Fabrazyme® (agalsidase beta) Preparation & Administration

SUPPLIES, PREMEDICATION AND EQUIPMENT:

1. Fabrazyme vials
2. Sterile Water for Injection, USP
3. 0.9% Sodium Chloride Injection, USP (infusion bag)
4. Syringes for reconstitution and dilution
5. Needles (do not use filter needles)
6. Intravenous administration pump and tubing
7. In-line low protein-binding 0.2 µm filter
8. Antipyretics (premedication)
9. Additional supplies as per institutional procedures

Note: Make sure the patient is ready to receive infusion before reconstituting the enzyme.
Fabrazyme does not contain any preservatives. Vials are for single use only and should not be stored for subsequent use once reconstituted. Discard any unused product. Use reconstituted and diluted solutions of Fabrazyme immediately. If immediate use is not possible, the reconstituted and diluted solution may be stored for up to 24 hours at 2°C to 8°C (36°F to 46°F).

DOSAGE:

The recommended dosage of Fabrazyme is 1 mg/kg body weight infused every two weeks as an intravenous (IV) infusion.

PREPARATION:

1. Verify patient dosage and remove the appropriate number of Fabrazyme vials from the refrigerator. The number of 35 mg and 5 mg vials needed is based on the patient's body weight and the recommended dose of 1 mg/kg.

To calculate dose:
Patient weight (in kg) = Patient dose (in mg) • Patient dose (in mg) ÷ 5 mg/mL = number of mL of reconstituted Fabrazyme required for patient dose • Based on the patient dose in mL, determine the number of 35 mg vials (7 mL extractable volume) and 5 mg vials (1 mL extractable volume) needed

2. Allow Fabrazyme vials and diluent to reach room temperature prior to reconstitution (approximately 30 minutes). DO NOT USE Fabrazyme after the expiration date on the vial.
3. Prepare a clean work area and organize supplies. Prepare infusion using aseptic technique.
4. Remove and discard plastic protective caps from vials.
5. Reconstitute each Fabrazyme vial by slowly injecting the appropriate volume of Sterile Water for Injection, USP to the inside wall of each vial. 35 mg vials require 7.2 mL and 5 mg vials require 1.1 mL.
6. Roll and tilt each vial gently. Avoid shaking or agitating the vials. Each vial will yield a 5 mg/mL clear, colorless solution.
7. Visually inspect the reconstituted vials for particulate matter and discoloration. Do not use the reconstituted solution if there is particulate matter or if it is discolored. If particulate matter is observed or if the solution is discolored, report to Sanofi Genzyme Medical Information at 800-745-4447 (option 2).
8. The reconstituted solution should be further diluted with 0.9% Sodium Chloride Injection, USP to a total volume based on patient weight (kg).

Total Infusion Volume Based on Patient Weight

Patient Weight (kg)	Minimum Total Volume (mL)
≤ 35	50
35.1 – 70	100
70.1 – 100	250
> 100	500

9. Obtain the appropriate size infusion bag. Prior to adding the volume of reconstituted Fabrazyme required for the patient dose, remove an equal volume of 0.9% Sodium Chloride Injection, USP from the infusion bag. Slowly withdraw the reconstituted solution from each vial up to the total volume required for the patient dose. Inject the reconstituted Fabrazyme solution directly into the Sodium Chloride solution. Do not inject into the air space within the infusion bag. Discard any vial with unused reconstituted solution.
10. Gently invert infusion bag to mix the solution, avoiding vigorous shaking and agitation.
11. Do not infuse Fabrazyme in the same intravenous line with other products.
12. Administer Fabrazyme using an in-line low protein-binding 0.2 µm filter.

