

Aldurazyme® (laronidase)

Home Infusion Guide for Healthcare Professionals (HCPs)

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

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 Health Care 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 to support HCPs in their management of patients receiving laronidase via home infusion therapy. Please refer to laronidase SmPC on www.medicines.ie.

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1 OBJECTIVES AND GOALS

- The main objective of this document is to provide guidance to healthcare professionals (HCPs) for the management of patients receiving laronidase at home to mitigate the important risks of **"medication errors in home infusion setting"** and **"infusion associated reactions (IARs) including hypersensitivity and anaphylaxis"**.
- The processes presented in this document serve as overall guidance but are subject to local medical practice and national rules and regulations.

2 INFORMATION FOR HCPS PRESCRIBING LARONIDASE

2.A) ROLES AND RESPONSIBILITIES

- The decision to transfer laronidase infusion to the patient's home setting is made by the treating/prescribing physician and should reflect patient and/or caregiver preferences and medical status.
- The home infusion will take place under the responsibility of the prescribing HCP. 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 trying to avoid risks of medication errors and reduce and mitigate the risk of IARs, particularly hypersensitivity reactions.
- The prescribing HCP is responsible for initiating all the administrative procedures authorising the other stakeholders (patient and/or caregiver(s), infusion HCP, home healthcare provider, pharmacy, etc.) to act and discuss with the patient and/or caregiver the level of support to be provided in the home setting.

2.B) CRITERIA TO DETERMINE ELIGIBILITY FOR HOME INFUSION

- Infusion of laronidase at home may be considered for patients who **are tolerating their infusions well** and have **no recent history of moderate or severe IARs for several months**. The decision to have a patient move to home infusion should be made after a complete medical evaluation and upon recommendation by the treating physician.
- **Home infusion infrastructure, resources, and procedures, including training, must be established and available to the HCP.** Home infusion should be supervised by a HCP who should be always available during the home infusion and for a specified time after infusion. Appropriate information should be given by the prescribing HCP and/or infusion HCP to the patient and/or caregiver prior to initiation of home infusion.
- Risks and necessary infrastructure and resources which need to be considered when evaluating whether an individual patient is suitable to move to home infusion:
 - *After a complete medical assessment, the patient's condition is deemed stable to receive infusions at home. The patient should be physically and mentally able to undergo the infusions at home.*
 - *A patient's underlying co-morbidities and ability to adhere to the home infusion requirements need to be considered when evaluating the patient for eligibility to receive home infusion.*
 - *Patients with advance disease may not be suitable for home infusion as they may be at higher risk of complications that require advanced medical resuscitation measures only available on a hospital setting.*
 - *The patient has reasonably uncomplicated venous access or may have a central venous access device placed that allows adequate infusion.*
 - *The patient and/or caregiver(s) have been informed by the prescribing HCP about the treatment to be provided at home, and the risks associated with the provision of medical assistance in this setting, like hypersensitivity reactions and medication errors. The patient/caregiver(s) must agree to the treatment at home after receiving this information.*
 - *The patient and/or caregiver(s) understand the illness, can recognise adverse events like hypersensitivity reactions and medication errors and understand the procedure to be followed should these occur.*
 - *The patient/caregiver must be informed that the infusion should always be administered in the presence of an experienced HCP, i.e., the infusion HCP who must be adequately trained in how to act in case of an IAR.*
 - *The patient must be willing and able to comply with home infusion procedures, patients' home environment should be adequate to perform the home infusion procedure.*

- o *The home environment must be favourable to home infusion therapy, including a clean environment with electricity, water, telephone access, refrigeration, and physical space to support storage of laronidase and other infusion supplies.*
- o *Home infusion infrastructure, resources, and procedures, including training, must be established and available to the infusion HCP.*
- o *The patient must adhere to regular disease monitoring as required by the prescribing HCP.*
- o *The patient and/or the caregiver must receive 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 guide, some contact data must be filled in by the prescribing HCP. This guide should be completed by the patient/caregiver, kept by the patient at home and be shown to the infusion HCP during regular follow-up visits.*

2.C) REQUIREMENTS AND ORGANISATION OF HOME INFUSION

- The prescribing HCP is responsible for the organisation of all necessary administrative actions required to initiate home infusion and needs to recommend the home infusion procedure. The infusion HCP will carry out the entire procedure for the infusions at the patient's home.
- The prescribing HCP is responsible for the initiation of all necessary administrative actions which will allow the other parties involved (patient and/or caregiver(s), infusion HCP, pharmacy) to proceed with home infusion and to discuss with the patient and/or caregiver the level of support to be provided in the home setting.
- The initial instructions and training of the infusion HCP will be provided by the health institution (hospital) or the correspondent experienced HCP and 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).
- Prescribing HCP is responsible for determining dose and infusion rate, which should remain constant while at home, and not be changed without supervision.
- Resuscitation equipment should be readily available in case of medical emergencies.
- Caution should be exercised if adrenaline is being considered for use in patients with MPS I due to the increased prevalence of coronary artery disease in these patients.
- Personalised patient specific pre-treatment and emergency treatment plan should be agreed between prescribing HCP and infusion HCP.

