ELFABRIO (pegunigalsidase alfa)
Home Infusion Therapy:

Guide for Fabry Disease Healthcare Professionals to minimise the risk of hypersensitivity reactions and medication errors in home settings

1. OBJECTIVE OF THIS GUIDE

The objective of this document is to provide relevant information for the Healthcare professional (HCP) to administer Elfabrio at home and to prevent medication errors.

Administration of Elfabrio at home may be considered for patients who are tolerating their infusions well.

The decision to transfer ELFABRIO treatment to the patient's home setting is made by the treating physician according to patient's preferences and medical status.

2. REQUIREMENTS AND ORGANISATION OF HOME INFUSION

The following set of requirements must be considered to ensure that ELFABRIO infusions can be safely, efficiently, and reliably delivered at the patient's home.

2.1. Checklist for home infusion organisation

- The patient and/or caregiver(s) have been informed by the treating physician about the treatment to be provided at home, the associated risks, and the provision of medical assistance at home, and agrees to the treatment at home.
- The patient and/or caregiver(s) understand the illness and have been trained to recognise possible adverse events, including IRRs and understand the procedure to be followed in case they occur (i.e., notify symptoms suggestive of ADRs to the healthcare professional for proper assessment and management).
- 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 ELFABRIO and other infusion supplies.
- Ensure that a healthcare professional is available at all times during at least 2 hours following the home infusion and a specified by the physician. The patient has been informed that the infusion should always be administered in the presence of a HCP adequately trained on how to manage in case of ADRs, IRRs and medication errors in agreement with the local requirements for the implementation of the home infusion therapy.

2.2. Drug and Infusion Equipment Supplies

Treatment medicine, pre-medication and emergency treatment and supplies, as well as all necessary equipment will be provided to the patient's home according to local arrangements and regulations (hospital/pharmacy to the patient or to a third party with the appropriate prescription).

Transport from the pharmacy/warehouse must comply with the following details of the transport chain as well as compliance with the following activities:

- Temperature control of drug during transport from pharmacy/wahrehouse to patient's home.
- The temperature monitoring device must be checked to confirm the drug experienced no temperature deviation during the shipping process (it is considered a deviation if temperature <2 or >8ºC).

2.2.1. ELFABRIO

Vials of ELFABRIO (20 mg per vial), will be provided as a liquid in clear glass 10 ml vials closed by rubber stoppers and sealed with aluminium seals. They must be stored in a clean refrigerator at a temperature of between +2°C and +8°C. Do not freeze or shake.

2.2.2. INFUSION EQUIPMENT

- IV Pole
- Infusion pump
- Bio-waste container
- Alcohol wipes
- Non-sterile gloves
- 30 ml syringe
- 2 x Needle free valves
- 2 x 0.9% Sodium Chloride 10 ml syringes
- IV catheter/Huber/extension set (as needed)
- IV Start Kit/Central Line Kit per access type
- Cadd In-line 0.2-micron IV tubing
- Vented vial access spike
- 18-gauge needle
- Tape
- 10 ml syringe
- 3 ml syringe
- Heparin 100u/ml PF 5ml/12ml syringe (for central lines only)
- Hibiclens
- Sodium Chloride 0.9% IV bag(s) according to the dilution needs
- Emergency Kit
- Tourniquet.
- PRE-INFUSION medication (if applicable)

2.2.3. PRE-INFUSION TREATMENT

Pre-infusion treatment (e.g., antihistamines, corticosteroids), if administered in the hospital or other medical setting, must be provided based on the patient-specific prescription and should be described in the Logbook.

This treatment must not be altered in the home setting, unless medically warranted at the discretion of the Treating Physician

2.2.4. EMERGENCY EQUIPMENT AND MEDICATION

The Treating Physician number must be called if an IRR occurs after completion of the infusion. Any IRR must be reported according to local rules and regulations.