ADMINISTRATION:

1. Explain the administration procedure to the patient.
2. Administer antipyretics to the patient prior to infusion (see Warnings and Precautions section of Full Prescribing Information).
3. Obtain appropriate baseline vital signs prior to the infusion.
4. Obtain intravenous access in the appropriate location; antecubital, wrist, or hand veins may be used.
5. Draw required blood work and flush line with 0.9% Sodium Chloride Injection, USP.
6. Connect the IV tubing to the Fabrazyme infusion bag.
7. Prime the tubing with Fabrazyme and expel any air prior to administration.
8. Attach the intravenous line to the infusion bag and begin the initial infusion at a rate no more than 0.25 mg/min (15 mg/hr). Slow the infusion rate in the event of infusion-associated reactions. For patients >30 kg, after patient tolerance to the infusion is well established, increase the infusion rate in increments of 0.05 to 0.08 mg/min (increments of 3 to 5 mg/hr) with each subsequent infusion.
   - For patients weighing < 30 kg, the maximum infusion rate is 0.25 mg/min (15 mg/hr)
   - For patients weighing ≥ 30 kg, the minimum infusion duration is 1.5 hours (based on individual patient tolerability)
9. Monitor the patient's vital signs at regular intervals.
10. When the infusion is complete, flush the infusion line with 0.9% Sodium Chloride Injection, USP to ensure the entire dose of Fabrazyme is delivered to the patient. Do not push the flush; rather, infuse at the last infusion rate tolerated by the patient.

IMPORTANT TREATMENT CONSIDERATIONS:

1. Life-threatening anaphylactic and severe hypersensitivity reactions have been observed in some patients during Fabrazyme infusions. If severe hypersensitivity or anaphylactic reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe hypersensitivty reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.
2. If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.
3. In clinical trials, some patients developed IgE or skin test reactivity specific to Fabrazyme. Physicians should consider testing for IgE in patients who experienced suspected hypersensitivity reactions. Re-administration of Fabrazyme to patients who have previously experienced severe or serious hypersensitivity reactions to Fabrazyme should be done only after careful consideration of the risks and benefits of continued treatment, and only under the direct supervision of qualified personnel and with appropriate medical support measures readily available.
4. Adverse events should be reported promptly to Sanofi Genzyme Medical Information at 800-745-4447 (option 2) or 617-768-9000 (option 2).

Please see Important Safety Information on reverse as well as accompanying full Prescribing Information.

Fabrazyme® (agalsidase beta)

INDICATION AND USAGE

Fabrazyme® is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Anaphylaxis and Hypersensitivity Reactions

In clinical trials and postmarketing safety experience with Fabrazyme, approximately 1% of patients developed anaphylactic or severe hypersensitivity reactions during Fabrazyme infusion.

Life-threatening anaphylactic and severe hypersensitivity reactions have been observed in patients during Fabrazyme infusions.

- Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.
- Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, antihistamines, epinephrine, and IV corticosteroids.
- If anaphylactic or severe hypersensitivity reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe hypersensitivity reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

In clinical trials with Fabrazyme, some patients developed IgE antibodies or skin test reactivity specific to Fabrazyme.

- Higher incidences of hypersensitivity reactions were observed in adult patients with persistent anti-Fabrazyme antibodies and in adult patients with high antibody titer compared to that in antibody negative adult patients.
- Physicians should consider testing for IgE antibodies in patients who experienced suspected hypersensitivity reactions and consider the risks and benefits of continued treatment in patients with anti-Fabrazyme IgE antibodies. Rechallenge of these patients should only occur under the direct supervision of qualified personnel, with appropriate medical support measures readily available.

Infusion-Associated Reactions

In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe. Infusion-associated reactions are defined as adverse reactions occurring on the same day as the infusion. The incidence of infusion-associated reactions was higher in patients who were positive for anti-Fabrazyme antibodies than in patients who were negative for anti-Fabrazyme antibodies.

- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment.
- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.
- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated. Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated. Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.
- Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions. Monitor closely patients with compromised cardiac function if Fabrazyme is administered to these patients.

ADVERSE REACTIONS

- Common adverse reactions reported (≥20% and >2.5% compared to placebo) were upper respiratory tract infection (53% vs 42%), chills (49% vs 13%), pyrexia (39% vs 22%), headache (39% vs 28%), cough (33% vs 25%), paresthesia (31% vs 18%), fatigue (24% vs 17%), peripheral edema (21% vs 7%), dizziness (21% vs 8%), and rash (20% vs 10%).

Please see full Prescribing Information for Fabrazyme.

www.fabrazyme.com/hcp

sanofi

MAT-US-2015550-v3.0-04/2023