Fabrazyme® (agalsidase beta)
Home Infusion Therapy:

Manual for patients with Fabry Disease who receive home infusion of agalsidase beta

VERSION NO. 2.0

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme. You can report via:

- The Yellow Card website www.mhra.gov.uk/yellowcard
- The free Yellow Card app available from the Apple App Store or Google Play Store
- Some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Suspected adverse reactions should also be reported to SANOFI on Tel: 0800 090 2314. Alternatively, send via e-mail to **UK-drugsafety@sanofi.com**.

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

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Contents

This patient manual contains important safety information you need to be aware of when receiving treatment with agalsidase beta.

Read all of this information carefully before you start home infusion.

Keep this information in an easily accessible place; you may need to read it again.

- If you have further questions, ask your treating physician.
- This medicine has been prescribed for you. Do not pass it on to others even if their symptoms are the same as yours as it may harm them.
- If you experience any side effects, you and/or your caregiver must notify your treating physician or infusion nurse.
- For further information please refer to the package leaflet provided with your medicine and available online at www.medicines.org.uk/emc

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1. YOUR DISEASE, TREATMENT AND HOME INFUSION

Together with your treating physician, you have decided to start home infusion therapy with agalsidase beta. **The objective of this document is to provide you with guidance on how to receive agalsidase beta at home.** The processes presented in this document serve as overall guidance but are subject to local medical practice and national rules and regulations. Your treating physician will provide you with the details that are applicable to your situation.

1.1 Fabry Disease and Treatment

Patients with Fabry disease have low or absent levels of an enzyme called alpha-galactosidase A. This enzyme is normally responsible for the breakdown of a fatty substance (globotriaosylceramide) and, as a result, abnormal deposits of this substance develop in blood vessel walls and other tissues throughout the body.

The main presenting childhood symptoms of Fabry disease in males include episodes of pain and burning sensations in the hands and feet, gastro-intestinal symptoms, skin rash and a decreased ability to sweat. Disease manifestations in adulthood are generally dominated by cardiac, renal and/or neurologic symptoms. In females, the course of the disease is variable, frequently - but not always - less severe than in affected males.

Agalsidase beta is an artificially produced enzyme which is intended to replace the natural enzyme alpha-galactosidase A that is lacking or not active enough in patients with Fabry disease. Agalsidase beta is used for the long-term treatment of patients who have a confirmed diagnosis of Fabry disease.

Refer to the agalsidase beta Package Leaflet for additional information.

1.2 Home Infusion

Currently, in some countries, people suffering from Fabry disease and treated with agalsidase beta receive their infusions at home. **The decision to receive home treatment should be made by you and your treating physician after initial infusions at the hospital to make sure you have no problems with the infusion.**

Home infusion of agalsidase beta will make it possible for you to receive treatment within your own living environment which increases comfort and flexibility of infusion timing. This does not require spending time travelling to and from the hospital, and you will be able to follow a normal schooling program and/or organise social and professional activities more easily. Home infusion also facilitates arranging treatment around family and friends.

The home infusion will take place under the responsibility of your treating physician. Distribution of the educational material should only be executed if the treating physician decides that the patient is eligible for home infusion treatment. **It is the responsibility of the treating physician to ensure a safe administration to the patient.** This should be checked and documented by the treating physician.

An appropriately trained infusion nurse will teach and assist you and/or your caregiver(s) in the beginning to ensure optimal treatment. The level of support required for home infusion will be discussed and agreed by you and/or your caregiver(s) and your treating physician. Should you prefer additional support for your infusion at home (after agreement of your treating physician), the infusion nurse can provide further assistance.

Note: The dose and rate of the infusion while at home must follow the guidelines provided by your treating physician as noted in the Logbook, and must not be changed without the prior agreement of your treating physician and supervision of the infusion nurse.

