HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fabrazyme safely and effectively. See full prescribing information forFabrazyme.

FABRAZYME® (agalsidase beta) for injection, for intravenous use

Initial U.S. Approval: 2003

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. (1)

DOSE AND ADMINISTRATION

• The recommended dosage is 1 mg/kg body weight given every two weeks as an intravenous infusion. (2.1)

• Administer antipyretics prior to infusion. (2.1)

• See the full prescribing information for the recommended infusion rate. (2.1)

DOSE FORMS AND STRENGTHS

For injection: 5 mg or 35 mg lyophilized cake or powder in a single-dose vial for reconstitution (3)

CONTRAINDICATIONS

For injection: 5 mg or 35 mg lyophilized cake or powder in a single-dose vial for reconstitution (3)

WARNINGS AND PRECAUTIONS

• 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-associated reactions. (5.1)

• Infusion-associated reactions occurred in 59% of patients during Fabrazyme administration in clinical trials. Some reactions were severe. In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms. (5.2)

• 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 as clinically indicated. (5.2)

• 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, and these patients should be monitored closely during Fabrazyme administration. (5.3)

• Readministration 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. (5.4)

ADVERSE REACTIONS

Most common adverse reactions (>20% and ≥2.5% compared to placebo) are: upper respiratory tract infection, chills, pyrexia, headache, cough, paresthesia, fatigue, peripheral edema, dizziness, and rash. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme at 1-800-745-4447 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosage
2.2 Preparation and Administration Instructions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Anaphylaxis and Allergic Reactions
5.2 Infusion-associated Reactions
5.3 Compromised Cardiac Function
5.4 Immunogenicity and Rechallenge
5.5 Monitoring: Laboratory Tests
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Immuneogenicity
6.3 Postmarketing Experience
7 PATIENT COUNSELING INFORMATION

FULL PRESCRIBING INFORMATION

1 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. (1)

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

• The recommended dosage of Fabrazyme is 1 mg/kg body weight infused every two weeks as an intravenous infusion. The initial intravenous infusion rate is no more than 0.25 mg/min (15 mg/hour). Slow the infusion rate in the event of infusion-associated reactions [see Warnings and Precautions (5.2)].

• Administer antipyretics prior to infusion of Fabrazyme [see Warnings and Precautions (5.2)].

• 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/hour) with each subsequent infusion.

• The maximum infusion rate for patients weighing less than 30 kg is 0.25 mg/minute (15 mg/hour).

• For patients weighing 30 kg or greater, the minimum infusion duration is 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 IgG may be successfully 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 upwards (doubled every 30 minutes up to a maximum rate of 0.25 mg/minute), as tolerated.

2.2 Preparation and Administration Instructions

Fabrazyme does not contain any preservatives. Vials are for single use only. Discard any unused reconstituted solution if there is particulate matter or if it is discolored.

Select a combination of 35 mg and 5 mg vials so that the total number of mg is equal to or greater than the patient’s body weight (kg) and the recommended dose of 1 mg/kg.

Select a combination of 35 mg and 5 mg vials so that the total number of mg is equal to or greater than the patient’s number of kg of body weight.

Select a combination of 35 mg and 5 mg vials so that the total number of mg is equal to or greater than the patient’s number of kg of body weight.

1. Allow Fabrazyme vials and diluent to reach room temperature prior to reconstitution (approximately 30 minutes). The number of 35 mg and 5 mg vials needed is based on the patient’s body weight (kg) and the recommended dose of 1 mg/kg.

2. Reconstitute each 35 mg vial of Fabrazyme by slowly injecting 7.2 mL of Sterile Water for Injection, USP down the inside wall of each vial. Roll and tilt each vial gently. Each vial will yield a 5 mg/mL clear, colorless solution (total extractable amount per vial is 35 mg, 7 mL).

3. Reconstitute each 5 mg vial of Fabrazyme by slowly injecting 1.1 mL of Sterile Water for Injection, USP down the inside wall of each vial. Roll and tilt each vial gently. Each vial will yield a 5 mg/mL clear, colorless solution (total extractable amount per vial is 5 mg, 1 mL).