- An available, rapid and reliable line of communication must be ensured to expedite emergency response in case immediate medical attention is required, as per indications included in the "Emergency Treatment Plan" reported in section 5.3 and the logbook (section 3)
- In the event the patient experiences an adverse event (see section 5.1) during or shortly after the infusion, the procedures indicated in section 5.3 as "Emergency Treatment Plan" are to be followed. The infusion should be discontinued immediately and the treating physician or his/her medical designate should be contacted to seek advice. Subsequent infusions may need to occur in a hospital or other medical setting.

Emergency equipment kit will consist of:

- Airway
- Ambu Mask
- Pulse Oximeter
- 1000cc Hartman or Lactated Ringer's
- Benadryl (and relevant brand) or equivalent medication (upon physician's approval)
- Any additional items per the physician's order (i.e., Epi-pen, methylprednisolone).
- 2 IV 0.2 µm filters
- Any additional items per the physician's order.

The *Emergency Medication Kit* will be provided in a locked Emergency Box, adequately labelled.

Should patients experience, or should the Home Nurse/Infusion Nurse identify, any ADR or any problem with the dilution and administration of ELFABRIO, they need to contact the Treating Physician or his/her medical designee immediately. Subsequent infusions may need to occur in a hospital or other medical setting at the discretion of the Treating Physician or his/her medical designee.

3. The Logbook

The Logbook is herewith attached as Appendix 10.1.

The Logbook serves as a means of communication for all involved in administering ELFABRIO in the home-setting.

The HCP will record the findings and actions from the initial interview and all relevant information from subsequent visits in the Logbook.

A *resource contact list* must be completed and available at home in the Logbook for the patient and/or caregiver(s).

The Logbook must be kept at the patient's home and will be updated by the infusion nurseeach time ELFABRIO is administered.

The patient must take the Logbook along to the hospital at each appointment and bring it home afterwards.

In the logbook, the treating physician clearly states the dose, the required infusion volume, infusion rate, as well as any changes. The treating physician clearly states what must be done and which procedures are to be followed and what medications are to be administered in the event of a serious IRR, in line with current medical standards for emergency treatment. The contact details of the treating physician and the country-specific national emergency number 101 are documented in the logbook (*resource contact list*).