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1.3 Safety Assessments (side effects and medication errors)

Like all medicines, this medicine can cause side effects, although not everybody gets them. In clinical studies **side effects were mainly seen while patients were being given the medicine or shortly after ("infusion related reactions").** Severe life-threatening allergic reactions ("anaphylactoid reactions") have been reported in some patients. **If you experience any serious side effect, you should contact your doctor immediately.**

Very common symptoms (may affect more than 1 in 10 people) include **chills, fever, feeling cold, nausea, vomiting, headache and abnormal feelings in the skin such as burning or tingling.** Your doctor may decide to lower the infusion rate or give you additional medicines to prevent such reactions from occurring. For the full list of all side effects reported with agalsidase beta, see the Package Leaflet.

In the event that you do not feel well due to the medication during the home infusion or shortly after the infusion, you must immediately stop the medication. The treating physician, his/her medical designate, or the emergency services (see instructions in the Logbook) must be contacted immediately. Subsequent infusions may need to occur in a clinical setting.

Any symptoms or side effects must also be recorded in the Logbook. If you become aware that a mistake was made in the preparation and/or administration of agalsidase beta, please contact the infusion nurse or the treating physician to determine appropriate action before starting or continuing with the infusion.

- In case you feel the treatment is not efficacious, please contact your treating physician.

2. ORGANISATION OF TREATMENT AT HOME

The organisation of treatment at home should be performed under the supervision of the treating physician. Your treating physician will be responsible for organising the treatment at home. The processes presented in this document serve as an overall guidance but are subject to local medical practice and national rules and regulations.

2.1 Patient

- **You and/or your caregiver(s) 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.
- **You and/or your caregiver(s) have an understanding of Fabry disease,** and are able to recognise side effects and understand the procedures to be followed should they occur.
- **The home environment must be conducive** to the provision of the home infusion therapy including a clean environment with electricity, water, telephone access, refrigeration, and physical space to support storage of agalsidase beta and other infusion supplies.
- **You have been informed that the infusion should always be administered in the presence of an adequately trained adult** (infusion nurse or, if self-infusion skills have been acquired, an adult knowledgeable about the infusion procedures and adequately trained on what to do in case of an infusion-associated reaction and medication errors, as assessed by the treating physician or infusion nurse).
- **You must be physically and mentally able** to undergo the infusions at home. The treating physician is responsible for determining whether you may receive agalsidase beta infusions at home.

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- **You have accessible blood veins** that allow an infusion needle to be inserted. When you have a central venous access device you should know how the infusion needle should be inserted into the septum.
- **You and/or your caregiver(s) must agree that you receive the treatment at home.**
- **You and/or your caregiver have been adequately trained** in the procedures of agalsidase beta preparation and infusion.

2.2 Treating Physician

- The treating physician **is responsible for the initiation of all necessary administrative actions,** allowing the other parties involved (the nurse, patient and/or caregiver(s) and pharmacist) to proceed.
- The treating physician **is responsible for determining the dose, the infusion rate, the pre-infusion treatment, and the emergency treatment,** to be described in the Logbook. Any changes must be clearly communicated to the patient and/or caregiver(s) and described in the Logbook.
- **The home infusion will take place under the responsibility of the treating physician.** Distribution of the educational material should only be executed if the treating physician decides that the patient is eligible for home infusion treatment. It is the responsibility of the treating physician to ensure a safe administration to the patient. This should be checked and documented by the treating physician.
- The treating physician **is responsible for setting up communication lines** in case immediate medical attention is required. This should be described in the Logbook.
- **Appropriate scheduling and monitoring of the infusions** is the responsibility of the treating physician and infusion nurse.

2.3 Pharmacy and Infusion Equipment

- Treatment and all necessary equipment will be provided according to local arrangements and regulations.

2.4 Infusion Nurse

- The infusion nurse **will establish with the treating physician and the patient and/or caregiver(s) the level of support necessary** at home during infusions.
- The infusion nurse **will have a coordinating task** together with the treating physician and you and/or your caregiver(s) in organising the treatment at home.
- The infusion nurse **is qualified to give intravenous (IV) infusions.**
- The infusion nurse **has been trained in administering agalsidase beta.**
- The infusion nurse **is aware of the possible side effects** (including serious allergic reactions) and the actions to be taken should they occur.
- The infusion nurse **will strictly follow the prescribed method of preparation and administering** agalsidase beta as stated in this Manual.
- The infusion nurse **will strictly follow the prescribed dose and infusion rate** of agalsidase beta as stated in the Logbook.
- The infusion nurse **will record each administration** of agalsidase beta in the Logbook.
- **Appropriate scheduling and monitoring of the infusions** is the responsibility of the treating physician and infusion nurse.