4. The reconstituted solution should be further diluted with 0.9% Sodium Chloride Injection, USP (agalsidase beta) for injection, for intravenous use

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

Patient dose (in mg) = Number of mL of reconstituted Fabrazyme required for patient dose

Example: Patient dose = 80 mg

80 mg ÷ 5 mg/mL = Number of mL of reconstituted Fabrazyme required for patient dose

Table 1

<table>
<thead>
<tr>
<th>Patient Weight (kg)</th>
<th>Minimum Total Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤35</td>
<td>50</td>
</tr>
<tr>
<td>35.1–70</td>
<td>100</td>
</tr>
<tr>
<td>70.1–100</td>
<td>250</td>
</tr>
<tr>
<td>&gt;100</td>
<td>500</td>
</tr>
</tbody>
</table>

Patient dose (in mg) = Number of mL of reconstituted Fabrazyme required for patient dose

Example: Patient dose = 80 mg

80 mg ÷ 5 mg/mL = 16 mL of Fabrazyme
Slowly withdraw the reconstituted solution from each vial up to the total volume required for the patient's dose. Inject the reconstituted Fabrazyme solution directly into the Sodium Chloride solution. Do not inject in the airspace within the infusion bag. Discard any vial with unused reconstituted solution.

5. Gently invert infusion bag to mix the solution, avoiding vigorous shaking and agitation.

6. Do not infuse Fabrazyme in the same intravenous line as other medications.

7. Administer Fabrazyme using an in-line low protein binding 0.2 µm filter.

### Storage

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 FORMS AND STRENGTHS

For injection: 5 mg or 35 mg of agalsidase beta as a white to off-white, lyophilized cake or powder in a single-dose vial for reconstitution.

### CONTRAINDICATIONS

None.

### WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis and Allergic Reactions

- Life-threatening anaphylactic and severe allergic 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, dyspnea, rash, dyspnea, flushing, chest discomfort, pruritis, and nasal congestion. Interventions have included cardiopulmonary resuscitation, oxygen supplementation, intravenous fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, epinephrine, and intravenous corticosteroids.

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

- If anaphylactic or severe allergic reactions occur, immediately discontinue the administration of Fabrazyme and institute necessary emergency treatment. Because of the potential for severe allergic reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

- The risks and benefits of readministering Fabrazyme following an anaphylactic or severe allergic reaction should be considered. Further medical support measures readily available, if the decision is made to readminister the product [see Warnings and Precautions (5.4) and Clinical Studies (14)].

5.2 Infusion-associated Reactions

- In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions during Fabrazyme administration, some of which were severe [see Warnings and Precautions (5.1)]. Severe infusion-associated reactions experienced by more than one patient in clinical studies with Fabrazyme included chills, vomiting, hypotension, and paresthesia. Other infusion-associated reactions included pyrexia, feeling hot or cold, dyspnea, nausea, flushing, headache, fatigue, pruritus, pain in extremity, hypertension, chest pain, throat tightness, abdominal pain, dizziness, tachycardia, nasal congestion, diaphoresis, edema peripheral, myalgia, urticaria, bradycardia, and somnolence.

- Most patients in clinical trials were pretreated with acetaminophen. In patients experiencing infusion-associated reactions, antipyretics and antihistamines were given to patients who continued to have symptoms.

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

- The most common adverse reactions reported with Fabrazyme were infusion-associated reactions, (Fabrazyme 59% vs placebo 27%) of which some were severe.

- Common adverse reactions which occurred in >20% of patients treated with Fabrazyme and >2.5% compared to placebo are: upper respiratory tract infection, chills, pyrexia, headache, cough, parasthesia, fatigue, peripheral edema, dizziness and rash.

### Table 2: Summary of Common Adverse Reactions in Clinical Trials of Patients with Fabry Disease

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Fabrazyme (n=60)</th>
<th>Placebo (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>44</td>
<td>30</td>
</tr>
<tr>
<td>Chills</td>
<td>43</td>
<td>12</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>39</td>
<td>22</td>
</tr>
<tr>
<td>Headache</td>
<td>39</td>
<td>28</td>
</tr>
<tr>
<td>Cough</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>31</td>
<td>18</td>
</tr>
<tr>
<td>Fatigue</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td>Dizziness</td>
<td>21</td>
<td>8</td>
</tr>
<tr>
<td>Rash</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Back pain</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Myalgia</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Feeling cold</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory tract congestion</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Toothache</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Fall</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Depression</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Wheezing</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Hypoacus</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Viral infection</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Hot flush</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

