FULL PRESCRIBING INFORMATION: CONTENTS

1 INDICATIONS AND USAGE
Fabrazyme (agalsidase beta) is indicated for use in patients with Fabry disease. Fabrazyme reduces globoside/sndose-3 (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose
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 (see Warnings and Precautions (5.2)).

The initial IV infusion rate should not be more than 0.25 mg/min (15 mg/hr). The infusion rate may be increased in increments of 0.05-0.08 mg/min increments of 15 mg/hr with each subsequent infusion. For patients weighing < 30 kg the maximum infusion rate should remain at 0.25 mg/min. For patients weighing >= 30 kg, the administration duration should not be less than 1.5 hours (based on individual patient tolerability).

Patients who have had a positive skin test to Fabrazyme or who have tested positive for anti-Fabrazyme IgE antibodies may be successfully re-challenged with Fabrazyme. The initial re-challenge administration should be a low dose at a slower infusion rate. Each 1/2 the initial standard recommended rate (0.05 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 optimized by slowly titrating upwards (every 30 minutes up to a maximum rate of 0.25 mg/min), as tolerated.

2.2 Instructions for Use
Fabrazyme does not contain any preservatives. Vials are for single use only. Discard any unused portion. Avoid shaking or agitating this product. Do not use filter needles during the preparation of the infusion.

3 DOSAGE FORMS AND STRENGTHS

3.1 Vials

Lysol powdered for reconstitution (1/2 mL) is 5 mg single-use vials (3)

4 CONTAINMENT DISCONTINUED

Note (5)

5 WARNINGS AND PRECAUTIONS

5.1 Infusion Reactions
In clinical trials with Fabrazyme, approximately 1% of patients developed IgE antibodies or a skin test reaction specific to Fabrazyme. Two or more patients in the re-challenge study discontinued treatment with Fabrazyme primarily due to recurrent infusion reactions. Severe infusion reactions have occurred in patients with a history of anaphylaxis. Fabrazyme is contraindicated for use in patients with IgE antibodies. See Warnings and Precautions (5.1) and Dosage and Administration (2.2).

5.2 Infusion Reactions
In clinical trials with Fabrazyme, approximately 50-55% of patients experienced infusion reactions during Fabrazyme administration. The most frequent infusion reactions reported were systemic and included chills, fever, feeling hot or cold, dyspnea, nausea, flushing, headache, vomiting, paresthesia, fatigue, pruritus, pain in extremity, hypotension, chest pain, throat tightness, abdominal pain, dyspnea, tachycardia, nausea, peripheral edema, syncope, facial edema, rash, and urticaria.

In clinical trials and post-marketing experience with Fabrazyme, approximately 1% of patients developed IgE antibodies or a skin test reaction specific to Fabrazyme. Two or more patients in the re-challenge study discontinued treatment with Fabrazyme primarily due to recurrent infusion reactions. Severe infusion reactions have occurred in patients with a history of anaphylaxis. Fabrazyme is contraindicated for use in patients with IgE antibodies. See Warnings and Precautions (5.1) and Dosage and Administration (2.2).

5.3 Compromised Cardiac Function
Patients with advanced Fabry disease may have compromised cardiac function, which may preclude them to a higher risk of severe complications from infusion reactions, and these patients should be monitored closely during Fabrazyme administration (5.3).

8.1 Pregnancy
Fabrazyme may cause fetal harm when administered to a pregnant woman. It is unknown whether Fabrazyme crosses the placenta. It is recommended that women of childbearing potential use effective contraception during and for at least 1 month after therapy discontinuation.

8.3 Nursing Mothers
Fabrazyme is excreted in human milk. It is not known whether Fabrazyme is excreted in human milk. Because animal breastfeeding studies are not available, and because of the potential for Fabrazyme to cause adverse reactions, breastfeeding should be avoided in mothers receiving Fabrazyme.

9.4 Local Viral Infections

9.5 Local Infections

15.2 Laboratory Data Changes

15.3 Other Laboratory Data Changes

15.4 Immune Reactions

15.5 Allergic Reactions

16 ADVERSE REACTIONS

In clinical trials with Fabrazyme, at least 20% of patients experienced infusion reactions during Fabrazyme administration or dose interruptions because of the potential for severe infusion reactions (5.1). Treatment-emergent adverse reactions (regardless of relationship) occurring in patients treated with Fabrazyme during one or more of the two placebo-controlled trials (Study 1) and Study 2 (see Clinical Studies (14)) are summarized in Table 2. Treatment-emergent adverse reactions (regardless of relationship) occurring during the double-blind treatment periods of the five placebo-controlled trials (Studies 1 and 2) are summarized in Table 2. Treatment-emergent adverse reactions (regardless of relationship) occurring during the double-blind treatment periods of the five placebo-controlled trials (Studies 1 and 2) are summarized in Table 2. Treatment-emergent adverse reactions (regardless of relationship) occurring during the double-blind treatment periods of the five placebo-controlled trials (Studies 1 and 2) are summarized in Table 2.