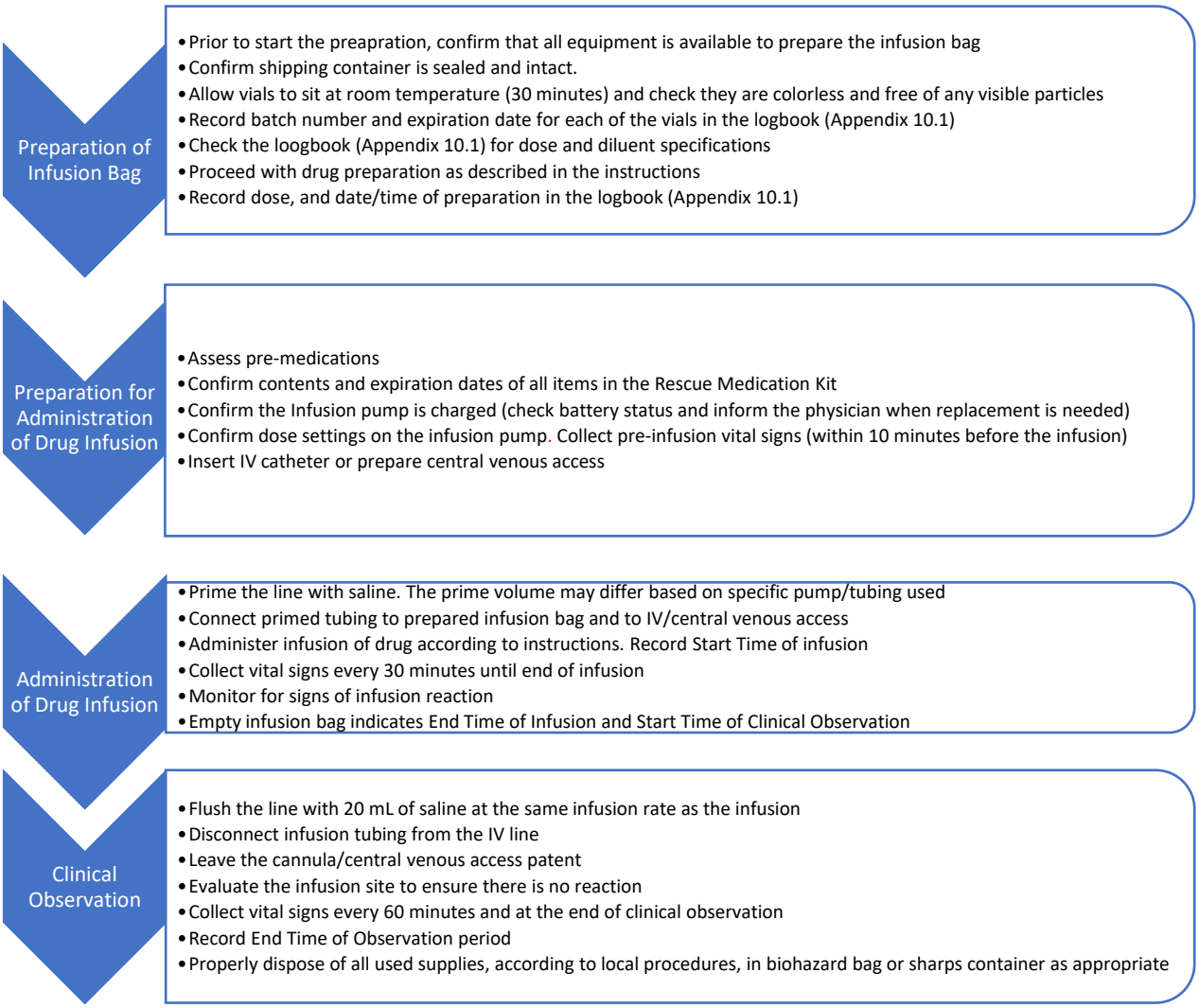
The ELFABRIO dose required, volume, infusion rate, premedication, emergency medication, as well as any changes will be determined by the treating physician. The prescription must be written in the Logbook (Appendix 10. 1). Any changes of this prescription (dose, volume or infusion rate) must again be reported in the Logbook. It is important to keep this guide handy and review the method of administration regularly. This will ensure optimal practice as well as an effective way of communicating with the treating physician.

4. STEP BY STEP INSTRUCTIONS ON PREPARING AND ADMINISTERING ELFABRIO

Each administration of ELFABRIO should be recorded in the Logbook (Appendix 10. 1). In case of any problems with the reconstitution and administration of ELFABRIO, the nurse should contact the treating physician to determine appropriate action before starting or continuing with the infusion as detailed in the Logbook.

The infusion should always be administered in the presence of a HCP knowledgeable about the infusion procedures and adequately trained on how to handle in case of an IRR and medication errors, as assessed by the treating physician or infusion personnel.

4.1. Drug Preparation and Administration – Process Flow Diagram



4.2. PREPARATION OF ELFABRIO INFUSION

If HCP becomes aware that a mistake was made in the preparation and/or administration of the drug, the HCP should inform the treating physician so he/she determines appropriate action.

Maintain strict asepsis while performing all preparation activities

1. Prepare a clean, flat, work area and lay out the requisites.
2. Keep the provided Emergency Kit nearby during the infusion.

   Verify if the number of vials received is correct Check lot numbers, expiration dates (do not use ELFABRIO after the labelled expiry date), and current prescription, then remove the correct number of boxes to prepare the prescribed dose. Vials are for single use only.

3. Allow the required number of vials to reach room temperature prior to dilution (approx. 30 min).

4. Wash hands with soap and water

5. Prepare the infusion bag provided to initiate the process.

6. Remove the vials of ELFABRIO from their boxes, inspect vials. Do not use if cap is missing or broken. Do not use if medication is discoloured or contains particulate matter.

7. Ensure vials of ELFABRIO have been allowed to warm to room temperature. Do not heat vials with hot water or in the microwave.

4.3. Dilution of ELFABRIO

The recommended dose should be diluted in 0.9% Sodium Chloride, to a total volume based on patient body weight. The recommended dose and infusion volume are detailed in the logbook (Appendix 10.1).