*Reported at rate of at least 5% in Fabrazyme-treated patients and greater than 2.5% compared to placebo-treated patients.
Serious and/or frequently occurring (≥5%) related adverse reactions based on a pooled analysis of 150 patients treated with Fabrazyme consisted of one or more of the following: chills, pyrexia, feeling hot or cold, dyspnea, nausea, flushing, headache, vomiting, parasthesia, 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, headache, syncope, rash, and somnolence. The occurrence of somnolence cannot be attributed to clinical trial specified pretreatment with antihistamines. Most infusion-related reactions requiring intervention were ameliorated with slowing of the infusion rate, temporarily stopping the infusion, and/or administration of antipruritics, antihistamines, or steroids. Other reported infusion-related reactions included: local pain, injection site edema, palpitations, hypotension, chest pain, abdominal pain, and hypertension.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other agalsidase products may be misleading.

The following data reflect the percentage of patients whose test results were considered positive for antibodies to Fabrazyme using an ELISA and radioimmuno precipitation (RIP) assay for antibodies. Ninety-five of 121 (79%) adult patients and 11 of 16 (69%) pediatric patients (106 of 137, 74% of all patients) treated with Fabrazyme in clinical studies have developed IgG antibodies to Fabrazyme. Most patients had low titer antibodies (Table 4). Three patients (4%) who were treated as per label for Fabrazyme and three patients (4%) who were treated as per label for Fabrazyme in this age group are supported by evidence from a multinational, multicenter, uncontrolled, open-label study in 16 pediatric patients with Fabry disease (14 males, 2 females) ages 8 to 16 years (see Clinical Studies (14)). The safety and effectiveness of Fabrazyme have not been established in pediatric patients less than 8 years of age.

8.4 Pediatric Use

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

8.6 Responses in Women

Fabby disease is an X-linked genetic disorder. However, some heterozygous women will develop signs and symptoms of Fabry disease due to the variability of the X-chromosome inactivation within cells. A total of 12 adult female patients with Fabry disease were enrolled in two separate randomized, double-blind, placebo-controlled clinical studies with Fabrazyme, and two female pediatric patients with Fabry disease, ages 11 years, were evaluated in an open-label, uncontrolled pediatric study (see Use in Specific Populations (8.4)). Although the safety and efficacy data available in female patients in these clinical studies are limited, there is no indication that female patients respond differently to Fabrazyme compared to males.

8.7 Lactation

There have been no reports of overdose with Fabrazyme. In clinical trials, patients received doses up to 3 mg/kg body weight. The adverse reactions experienced by patients who received treatment with 3 mg/kg were similar to the adverse reactions experienced by patients who received treatment with 1 mg/kg. The adverse reactions experienced by patients who received treatment with 3 mg/kg were similar to the adverse reactions experienced by patients who received treatment with 1 mg/kg.

Fabrazyme (agalsidase beta) for injection is intended for intravenous infusion. It is supplied as a sterile, nonpyrogenic, preservative-free, white to off-white, lyophilized cake or powder for reconstitution with Sterile Water for Injection, USP. Each 35 mg vial contains 37 mg of agalsidase beta, as well as 222 mg mannitol, 20.4 mg sodium phosphate monobasic monohydrate, and 59.2 mg sodium phosphate dibasic heptahydrate. Following reconstitution as directed, 35 mg of agalsidase beta (7 mL) may be administered from each 35 mg vial.

12.1 Mechanism of Action

Fabry disease is an X-linked genetic disorder of glycosphingolipid metabolism. Deficiency of the lysosomal enzyme α-galactosidase A leads to progressive accumulation of glycosphingolipids, predominantly GL-3, in many body tissues, starting early in life and continuing over decades. Clinical manifestations of Fabry disease include renal failure, cardiomyopathy, and cerebrovascular accidents. Accumulation of GL-3 in renal endothelial cells may play a role in renal failure. Fabry disease is intended to provide an exogenous source of α-galactosidase A in Fabry disease patients. Nonclinical and clinical studies evaluating a limited number of cell types indicate that Fabrazyme may alter the hydrolysis of glycosphingolipids, including GL-3.