Typhilitis 6(8) 2(3)
Hypertension 4(5) 0
Taste perversion 7(9) 1(2)
Dysuria 20(25) 12(20)
Procedural pain 20(25) 12(20)
Fever 5(6) 2(3)
Excoriation 7(9) 1(2)
Post-procedural complication 8(10) 1(2)
Blood creatinine increased 7(9) 1(2)
Musculoskeletal and Connective Tissue Disorders

5.4 Immunogenicity and Re-challenge

5.5 Monitoring Laboratory Tests

5.6 Observed Reactions

6 ADVERSE REACTIONS

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Table 2. Continued

Summary of Adverse Reactions (regardless of relationship) Occurring in Fabrazyme®-Treated Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Regimen</th>
<th>Dose</th>
<th>Dose (mg/kg)</th>
<th>Adverse Reaction</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.4 Pediatric Use</td>
<td>Phase 01/02: Phase 1/2 Study in Adult Patients with Fabry Disease</td>
<td>0.5 mg/kg</td>
<td>0.5</td>
<td>0.5 mg/kg</td>
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<td>1 mg/kg</td>
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<td>3 mg/kg</td>
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<td></td>
<td>Study AGAI-AG10: Open-label Extension Study in Adult Patients with Fabry Disease</td>
<td>0.5 mg/kg</td>
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<td>3 mg/kg</td>
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14 CLINICAL STUDIES

The safety and efficacy of Fabrazyme were assessed in four clinical studies in patients with Fabry disease. Study 1 was a randomized, double-blind, placebo-controlled, multi-center, multi-study of Fabrazyme in 58 patients (56 males and 2 females), ages 16 to 67 years, all naïve to enzyme replacement therapy. Patients received either 1 mg/kg or placebo every 4 weeks for 5 months (12 patients per group for a total of 114 patients). All patients were pretreated with acetaminophen and an antihistaminic to decrease or prevent infusion reactions. One death occurred in the placebo group, related to the development of encephalopathy and an increase in creatinine. No patients withdrew from the trial due to the development of any serious adverse event. The primary efficacy endpoint of 0.3 increases in renal interstitial capillary endothelial cells, was assessed by light microscopy and was graded on an 11-point system, scoring ranging from 0 (normal) to 3 (severe). Patients were randomized to Fabrazyme or placebo. A GL-3 increase of >=10% was achieved in 20 of 28 (71%) patients treated with Fabrazyme compared to 20 of 28 treated with placebo (p=0.001). Similar reductions in GL-3 increases were observed in the capillary endothelial of the heart and skin.

Table 4

Reduced GL-3 Inclusion by Normal or Near Normal Levels (N=28) in the Capillary Endothelium of the Heart, Skin, and Kidney

<table>
<thead>
<tr>
<th>Group</th>
<th>Regimen</th>
<th>Dose (mg/kg)</th>
<th>Dose (mg/kg)</th>
<th>Density</th>
<th>Density</th>
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6.5 Genetic Use

Clinical trial of Fabrazyme did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

6.6 Adverse Reactions in Women

Adverse reactions (regardless of relationship) resulting in death reported in the postmarketing setting with FABRAZYME included pharyngeal edema, face swelling, and swollen tongue), generalized urticaria, bronchospasm, and hypotension.

It is not known whether Fabrazyme is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Fabrazyme is administered to a nursing mother.

3.2 Labeling and Delivery

There is no information on the effect of Fabrazyme during labor and delivery. Pregnant females are encouraged to enroll in the Fabry Registry. The registry will monitor the effect of Fabrazyme on the mother and her offspring. More information can be found at www.FabryRegistry.info.

3.3 Nursing Mothers

Fabrazyme is supplied as a sterile lyophilized cake or powder.Fabrazyme 55 mg is supplied as a single-use, clear Type glass vial (20 mL) (NDC 04846-0041-1). The container consists of a siliconized between and a 5-ml sterile syringe. FABRAZYME and Genzyme are registered trademarks of Genzyme Corporation. 03/01/17

11.3 Caringogenesis, Mutagenesis, Impairment of fertility

Potential adverse reactions associated to enroll in the Fabry Registry (see Use in Specific Populations 8.1 and Parenterl Counseling Information 17).