1. Remove the protective lids from the ELFABRIO vials, and aseptically wipe each rubber seal with an alcohol pad, using one pad for each vial, and allow to dry.
2. Wipe the injection port of the IV bag of 0.9% Sodium Chloride with an alcohol pad and allow to dry.
3. Attach an 18-gauge needle to the needle free valve.
4. Remove needle cap and insert the needle into the IV bag injection port.
5. Secure the connection of the needle-free valve to injection port of the IV bag with tape.
6. Cleanse the valve with a new alcohol pad and allow to dry completely.
7. Prior to adding ELFABRIO to the 0.9% Sodium Chloride IV bag, an equal volume of Sodium Chloride must be removed from the IV bag.

   Example:

   - Patient weight is 80 kg
   - Patient prescribed dose is 1 mg/kg = 80mg
   - ELFABRIO vial concentration is 20 mg/10 ml (2 mg/ml)
   - An 80 kg patient would receive 40 ml of ELFABRIO and need 40 ml of Sodium Chloride removed from the IV bag prior to adding ELFABRIO
8. Attach 30 ml syringe to needle free valve/clave and remove appropriate amount of 0.9% Sodium Chloride from IV bag, discard in the trash.
9. Attach a vented vial access spike to a sterile 10 ml syringe (and 3 ml syringe as needed).
10. Remove the protective cap of the vented vial access spike. While holding the vial of ELFABRIO firmly on the table, insert the spike into the center of the rubber seal.
11. Invert the vial and withdraw the contents into the syringe.

12. Unscrew the syringe from the spike and attach the syringe directly from the needle free valve at the injection port of the IV bag. Slowly inject the medication in to the IV bag.
13. Reattach the syringe to the spike and remove the spike from the empty vial. Now insert it into the next vial of ELFABRIO, while maintaining aseptic technique.
14. Repeat these steps until the total calculated dose of ELFABRIO has been transferred into the IV bag.

    NOTE: calculated volume may require removal of less than maximum volume (10 mL) from the last vial used for the infusion (partial vial use).

15. Remove the needle free valve and 18-guage needle from the injection port and dispose of in the bio-waste receptacle.
16. Discard all ELFABRIO vials in the biowaste container and document any amount of medication discarded in the logbook.
17. Gently invert IV bag to mix the solution, avoiding vigorous shaking or agitation

4.4. Administration

Diluted solutions of ELFABRIO should be used immediately. If immediate use is not possible, the diluted solution may be stored for up to 24 hours in the refrigerator (2 °C-8 °C) or 8 hours at room temperature (stored below 25 °C), away from light.

If medication cannot be used during these time frames it must be discarded. IMMEDIATELY CONTACT the treating physician's emergency line.

Time of preparation should be the time when the infusion preparation is finished and ready to be administered to the patient.

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

The treatment must not be altered in the home setting, unless medically warranted at the discretion of the treating physician.

Infusion will be administered intravenously using a pre-programmed pump over a specified time period. The pump will be pre-set by the physician's team before the first home infusion.

NOTE: Settings on the pump will remain the same as programmed infusion settings. Monitor the pump screen display that indicates the amount infused. Note it in the logbook (Appendix 10.1)

4.4.1. Venous access 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.

4.4.2. Inserting the Needle in the Vein

1. Ensure that some strips of tape are hanging ready for use and that the start of the infusion system is within reach. Place the alcohol wipes close by along with some gauzes.
2. Remove the infusion needle from the packaging.

3. Have the patient sit down and rest one arm on the table (preferably on a 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. Use tape to keep the needle into place.