12.2 Pharmacodynamics

In a placebo-controlled study conducted in patients with Fabry disease after intravenous administration of 1 mg/kg of Fabrazyme every two weeks for 20 weeks, a reduction of GL-3 was observed in the plasma and in the glomerular mesangial region (AUC) and in the clearance (CL) did not increase proportionately with increasing doses, demonstrating that the enzyme follows non-linear pharmacokinetics (Table 3). Plasma pharmacokinetic profiles were also characterized in adult patients with Fabry disease given 1 mg/kg Fabrazyme every 14 days for a total of 11 infusions. AUC and CL are shown in Table 3 below for more details.

In 15 pediatric Fabry patients (ranging in age from 8 to 16 years old and weighing between 27.1 to 64.9 kg) who were dosed with 1 mg/kg every 14 days, Fabrazyme pharmacokinetics were not weight-dependent (Table 3). Fabrazyme concentrations were about five times higher after IgG seroconversion, with no detectable impact on GL-3 clearance. IgG seroconversion in pediatric patients was associated with prolonged half-life and plasma concentrations of Fabrazyme, a phenomenon rarely observed in adult patients. A possible cause for this prolongation likely pertains to the ability of antibodies to act as "carriers" for their antigens. Among the 14 female patients exposed to Fabrazyme in clinical studies, six (adult females) treated with Fabrazyme in clinical studies have developed IgG antibodies to Fabrazyme. Most patients who have had a positive skin test to Fabrazyme, or who have tested positive for Fabrazyme-specific IgE antibodies in clinical trials with Fabrazyme have been rechallenged (see Clinical Studies (14), Warnings and Precautions (5.4), and Dosage and Administration (2.1)).
### Table 3: Fabrazyme Pharmacokinetic Summary

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Regimen</th>
<th>Mean Infusion Length (min)</th>
<th>Infusion number (n=15)</th>
<th>AUC (mg · h/L) (min/mL)</th>
<th>Cmax (mg/L)</th>
<th>Half-life (min)</th>
<th>CL mL/min/kg</th>
<th>Vss mL/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>q14 days x 5</td>
<td>132</td>
<td>1 (n=15)</td>
<td>72 ± 24</td>
<td>0.6 ± 0.2</td>
<td>92 ± 27</td>
<td>4.1 ± 3.2</td>
<td>225 ± 62</td>
</tr>
<tr>
<td>1</td>
<td>q14 days x 5</td>
<td>115</td>
<td>1 (n=15)</td>
<td>406 ± 137</td>
<td>5.0 ± 6.7</td>
<td>67 ± 12</td>
<td>2.1 ± 0.7</td>
<td>112 ± 16</td>
</tr>
<tr>
<td>3</td>
<td>q14 days x 5</td>
<td>120</td>
<td>5 (n=2)</td>
<td>466 ± 382</td>
<td>4.7 ± 4.3</td>
<td>45 ± 3</td>
<td>3.2 ± 2.6</td>
<td>243 ± 23</td>
</tr>
<tr>
<td>1 mg/kg</td>
<td>q14 days x 11</td>
<td>280</td>
<td>1 (n=15)</td>
<td>649 ± 226</td>
<td>3.5 ± 1.6</td>
<td>89 ± 20</td>
<td>1.8 ± 0.8</td>
<td>120 ± 80</td>
</tr>
<tr>
<td>3 mg/kg</td>
<td>q14 days x 11</td>
<td>300</td>
<td>11 (n=11)</td>
<td>784 ± 621</td>
<td>3.9 ± 2.6</td>
<td>119 ± 46</td>
<td>2.3 ± 2.2</td>
<td>280 ± 230</td>
</tr>
<tr>
<td>1 mg/kg</td>
<td>q14 days x 24</td>
<td>108</td>
<td>1 (n=9-9)</td>
<td>344 ± 307</td>
<td>2.2 ± 1.2</td>
<td>86 ± 27</td>
<td>5.8 ± 4.6</td>
<td>1097 ± 912</td>
</tr>
<tr>
<td>3 mg/kg</td>
<td>q14 days x 24</td>
<td>111</td>
<td>12 (n=15)</td>
<td>1007 ± 688</td>
<td>4.9 ± 2.4</td>
<td>130 ± 41</td>
<td>1.6 ± 1.2</td>
<td>292 ± 165</td>
</tr>
<tr>
<td>1 mg/kg</td>
<td>q14 days x 24</td>
<td>108</td>
<td>24 (n=10-10)</td>
<td>1238 ± 547</td>
<td>7.1 ± 4.4</td>
<td>151 ± 59</td>
<td>1.1 ± 0.8</td>
<td>247 ± 146</td>
</tr>
</tbody>
</table>

*Vss = volume of distribution at steady state

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

There are no animal or human studies to assess the carcinogenic or mutagenic potential of Fabrazyme. A study to evaluate the effects of agalsidase beta on fertility and general reproduction was performed in male and female rats at various dose levels, and no adverse effects on fertility were observed.

