UNDERSTANDING ELAPRASE® (IDURSULFASE) THERAPY:

A guide for Hunter syndrome (MPS II) patients and their families

Important Safety Information

Life-threatening anaphylactic reactions have occurred in some patients during and up to 24 hours after ELAPRASE therapy.

Patients who have experienced anaphylactic reactions may require prolonged observation. Symptoms of anaphylaxis include difficulty breathing, low blood pressure, hives, and/or swelling of the throat and tongue.

Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions.¹

Please see the accompanying full Prescribing Information, including the Boxed Warning.
ELAPRASE® (IDURSULFASE): A TREATMENT OPTION FOR HUNTER SYNDROME (MPS II)

Introduction to ELAPRASE

Indication and usage

ELAPRASE® (IDURSULFASE): THE FIRST AND ONLY ENZYME REPLACEMENT THERAPY (ERT) FOR HUNTER SYNDROME AVAILABLE IN THE USA

Indication and supporting clinical trial efficacy data

Adverse reactions (side effects)

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions including anaphylaxis

Risk of hypersensitivity, serious adverse reactions and antibody development in Hunter syndrome patients with severe genetic mutations

Risk of acute respiratory complications

Risk of acute cardiorespiratory failure

HOW ELAPRASE® (IDURSULFASE) IS ADMINISTERED

ONEPATH® PRODUCT SUPPORT SERVICES

How can OnePath help eligible patients?

How to enroll in OnePath

FREQUENTLY ASKED QUESTIONS ABOUT ELAPRASE® (IDURSULFASE)

TALK WITH YOUR HEALTHCARE PROVIDER ABOUT ELAPRASE® (IDURSULFASE)
As you know, living with Hunter syndrome (mucopolysaccharidosis II, MPS II), can be a challenge. For those with Hunter syndrome and their families, each day presents new opportunities to learn more about this genetic disorder and the ways in which it can be managed.

This booklet provides information about a treatment option for people with Hunter syndrome.

Most likely, you’ve already learned that Hunter syndrome is caused by the body’s inability to break down certain elements in the body called mucopolysaccharides (mew-ko-pol-ee-sak-ah-rides), also known as glycosaminoglycans (gli-ko-sah-mee-no-gli-cans) or GAGs. The build-up of GAGs is due to deficient or absent activity of the enzyme iduronate-2-sulfatase (I2S).

ELAPRASE® is a purified form of the I2S enzyme targeted to replace
the deficient or malfunctioning I2S enzyme in Hunter syndrome patients.\textsuperscript{1,2} Together with your healthcare providers, you can decide if ELAPRASE is right for you or your child.

\section*{Indication and usage}

ELAPRASE is indicated for patients with Hunter syndrome. ELAPRASE has been shown to improve walking capacity in patients aged 5 years and older.

In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long-term clinical outcome; however, treatment with ELAPRASE has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of ELAPRASE have not been established in pediatric patients younger than 16 months of age.\textsuperscript{1}
ELAPRASE® (idursulfase): The first and only FDA-approved enzyme replacement therapy (ERT) for Hunter syndrome

ELAPRASE is indicated for patients with Hunter syndrome.¹ ELAPRASE has been shown to improve walking capacity in patients aged 5 years and older.¹

The safety and efficacy of ELAPRASE were evaluated in a clinical study of 96 Hunter syndrome patients aged 5–31 years. Patients in the ELAPRASE weekly treatment group exhibited a significant improvement, compared with patients who received placebo, in the primary efficacy endpoint: a two-component score based on a statistical analysis of (1) the distance walked during a 6-minute walking test (6-MWT) and (2) a common measure of lung function called % predicted forced vital capacity (% predicted FVC).¹

When individual components were examined separately, in an adjusted analysis, patients exhibited a 35-meter greater mean increase in the distance walked in 6 minutes compared with placebo, while the changes in % predicted FVC were not statistically significant.¹

In Hunter syndrome patients, high levels of GAGs can be detected in the urine and the build-up of GAGs within organs such as the liver and spleen results in enlarged organ size.³

ELAPRASE once weekly was shown to reduce liver and spleen volumes and decrease mean urinary GAG levels, although in half of the ELAPRASE-treated patients, the urine GAG levels were still considered higher than normal.¹