- **In the event of an IAR, the infusion nurse must discontinue the infusion and phone the treating physician and/or the emergency services as described in the Logbook. The treating physician or the emergency services must also be contacted immediately if an IAR occurs shortly after completion of the infusion. Any IAR must be recorded in the Logbook.**

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2.5 Pre-treatment and Emergency Treatment

- If necessary, **your treating physician will prescribe pre-treatment medication.** Your treating physician will include the information on this medication in the Logbook.
- Your treating physician **will prescribe medication to respond to an emergency situation,** if necessary. Your treating physician will include the information on this medication in the Logbook. This emergency medication should be available during the infusions at home.

2.6 The Logbook

- **You have been provided a logbook by your physician.** This will serve as a **means of communication** for everyone involved in administering agalsidase beta at home.
- The Logbook **must be kept at your home** and will be kept up to date by you, your caregiver(s), your treating physician and/or the infusion nurse.
- **The prescribed dose and infusion rate of agalsidase beta as stated in the Logbook should be strictly followed.** The treating physician is responsible for describing the dose and the infusion rate, as well as any changes.
- **Each administration of agalsidase beta at home should be recorded in the Logbook.**
- You and/or your caregiver(s) **must take the Logbook along to the hospital** at each appointment for a check-up and bring it home afterwards.
- **The infusion nurse records the findings and actions from the initial interview** and you, your caregiver(s) or the infusion nurse notes all relevant information from subsequent visits in the Logbook.

> - **In the Logbook, the treating physician must clearly state what has to be done and administered in the event of an infusion side effect. In case of any reaction to an infusion, the infusion needs to be stopped.**

- Any infusion associated side effect and/or medication error should be recorded in the Logbook.

3. TRAINING ON PREPARATION AND ADMINISTRATION OF AGALSIDASE BETA

The initial instructions will be given at the hospital. The level of support required for home infusion will be discussed and agreed by you and/or your caregiver(s) and your treating physician.

- **Your treating physician is responsible for the organisation of the home infusion** and needs to agree upon the home infusion procedure.
- **Should you prefer to carry out the procedure yourself or with the assistance of your caregiver(s), you and/or your caregiver(s) will receive training from the infusion nurse.** The infusion nurse will explain and demonstrate the complete infusion procedure to you and/or your caregiver(s), including training in hand hygiene, proper disinfection and aseptic handling when preparing the infusion.
- **At subsequent visits, the infusion nurse will be present to assist, if required,** until you and/or your caregiver(s) feel confident with the entire infusion procedure.
- While preparing and administering agalsidase beta, the procedures described in the Package Leaflet must be closely followed and as described in this Manual must be adhered to.
- **Each administration of agalsidase beta should be recorded in the Logbook.**
- **The infusion should always be administered in the presence of an adult** knowledgeable about the infusion procedures and adequately trained on how to handle in case of an infusion-associated reaction and medication errors (as assessed by the treating physician or infusion nurse).

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4. HOW DO I PREPARE AND ADMINISTER AGALSIDASE BETA?

4.1 Supplies

Supplied by the hospital/pharmacy to you or to a third party, and as prescribed by the treating physician.

- Vials of agalsidase beta (5 mg or 35 mg per vial); must be stored in a clean refrigerator at a temperature between +2°C and +8°C.
- Sterile water for injection to reconstitute agalsidase beta.
- NaCl 0.9% solution, 2 x 250 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 2 ml, 10 ml and 50 ml syringes depending upon dose of agalsidase beta.
- 3 x sterile hypodermic needles (1.1 x 40 mm).
- 1 x infusion needle.
- In-line low protein-binding 0.2 micron filter.
- Infusion-administration set (infusion line).
- Tape.
- Sterile skin cleansing swabs.
- Sharps bin.
- Hand wash.
- Tourniquet.
- Additional requisites if using a venous access device:
  - Heparin.
  - NaCl 0.9% solution.
  - Needles.
  - Syringes.
  - Dressing pack.
  - Sterile gloves.
  - Gripper needle.
- Pre-treatment medication (if applicable).
- Emergency medication (See Logbook for instructions by treating physician).