2.D) PRESCRIPTION

- The laronidase dose, required volume, infusion rate, pre-medication, emergency medication, as well as any changes should be determined by the prescribing HCP.
- Due to the frequent weight variation in this patient population, it is highly recommended to have an up-to-date weight measurement to ensure correct dosing of the medication.
- The prescribing HCP should be consulted in case of body weight changes. Any changes of the prescription (dose or infusion rate) must be documented. The prescription must be written in accordance with local regulations. Please refer to section 3.C within this document for more information on infusion preparation.
- The infusion rate will be set following the infusion rate of laronidase that was previously tolerated by the patient in hospital or outpatient setting. **To mitigate the risk of medication errors in the home infusion setting, the correct determination of infusion volume and rate is of high importance and must be defined by the prescribing HCP.**

3 INFORMATION FOR HCPS ADMINISTERING LARONIDASE

Instructions for use on dilution and administration can be found in the SmPC of laronidase, available on www.medicines.ie. A detailed description is provided in this section.

- Pharmacy and Infusion Equipment Treatment and all necessary equipment will be provided according to local arrangements and regulations.
- It is recommended that the diluted laronidase solution be administered to patients using an infusion set equipped with a 0.2 µm in-line filter.
- Laronidase 100 U/ml concentrate for solution for infusion reconstituted in 0.9% sodium chloride has an osmolality of 415 – 505 mOsm/kg and a pH of 5.2 – 5.9.

3.A) INFUSION HCP

- Together with the prescribing HCP and the patient and/or caregiver(s), the infusion HCP will have a coordinating role in terms of organizing the treatment at home, and will establish with the treating/prescribing HCP, patient and/or caregiver(s) the level of support necessary in the home.
- The infusion HCP must be qualified to give intravenous (IV) infusions and be appropriately trained on MPS I and the administration of laronidase. In addition, he/she must be trained in recognizing adverse events likely to occur (including serious adverse events such as anaphylactic reactions) and in the actions to be implemented to manage adverse events. (See section 4.a "Information on signs and symptoms related to IARs").
- The Infusion HCP should verify the presence of the prescribed pre-medication, emergency medication, the prescribed number of laronidase vials and equipment.
- The infusion HCP must strictly follow the prescribed method of preparation and administration of laronidase and monitor the infusion, as prescribed by the prescribing HCP.
- Dose and infusion protocol should remain constant while at home. The infusion HCP does not change the dose of laronidase and the infusion protocol (rate, duration, and steps of infusion) of laronidase prescribed by the prescribing HCP, unless necessary due to safety considerations.
- Appropriate scheduling and monitoring of the infusions are the responsibility of the prescribing HCP and 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 HCP must follow the patient-specific emergency measures provided by the prescribing HCP in an emergency plan. This can include lowering the infusion rate, stopping temporarily or discontinuing the infusion. An appropriate medical treatment should be initiated; refer to SmPC for full details, available on www.medicines.ie. Subsequent infusions may need to occur in a hospital or in an appropriate setting of outpatient care until no such adverse reaction is present.
- In case of adverse events, the infusion HCP immediately contacts the prescribing HCP and/or calls 112. The infusion HCP documents the adverse event in the Infusion Diary (within manual for patients and caregivers with Mucopolysaccharidosis Type I (MPS I) Disease who receive home infusion of laronidase or equivalent and reports any adverse events, including medication errors in the home infusion setting. Healthcare professionals are asked to report any suspected adverse reactions by contacting HPRA Pharmacovigilance, website: www.hpra.ie. Adverse reactions can also be reported to Sanofi: Tel: 01 403 5600, e-mail: IEPharmacovigilance@sanofi.com.

3.B) REQUIRED SUPPLIES

Supplies are generally provided by the hospital/pharmacy to the patient or to a third party by appropriate prescription from the prescribing HCP:

- Vials of laronidase (500 U per vial-5 ml per vial, 100 U/ml); must be stored in a clean refrigerator at a temperature of between +2°C and +8°C.