4.4.3. Procedure

- Remove the protective cap from the 0.2-micron Cadd administration tubing spike and insert into the infusion port of the IV bag containing ELFABRIO.
- Hang IV bag on IV pole and attach Cadd Cassette to pump.
- Obtain IV access (see section 4.4.1 and/or section 4.4.2.**שגיאה! מקור ההפניה לא נמצא**)
- Prime the tubing and connect to the patient to start infusion. DO NOT prime fluid with the tubing connected to the patient.
- Ensure medication is administered at infusion rate **as prescribed by the Treating Physician** The patient should be sat down and relaxed while the infusion takes place.
- Should any alarm occur, resolve the problem as per pump specific instructions
    - In case of "air in line", stop the infusion, disconnect the line from the patient and gently tap the line to move all bubbles close to the end of the line (to limit any study drug wasting) and prime the line to ensure all air is removed.
    - In case of "down occlusion alarm" check patency of the infusion line and cannula. If the needle or cannula is occluded, do not flush; instead place a new needle or cannula in a different insertion point and remove the occluded cannula.
- In the case of a hypersensitivity reaction to the medication, or emergency, refer to section 5.1 section 5.2 and section 5.3.
- The pump will alarm at the end of the infusion. An empty infusion bag indicates the end time of Infusion and the start time of the clinical observation period (see section 4.3).

NOTE: Do not remove the IV access at this time.

- Flush the infusion line with 20 mL of saline.
- Once the pump indicates 20 mL has been infused, manually stop the pump.
- Remove the infusion tubing from the patient's IV cannula or Central Venous Access Device.

NOTE: The IV access should remain in place throughout the end of infusion monitoring period.

At the end of the infusion, all *IV bags and administration tubing* can be disposed of into the household trash unless contaminated with visible blood. *Contaminated tubing and IV needles* should be disposed of into the Bio-waste container.

4.4.4. Measurement of Vital Signs

Vital signs (blood pressure, body temperature, respiratory rate, and heart rate) will be collected at least 10 minutes pre-infusion, every 30 minutes during infusion and at end of the infusion.

During the post-dosing clinical observation period, vital signs will be collected every 60 minutes and at the end of the visit/observation period.

4.5. Observation Period

The patient should be observed for two hours after the infusion in case of IRR. Collect vital signs every 60 minutes until the observation duration has concluded, and again at the end time of the observation period.

In case of any ADR/IRR or other safety concern, follows the indication included in the "Emergency Treatment Plan" (see section 5.3) and record any clinical finding in the Logbook (Appendix 10.1).

Once the observation period is complete, remove patient's *IV/Central Venous access* and properly dispose of all used supplies in biohazard bag or sharps container as appropriate.

Additionally, there will be a nurse call to the patient one hour after the observation period to follow up on tolerability post infusion.

5. ELFABRIO SAFETY INFORMATION: INFUSION RELATED REACTION (IRR)

ELFABRIO has been shown to have good tolerability, however, being an IV protein product, hypersensitivity reactions including severe ones cannot be ruled out and these are commonly known as infusion-related reactions (IRRs).

IRRs defined as any related adverse events with onset after start of infusion and up to 2 hours after end of infusion have been reported (see also sections 4.4 and 4.8 of SmPC).

The most observed symptoms of IRRs were hypersensitivity, itching, nausea, dizziness, chills and muscular pain. As with any intravenous protein product, allergic-type hypersensitivity reactions may manifest and can include localised angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalised urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.

5.1. Identification

IRRs, including severe hypersensitivity reactions or anaphylactic reactions can occur following treatment with ELFABRIO. The most commonly observed symptoms of IRRs with ELFABRIO were hypersensitivity, itching, nausea, dizziness, chills and muscular pain.

Symptoms of hypersensitivity and serious allergic reactions include excessive and prolonged contraction of the airway muscles causing breathing difficulty (bronchospasm), swelling of the face, mouth and throat, wheezing, low blood pressure, hives, difficulty swallowing, rash, shortness of breath, flushing, chest discomfort, itchiness, sneezing and nasal congestion.

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5.2. Treatment and management

The following guidelines indicate the first aid procedures that should be used to manage a severe hypersensitivity reaction during home administration of the drug.

<u>At the first signs of a reaction:</u>

- Immediately stop administering the drug
- Maintain venous access with saline solution

- Place the patient in a comfortable position and, if possible, in the Trendelenburg position (with the legs raised to prevent hypotension). If the patient has difficulty breathing, a seated position is preferable to lying down;
- If the signs and symptoms are severe or deteriorate rapidly, take live saving actions and then immediately call the Treating Physician who will then provide the guidance to proceed following instruction reported in Table 2.
- Any action taken following an IRR will be documented in the Logbook (Appendix 10.1).
- Drug supplies available to the HCP will be managed according to local requirements and regulations.