#### 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, multinational, multicenter study of 58 Fabry patients (56 males and 2 females), ages 16 to 61 years, all naive to enzyme replacement therapy. Patients received either 1 mg/kg of Fabrazyme or placebo every two weeks for up to a maximum of 18 months. There was a statistically significant reduction in mean plasma GL-3 levels with durability of effect through the additional 18 months of treatment in the extension study from pretreatment baseline.

Study 2 was an open-label, uncontrolled, multinational, multicenter study to evaluate safety, pharmacokinetics, and pharmacodynamics of Fabrazyme treatment in 16 pediatric patients with Fabry disease (14 males, 2 females), who were ages 5 to 18 years. All patients had plasma GL-3 levels >7.03 mg/L, whereas the two female patients had normal plasma GL-3 levels. Twelve of the 14 male patients and no female patients had GL-3 reductions observed in the capillary endothelium of skin biopsies at baseline. At Weeks 24 and 48 of treatment, all 14 males had plasma GL-3 within the normal range. The 12 male patients with GL-3 reductions in capillary endothelium at baseline achieved GL-3 inclusion scores of 0 at Weeks 24 and 48 of treatment. The two female patients’ plasma GL-3 levels remained normal through study Week 48.

Study ALSG-0106-01: Phase 2 Study in Pediatric Patients with Fabry Disease

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Regimen</th>
<th>Mean Infusion Length (min)</th>
<th>Infusion number (n=15)</th>
<th>AUC (mg · h/L) (min/mL)</th>
<th>Cmax (mg/L)</th>
<th>Half-life (min)</th>
<th>CL mL/min/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg/kg</td>
<td>q14 days x 24</td>
<td>208</td>
<td>1 (n=9-9)</td>
<td>344 ± 307</td>
<td>2.2 ± 1.2</td>
<td>86 ± 27</td>
<td>5.8 ± 4.6</td>
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<tr>
<td>3 mg/kg</td>
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<td>111</td>
<td>12 (n=15)</td>
<td>1007 ± 688</td>
<td>4.9 ± 2.4</td>
<td>130 ± 41</td>
<td>1.6 ± 1.2</td>
</tr>
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<td>1 mg/kg</td>
<td>q14 days x 24</td>
<td>108</td>
<td>24 (n=10-10)</td>
<td>1238 ± 547</td>
<td>7.1 ± 4.4</td>
<td>151 ± 59</td>
<td>1.1 ± 0.8</td>
</tr>
</tbody>
</table>

### 16 HOW SUPPLIED/STORAGE AND HANDLING

Fabrazyme (agalsidase beta) for injection is supplied as a sterile, nonpyrogenic, white to off-white lyophilized cake or powder in single-dose vials. 35 mg vial: NDC 58468-0040-1 5 mg vial: NDC 58468-0041-1 Refrigerate vials of Fabrazyme at 2°C to 8°C (36°F to 46°F). Do not use Fabrazyme after the expiration date on the vial. This product contains no preservatives. Reconstituted and diluted solutions of Fabrazyme should be used immediately. If immediate use is not possible, the reconstituted and diluted solution may be refrigerated for up to 24 hours at 2°C to 8°C (36°F to 46°F) [see Dosage and Administration (2.1)].

### 17 PATIENT COUNSELING INFORMATION

Informs patients that a Registry has been established in order to better understand the variability and progression of Fabry disease in the population as a whole and in women [see Use in Specific Populations (8.4)] and to monitor and evaluate long-term treatment effects of Fabrazyme. The Registry will also monitor the effect of Fabrazyme on pregnant women and their offspring. Encourage patients to participate: Advise patients that their participation is voluntary and may involve long-term follow-up. For more information, visit www. registrytm.com or call 1-800-745-4447, extension 15600.

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