure, respiratory rate and body temperature.
- The initial infusion rate should not be higher than 1 mg/kg body weight/hour to minimize the risk of IARs. If the infusion is well tolerated, increase the infusion rate stepwise (by 2 mg/kg body weight/hour) every 30 minutes until a maximum rate of 7 mg/kg body weight/hour.
- After the infusion is complete, the intravenous line should be flushed with 0.9% NaCl solution at the same rate to remove any residual alglucosidase alfa from the tubing.

- Disconnect the infusion line from the patient's vein path and remove the needle. Discard any supply according to local regulations.
- Alglucosidase alfa should not be infused in the same intravenous line with other medicinal products.

The alglucosidase alfa dose, infusion rate, as well as any changes, will be determined by the prescribing HCP. The treatment must not be altered in the home setting, unless medically warranted at the discretion of the prescribing HCP. The infusion and any observations should be documented in an Infusion Diary.

Note: The patients with an impaired cardiac and/or respiratory function have the risk of an infusion-related volume overload which may lead to a severe deterioration of the cardiac and/or respiratory condition to the point of cardiorespiratory failure. The stepwise increase of infusion rate is done every 30 minutes and may only be considered in the absence of infusion-associated reactions.

Recognition and handling of infusion-associated reactions (IARs)

Recognition of IARs

The most frequently reported adverse events are IARs, whether administered at hospital or in another appropriate setting of outpatient care.

An IAR is defined as any adverse event occurring during the infusion, or during the hours following infusion, and assessed as potentially causally related to the administration of the product (alglucosidase alfa-related events occurring after the post-infusion period may be considered IARs at the discretion of the reporter).

IARs may occur at any time during and/or within a few hours of the infusion and are more likely with higher infusion rates.

Hypersensitivity reactions, including anaphylaxis, have also been reported in alglucosidase alfa-treated patients.

Summary of the safety profile

Infantile-onset Pompe disease

In clinical trials, adverse reactions were mostly mild to moderate in intensity and almost all occurred during the infusion or during the 2 hours following the infusion (infusion-associated reactions, IARs). Serious infusion reactions including urticaria, rales, tachycardia, decreased oxygen saturation, bronchospasm, tachypnoea, periorbital oedema and hypertension have been reported.

Late-onset Pompe disease

The most common adverse reactions observed in placebo-controlled clinical trial were IARs. The majority of these reactions were non-serious, mild to moderate in intensity and resolved spontaneously. Serious adverse reactions reported in patients treated with alglucosidase alfa were: angioedema, chest discomfort, throat tightness, non-cardiac chest pain and supraventricular tachycardia and IgE-mediated hypersensitivity reactions.

Please refer to section 4.8 of the SmPC for complete information on the safety profile of alglucosidase alfa.

Pre-treatment, special populations, and monitoring

- Antihistamines, antipyretics, and/or corticosteroids can be given to prevent or reduce IARs. However, IARs may still occur in patients after receiving pre-treatment.
- Patients with an acute underlying illness at the time of alglucosidase alfa infusion appear to be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from infusion-associated reactions.
- Patients with impaired cardiac and/or respiratory function have the risk of infusion-related volume overload which may lead to a severe deterioration of the cardiac and/or respiratory condition to the point of cardiorespiratory failure.
- Patients should be monitored after the infusion for a time span defined by the prescribing HCP.

Clinical management of adverse events

The majority of reported IARs and hypersensitivity reactions were mild or moderate and were managed with standard clinical practices (refer to alglucosidase alfa SmPC for further details).

Appropriate measures for emergency support and monitoring as determined by the prescibing HCP (and documented within the Infusion Diary) should be in place according to the patient's individual emergency plan.

If the patient experiences IARs, including hypersensitivity and anaphylactic reactions, during the home infusion, the infusion process should be stopped immediately but not removed. The measures indicated in the individual emergency plan should be followed based on the severity of the IAR, i.e., stopping temporarily or completely, and initiating appropriate medical treatment if needed.

Subsequent infusions may need to occur in a hospital or in an appropriate setting of outpatient care until no such adverse reactions occur and the prescribing HCP determines that it is acceptable to return to home infusion.

Dose and infusion rate must not be changed by the infusion HCP for subsequent infusions without consulting the prescribing HCP.

Reporting of adverse events

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

If the patient becomes aware that a mistake was made in the preparation and/or administration of the drug, the patient or infusion HCP should inform the prescribing HCP to determine appropriate action. Any medication errors should be reported to Sanofi, Tel: 01 403 5600 or e-mail: IEPharmacovigilance@sanofi.com by the prescribing HCP.

Additional information

Please refer to the SmPC on medicines.ie for full prescribing information relating to alglucosidase alfa:

https://www.medicines.ie/medicines/myozyme-50-mg-powder-for-concentrate-for-solution-for-infusion--32971/spc#tabs

References

1. Myozyme SmPC available on medicines.ie:

   https://www.medicines.ie/medicines/myozyme-50-mg-powder-for-concentrate-for-solution-for-infusion--32971/spc#tabs