- Saline Solution 0.9% for IV administration. Bags of 100 ml for patients weighing 20 kg or less and bags of 250 ml for patients weighing more than 20 kg.
- Appropriate number of 10 ml, 20 ml and 50 ml syringes depending on dose of laronidase.
- Sterile hypodermic needles (caliber Gauge 20G or 21G). Plan 2 needles per 4 vials.
- In-line low protein-binding 0.2 µm filter.
- Supply for the installation of a peripheral venous path or management of central venous path according to local guidelines.
- Supply needed for IV 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-treatment medication (when applicable).
- Emergency medication according to local Standard of Care.

3.C) PREPARATION

The instructions for use (dilution and administration) can be found in the laronidase SmPC, available on www.medicines.ie.

Medical evaluation of the patient prior to administration of the infusion at home

Before the infusion, the infusion HCP must evaluate the patient to check their general condition.

The infusion HCP must evaluate the patients' medical status including vital signs, and sign of fever or infection. Patients with an acute underlying illness, including a respiratory infection that may prompt respiratory distress, at the time of laronidase infusion 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 preparation of the infusion, 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 laronidase infusion can be administered immediately after its preparation.

Any abnormalities should be noted on the infusion diary. If the patient has any acute illnesses, the prescribing HCP should be consulted before proceeding with the infusion.

Preparation of medication

Infusion HCP should make sure the vials get to 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 20 minutes to allow them to reach room temperature (below +30°C).

- The recommended dosage regimen of laronidase is 100 U/kg body weight administered once every week.
- Check the number of vials is appropriate to the patient's weight.
 - *Due to the frequent weight variation in this patient population, it is highly recommended to have an up-to-date weight measurement to ensure correct dosing of the medication. The prescribing HCP should be consulted in case of body weight changes. Please see section 2.C.*
- Check the expiry date printed on the bottom of the vial pack (do not use laronidase after the labelled expiry date).
- Check that the solution contained in the vials is clear and without any residue. Solution should be transparent.
- Vials should not be shaken.

3.D) DILUTION

Once the number of vials to be required for the infusion has been determined and they have reached room temperature, the preparation of the infusion solution should be immediately started.

- Before dilution, each vial of laronidase should be visually inspected for particulate matter and discoloration. The clear to slightly opalescent and colorless to pale yellow solution should be free of visible particles. Vials exhibiting particles or discoloration should not be used. Information for proceeding with this step can also be found in the SmPC for laronidase, available on www.medicines.ie.
- Laronidase solution should be diluted in 0.9% saline solution using aseptic technique. Determine the total volume of infusion based on the individual patient's weight, either 100 ml (if body weight is less or equal than 20 kg) or 250 ml (if body weight is more than 20 kg) of sodium chloride 9 mg/ml (0.9%) solution for infusion.
- **If the patient's weight is up to 20 kg, the total infusion volume should be 100 ml of prepared infusion.**
 - *Example: patient weight: 15 kg.*
 - *Considering each 1 ml of laronidase contains 100 U, and weekly dose for laronidase is 100 U/kg/week, this equals 1 ml/kg/week. So, for this patient 15 ml of laronidase will be needed. Each vial of laronidase contains 5 ml. This patient will require 3 vials. The total volume of laronidase is 15 ml. Once determined, you should add the volume of laronidase to complete the 100 ml of infusion solution with 0.9% saline.*
- **If a patient's weight is higher than 20 kg, the total infusion volume should be 250 ml.**
 - *Example: patient's weight: 35 kg.*
 - *Considering each 1 ml of Laronidase contains 100 U, and weekly dose for Laronidase is 100 U/kg/week, this equals 1 ml/kg/week. So, for this patient 35 ml of Laronidase will be needed. Each vial of Laronidase contains 5 ml, so you will need 7 vials. You should add the volume of Laronidase to complete the 250 ml of infusion solution with 0.9% saline.*
- Insert the needle in the cap of the infusion bag and withdraw and discard a volume of 0.9% saline solution, equivalent to the volume of the laronidase solution to be added.
- Withdraw the required volume from the laronidase vials and combine the withdrawn volumes.
- Laronidase solution should be added slowly and directly into the 0.9% saline solution. Foaming or agitation of the infusion bag should be avoided. Air introduction into the infusion bag should be avoided.
- Mix the infusion bag solution by gently inverting or massaging the infusion bag. Vials must not be shaken, because this abrupt movement can denaturalize (brake) the enzyme, and it would lose effectiveness.