ELFABRIO has been shown to have good tolerability. However, IRRs, including hypersensitivity reactions, cannot be ruled out. For this reason, emergency management procedures are described in Table 2

5.3. Emergency treatment plan

Any patients experiencing adverse events during the home infusion need to immediately stop the infusion process and seek the attention of a healthcare professional. Subsequent infusions may need to occur in a clinical setting.

The management of IRRs must be based on the severity of the reaction. For mild to moderate reactions, management should include slowing the infusion rate and treatment with medicinal products such as antihistamines, antipyretics and/or corticosteroids. If severe hypersensitivity reactions or anaphylactic reactions occur, immediately seek medical attention and stop the infusion. The Treating Physician will provide medical attention if required

6. Appendix 10. 1 - Logbook

Logbook for ELFABRIO Home Infusion

General data (*to be completed by treating physician*) Emergency number:		
CONTACT DETAILS		
Patient	Name:	
	Date of Birth:	
	Address:	
	Zip / City:	
	Telephone:	
	Name:	
	Address:	
	Zip / City:	
	Telephone	
Infusion Nurse/Home Nurse	Name:	
	Organisation:	
	Address:	
	Zip / City:	
Treating Physician	Name:	
	Hospital:	
	Address:	
	Zip / City:	
	Telephone:	
	Emergency number	
Pharmacy	Name:	
	Address:	
	Zip / City:	
	Telephone:	
Emergency treatment	Emergency number: 101	

Administration details *(to be completed by treating physician)*

ELFABRIO administered since	Date (dd-mmm-yyyy):
ELFABRIO dosing regimen	
- Dose	
- Frequency	
- Rate of infusion	
- Required reconstituted volume (ml)	
- Total volume in infusion bag (ml)	
Reasons for ELFABRIO infusion at home	
Indicate support to be provided by infusion nurse at home	

Infusion session form *(To be complete at each infusion session)*

- The patient and/or caregiver(s) have been informed about the associated risks of home infusion of ELFABRIO, and proper education on the use of emergency medications has been provided. The management of IRRs must be based on the severity of the reaction. For mild to moderate reactions, management should include slowing the infusion rate and treatment with medicinal products such as antihistamines, antipyretics and/or corticosteroids. If severe hypersensitivity reactions or anaphylactic reactions occur, immediately seek medical attention and stop the infusion. The Treating Physician will provide medical attention if required.
  Any patients experiencing adverse events during the home infusion need to immediately stop the infusion process and seek the attention of a healthcare professional. Subsequent infusions may need to occur in a clinical setting.

- Necessary actions in the event of a serious infusion-associated reaction, including emergency contact details, are described in Emergency Treatment Plan[1]. Keep this information readily available during the infusion procedure.

Date of Infusion	Date (mm-dd-yyy)
Patient's general health status - Describe any new health issues that you are currently experiencing prior to infusion, if any	
Dose	
Required reconstituted volume (ml)	
Number of vials used	
Duration of administration	
Infusion rate	

[1] See Section 6 and Appendix 10.4 of the HCP brochure and Section 5 in the Guide for Fabry Disease Healthcare Professionals to aid in the infusion at home to prevent medication errors

Problems/Remarks related to the infusion, if any (including infusion related reaction(s), action taken, and outcome)	
Name of person responsible for infusion, and date - Nurse -	

CALL FOR REPORTING

Reporting suspected adverse reactions is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

Company's contact point:

Megapharm LTD

Email: AERMEGA@MEGAPHARM.CO.IL

Tel: 09-7604596

If the patient, caregiver or infusion nurse/home nurse becomes aware that a mistake was made in the preparation and/or administration of the drug, they should inform the treating physician to determine appropriate action. Any medication errors should be reported as a spontaneous report to by the treating physician.

For full details please see the enclosed Israeli physician leaflet
This guide, format and content have been approved by the Ministry of Health on October 2024

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