4.2 Preparation

NOTE: The instructions for use (reconstitution, dilution and administration) can be found in the Package Leaflet (available online at: www.medicines.org.uk/emc). A detailed description is provided in this section.

1. Prepare a clean work area and lay out the supplies.
2. The vials of agalsidase beta must be removed from the refrigerator to reach room temperature approximately 30 minutes before preparation.
3. Check the expiry date printed on the bottom of the vial pack (do not use agalsidase beta after the labelled expiry date).
4. Verify if the number of vials received is correct.
5. Prepare only the number of vials required for one infusion.

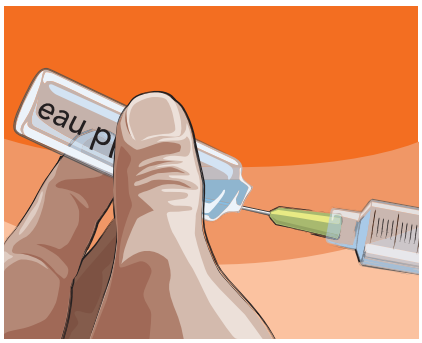
Note: The storage instructions are described in the instructions for use in the Package Leaflet (a copy of the package leaflet can be found online at: www.medicines.org.uk/emc), and must be followed.

4.2 STEP 1: Preparation of the materials

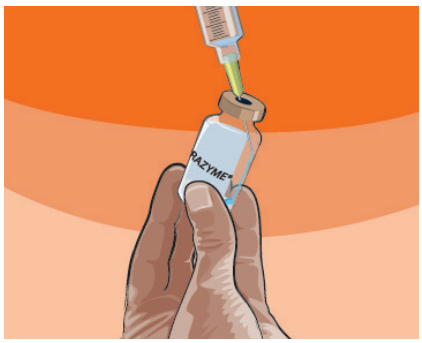
4.3 Reconstituting agalsidase beta

1. Remove the flip-off cap from the agalsidase beta vial.
2. Disinfect the rubber stopper of the agalsidase beta vial with chlorhexidine and allow to air dry.
3. Open the sterile water for injection.
4. Draw the required amount (ml) of sterile water into the syringe.
   - For 35 mg vials, reconstitute each vial with 7.2 ml water for injection.
   - For 5 mg vials, reconstitute each vial with 1.1 ml water for injection.
5. Avoid forcefully ejecting the water for injection from the syringe onto the powder, to minimise foaming. This should be done by slow drop-wise addition of the water for injection down the inside of the vial. Roll and tilt each vial gently. Do not invert, swirl or shake the vial.
6. Repeat the process for more agalsidase beta vials if required.
7. Small bubbles may appear after the mixing.
8. Let the solution settle for a few minutes to allow any bubbles present to disappear and to ensure that the powder is properly reconstituted.
9. After reconstitution, agalsidase beta must be inspected visually before use. The reconstituted solution must be a clear, colourless liquid and free from foreign matter. Because this is a protein solution, slight flocculation/ cloudiness (in the form of thin translucent fibres) may occur occasionally after dilution.
10. If you notice any foreign matter or discolouration of the liquid, do not use the product and contact the infusion nurse and/or treating physician.
11. It is recommended that the vials be diluted promptly after reconstitution, to minimise protein particle formation over time.
12. Any unused product or waste material must be disposed of in accordance with local requirements.