3.E) ADMINISTRATION

- Prior to use visually inspect the solution for particulate matter. Only clear and colourless solutions without visible particles should be used.
- Once laronidase has been diluted, attach the tubing to the infusion bag.
- Connect a low protein binding, 0.2 µm in line filter to the infusion bag.
 - *This step avoids administration of inadvertently introduced particles during dose IV preparation.*
- Before starting the infusion, check the patient's pulse, blood pressure, respiratory rate and body temperature.
- The initial infusion rate of 2 U/kg/h may be incrementally increased every fifteen minutes, if tolerated, to a maximum of 43 U/kg/h.

The total volume of the infusion is determined by the patient's body weight and should be delivered over approximately 3 to 4 hours.

- Laronidase should not be infused in the same intravenous line with other medicinal products.

From a microbiological safety point of view, the product should be used immediately. If not used immediately, in-use storage should not be longer than 24 hours at +2°C to +8°C provided that dilution has taken place under controlled and validated aseptic conditions.

The laronidase 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 a Patient/Caregiver Infusion Diary.

4 LARONIDASE SAFETY INFORMATION

Please refer to section 4.8 of the SmPC on www.medicines.ie for full safety profile information.

4.A) INFORMATION ON SIGNS AND SYMPTOMS RELATED TO IARS

The most frequently reported adverse drug reactions (ADRs) are IAR whether administered at hospital or in another appropriate setting of outpatient care.

An IAR is defined as any adverse event (AE) occurring during the infusion or during the hours following the infusion and assessed as potentially causally related to the administration of laronidase. 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 after the infusion and are more likely with higher infusion rates.

Examples of potential IARs that have been reported in laronidase treated patients include hypersensitivity reactions, very severe generalised allergic reactions, anaphylactic shock, respiratory failure/distress, stridor, and other disorders due to obstruction of airways, bronchospasm, hypoxia, urticaria. The majority of IARs and hypersensitivity reactions were mild or moderate and were managed with standard clinical practices, refer to the SmPC for further details, available on www.medicines.ie.

Recommended pre-treatment

- For initial administration of laronidase or upon re-administration following interruption of treatment, it is recommended that patients be administered pre-treatment medicines (antihistamines and/or antipyretics) approximately 60 minutes prior to the start of the infusion, to minimise the potential occurrence of IARs.
- If clinically indicated, administration of pre-treatment medications with subsequent infusions of laronidase should be considered.
- As there is little experience on resumption of treatment following prolonged interruption, use caution due to the theoretical increased risk of hypersensitivity reaction after treatment interruption.

4.B) RECOMMENDED ACTIONS FOR THE MANAGEMENT OF THE ADRS IF SYMPTOMS OCCUR

Appropriate measures for emergency support and monitoring should be in place according to the patients' individual emergency plan, as determined by the prescribing HCP.

If the patient experiences IAR including hypersensitivity and anaphylactic reactions during the home infusion, the infusion process should be stopped immediately but the venous access should not be 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 reaction is present.

Severe IARs have been reported in patients with pre-existent severe underlying upper airway involvement and therefore specifically these patients should continue to be closely monitored and only be infused with laronidase in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available.

In case of a single severe IAR, the infusion should be stopped until the symptoms are resolved and symptomatic treatment (e.g. with antihistamines and antipyretics / anti-inflammatories) should be considered. The benefits and risk of re-administering laronidase following severe IARs should be considered. The infusion can be restarted with a reduction of the infusion rate to 1/2 – 1/4 the rate of the infusion at which the reaction occurred.

In case of a recurrent moderate IAR or re-challenge after a single severe IAR, pre-treatment should be considered (antihistamines and antipyretics/anti-inflammatories and/or corticosteroids) and a reduction of the infusion rate to 1/2 – 1/4 the rate of the infusion at which the previous reaction occurred. In case of a mild or moderate IAR, symptomatic

treatment (e.g. with antihistamines and antipyretics/anti-inflammatories) should be considered and/or a reduction in the infusion rate to half the infusion rate at which the reaction occurred.

Once a patient tolerates the infusion, the dose may be increased to reach the approved dose. Please see SmPC for full information on IAR management.

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

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

4.C) 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 by contacting HPRA Pharmacovigilance, website: www.hpra.ie.

Adverse reactions can also be reported to Sanofi: Tel: 01 403 5600, 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's Pharmacovigilance Department by the prescribing HCP.

4.D) ADDITIONAL INFORMATION

Please refer to the SmPC for complete indication statements and further information about the approved use of laronidase. Other detailed information on laronidase is available on www.medicines.ie.

REFERENCES

1. Laronidase SmPC: [Medicines List - Search PIL, SPC & EDM | Medicines.ie](#)