

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.

DOSAGE:

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

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

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.

9. Gently invert infusion bag to mix the solution, avoiding vigorous shaking and agitation.
10. Do not infuse Fabrazyme in the same intravenous line with other products.
11. 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). The infusion rate may be slowed in the event of infusion reactions. After patient tolerance to the infusion is well established, the infusion rate may be increased 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 should remain at 0.25 mg/min (15 mg/hr)
 - For patients weighing ≥ 30 kg, the administration duration should not be less than 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 allergic reactions have been observed in some patients during Fabrazyme infusions. If severe allergic or anaphylactic reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Appropriate medical support measures should be readily available when Fabrazyme is administered because of the potential for severe infusion reactions.
2. If an infusion reaction occurs, regardless of pretreatment, decreasing the infusion rate, temporarily stopping the infusion, and/or administration of additional antipyretics, antihistamines and/or steroids may ameliorate the symptoms.
3. Patients who have had a positive skin test to Fabrazyme or who have tested positive for anti-Fabrazyme IgE antibodies may be rechallenged with Fabrazyme. The initial rechallenge administration should be a low dose at a lower infusion rate, e.g., 1/2 the therapeutic dose (0.5 mg/kg) at 1/25 the initial standard recommended rate (0.01 mg/min). Once a patient tolerates the infusion, the dose may be increased to reach the approved dose of 1 mg/kg and the infusion rate may be increased by slowly titrating upward (double every 30 minutes up to a maximum rate of 0.25 mg/min), as tolerated.
4. Adverse events should be reported promptly to 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

Fabrazyme® (agalsidase beta)

Indications and Usage

Fabrazyme is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.

Important Safety Information

Life-threatening anaphylactic and severe allergic reactions have been observed in patients during Fabrazyme infusions. In clinical trials and postmarketing safety experience, approximately 1% of patients developed anaphylactic or severe allergic reactions 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 severe allergic or anaphylactic reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe allergic reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

In patients experiencing infusion reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion reactions occurred in some patients after receiving pretreatment with antipyretics, antihistamines, and oral steroids. If an infusion reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms. If severe infusion 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 reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

Re-administration of Fabrazyme to patients who have previously experienced severe or serious allergic 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.

The most common adverse reactions reported are infusion reactions, some of which were severe. Infusion reactions occurred in approximately 50-55% of patients during Fabrazyme administration in clinical trials. Serious and/or frequently occurring ($\geq 5\%$ incidence) related adverse reactions consisted of one or more of the following: chills, fever, feeling hot or cold, dyspnea, nausea, flushing, headache, vomiting, paresthesia, fatigue, pruritus, pain in extremity, hypertension, chest pain, throat tightness, abdominal pain, dizziness, tachycardia, nasal congestion, diarrhea, edema peripheral, myalgia, back pain, pallor, bradycardia, urticaria, hypotension, face edema, rash, and somnolence.

Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion reactions. Patients with compromised cardiac function should be monitored closely if the decision is made to administer Fabrazyme.

Other serious adverse events reported in clinical studies included stroke, pain, ataxia, bradycardia, cardiac arrhythmia, cardiac arrest, decreased cardiac output, vertigo, hypoacusis, and nephrotic syndrome. These adverse events also occur as manifestations of Fabry disease; an alteration in frequency or severity cannot be determined from the small numbers of patients studied.

Severe and serious infusion related reactions have been reported in postmarketing experience, some of which were life threatening including anaphylactic shock. In addition to the above adverse reactions, the following have been reported during postmarketing use of Fabrazyme: arthralgia, asthenia, erythema, hyperhidrosis, infusion site reaction, lacrimation increased, leukocytoclastic vasculitis, lymphadenopathy, hypoesthesia, oral hypoesthesia, palpitations, rhinorrhea, oxygen saturation decreased and hypoxia.

Adverse reactions (regardless of relationship) resulting in death reported in the postmarketing setting with Fabrazyme treatment included cardiorespiratory arrest, respiratory failure, cardiac failure, sepsis, cerebrovascular accident, myocardial infarction, renal failure, and pneumonia. Some of these reactions were reported in Fabry disease patients with significant underlying disease.

The safety and efficacy in patients younger than 8 years of age have not been evaluated.

Most patients who develop IgG antibodies do so within the first three months of exposure. IgG seroconversion in pediatric patients was associated with prolonged half-life of Fabrazyme, a phenomenon rarely observed in adult patients.

In clinical trials, a few patients developed IgE or skin test reactivity specific to Fabrazyme. Physicians should consider testing for IgE in patients who experienced suspected allergic reactions and consider the risks and benefits of continued treatment in patients with anti-Fabrazyme IgE antibodies.

Fabrazyme is available by prescription only. Side effects should be reported promptly to Genzyme Medical Information at 800-745-4447, option 2. To learn more, please see the full prescribing information, visit www.fabrazyme.com, or contact Genzyme at 1-800-745-4447.

Please see accompanying full Prescribing Information.

www.fabrazyme.com

genzyme

©2011 Genzyme Corporation. Fabrazyme is a registered trademark of Genzyme Corporation. All rights reserved. FZ-US-P003-04-11