4.3 STEP 2: Disinfect the vial



4.3 STEP 4: Draw the required amount of sterile water into the syringe



4.3 STEP 5: Avoid forcefully ejecting the water for injections from the syringe

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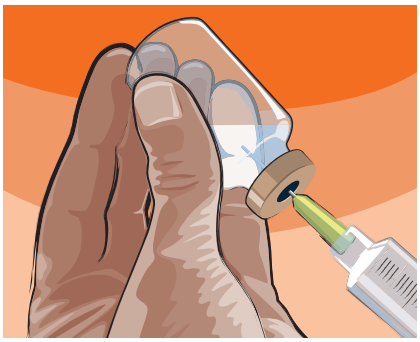
4.4 Dilution

1. Disinfect the cap/opening of 1 or 2 bags of NaCl 0.9% solution using chlorhexidine and allow to air dry.
2. The volume of reconstituted agalsidase beta solution must be the same as the prescribed volume in the Logbook.
3. Insert the needle in the cap of the infusion bag and slowly withdraw a volume of NaCl 0.9% solution, equivalent to the volume of the reconstituted agalsidase beta solution to be added.

   For instance, if the prescribed reconstituted volume is 14 ml, remove 14 ml of NaCl solution from the bag of NaCl solution. Never remove more than half the content of the bag of NaCl solution to ensure that at least half the diluted solution consists of NaCl solution.
4. Remove the airspace within the infusion bag by withdrawing the air into a 50 ml syringe.
5. Slowly withdraw the reconstituted solution from each vial up to the total volume required. At the point when these quantities are withdrawn, the reconstituted product should not contain any foam.
6. Gently inject the total volume of the reconstituted agalsidase beta solution into the infusion bag of NaCl 0.9% solution.
7. Carefully mix this agalsidase beta solution by gently inverting or lightly massaging the infusion bag. Do not shake or excessively agitate the infusion bag.
8. The diluted solution should be filtered through an in-line low protein-binding 0.2 micron filter during administration.

4.4 STEP 3: Slowly withdraw the required volume of NaCl 0.9% solution, equivalent to the volume of the reconstituted agalsidase beta



4.4 STEP 5: Slowly withdraw the reconstituted solution from each vial up to the total volume required

4.4 STEP 5: The reconstituted product should not contain any foam

4.5 Administration

4.5.1 Filling the Infusion Line

1. Remove the infusion system from the package and close it using the roller clamp. Connect the in-line filter to the infusion line.
2. Connect the spike in the NaCl 0.9% solution bag that does not contain agalsidase beta and fill the infusion system by holding the drip chamber upside down and opening the clamp.
3. Fill the entire system, remove any air bubbles that may be present and close the roller clamp.
4. Connect the infusion bag containing agalsidase beta to the y-system. Keep the clamp closed.

4.5.2 Inserting the Needle in the Vein

In case of self-infusion, the adult person present during the infusion session should have been adequately trained (by the infusion nurse, treating physician, or his/her medical designate) on the technique of needle insertion.

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 chlorhexidine solution close by, along with some gauzes.
2. Remove the needle from the packaging.
3. Sit down and rest one arm on the table (preferably on a clean cloth).
4. Apply the tourniquet, look for an appropriate vein, 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. Connect the system with filter to the needle.
7. Remove the tourniquet; 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 using a new needle. Open the clamp for NaCl 0.9% solution.
8. Adjust the infusion rate according the prescription (see the Logbook), and open the valve. Sit down and relax while the infusion takes place. Keep the Logbook close in case information on emergency procedures is needed.

4.5.3 Administration

- From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage and conditions are the responsibility of the user. The product diluted in NaCl 0.9% solution will retain chemical stability up to 24 hours if stored at a temperature between 2°C and 8°C and away from light.
- The agalsidase beta 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.
- After the agalsidase beta infusion has been completed, the system is flushed with NaCl 0.9% solution at the same rate, and the needle is then removed.

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4.5.4 Preparation of the agalsidase beta infusion in case of a central venous access device

When you have a venous access device for the delivery of agalsidase beta, you and/or your caregiver(s) will be shown how to care for the device by the infusion nurse, if this has not already been demonstrated during hospital-based infusions.

Proper care of a venous access device involves regular irrigation with a drug called heparin to prevent clotting and attention to a sterile technique to keep the device free of infection. The following steps are necessary:

- When in use, cover site with transparent occlusive dressing. No dressing required when not in use.
- Flush with 5 ml NaCl 0.9% solution before and after each use.
- Flush with 5 ml heparin (100 U/ml) after each use.