All patients in this trial were invited to receive weekly ELAPRASE treatment by participating in a 24-month extension study. In patients who were treated with ELAPRASE in the first study, improvements in the 6-MWT continued for a further 8 months.¹

In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long-term clinical outcome; however, treatment with ELAPRASE has reduced spleen volume similarly to that of adults and children 5 years of age and older.¹ The safety and efficacy of ELAPRASE have not been established in pediatric patients younger than 16 months of age.¹
Adverse reactions

The most common adverse reactions (side effects) occurring in at least three patients (≥9%) aged 5+ years were headache, itching, muscle and bone pain, hives, diarrhea, and cough. Among patients aged 7 years or younger, the most common adverse reactions (≥10%) were fever, rash, vomiting, and hives.

In all clinical trials, the most common adverse reactions requiring medical intervention were hypersensitivity ("allergic") reactions, and included rash, hives, itching, flushing, fever, and headache.¹

Please see the accompanying full Prescribing Information, including the Boxed Warning.
Important safety information

Hypersensitivity reactions including anaphylaxis

Some patients have experienced serious hypersensitivity (“allergic”) reactions, including anaphylactic reactions, during and up to 24 hours after ELAPRASE infusions, regardless of how long a patient has been taking ELAPRASE. Anaphylactic reactions are immediate and life-threatening allergic reactions. Anaphylactic reactions included breathing difficulties, low oxygen levels, low blood pressure, hives and/or swelling of the throat or tongue.¹

Patients will be closely monitored during, and for a period of time after, ELAPRASE infusions and their healthcare team should be prepared to manage anaphylactic reactions. Patients should notify their healthcare team immediately if any symptoms of an allergic reaction occur.¹

Risk of hypersensitivity, serious adverse reactions and antibody development in Hunter syndrome patients with severe genetic mutations

In a clinical trial of patients aged 7 years or younger, patients with certain types of genetic mutations experienced a higher incidence of hypersensitivity reactions, serious
adverse reactions and development of an immune response to ELAPRASE. This immune response can potentially interfere with the efficacy of ELAPRASE.¹

Risk of acute respiratory complications

Patients with respiratory problems or those who have a fever or respiratory illness at the time of ELAPRASE infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Physicians should consider delaying ELAPRASE infusion in these patients.¹

Risk of acute cardiorespiratory failure

Patients with respiratory illness or heart/respiratory problems may be at higher risk of fluid overload during ELAPRASE infusions. The healthcare team should be appropriately trained to monitor signs and symptoms of fluid overload and provide the necessary medical support. Patients susceptible to fluid overload may require prolonged observation time.¹
How ELAPRASE® (idursulfase) is administered

ELAPRASE is a weekly infusion therapy, which means it’s given intravenously (IV).¹ To receive ELAPRASE therapy, you will initially have to go to a treatment center every week (patients who tolerate the infusions well for several months may be able to instead receive infusions at home under the supervision of a healthcare professional).

Typically, the infusion can take up to 3 hours, but there may be additional time needed for preparation and observation. Patients may require longer infusion times if hypersensitivity reactions occur; however, infusion times should not exceed 8 hours.¹

Your healthcare provider can give you more details about what to expect and can help you plan ahead.

At the treatment center, a healthcare professional will deliver the therapy and will be able to answer any questions you may have. Each infusion center has its own guidelines about what patients are permitted to do while undergoing therapy, and it may be OK to engage in a quiet activity such as reading a book, watching TV, or doing homework.

Check with your treatment center before you arrive to find out which activities are acceptable.

As with any new experience, the ELAPRASE infusion might be unfamiliar at first, or the process might even make you nervous. Talk to your doctor about any concerns you may have.
OnePath® product support services

If you and your doctor choose to include ELAPRASE treatment in your care plan, OnePath can provide product support services. Eligible patients who enroll in OnePath will be assigned a dedicated Patient Support Manager.

How can OnePath help eligible patients?

OnePath Patient Support Managers offer product support in multiple ways:

- **Confirm insurance coverage:** reviews your insurance benefits to help you understand your insurance coverage
- **Provide information about treatment center options:** investigates potential sites for receiving ELAPRASE infusions (doctor’s office, infusion center)
- **Facilitate access and refill requests:** specialty pharmacy coordination

How to enroll in OnePath:

1. Review and sign the OnePath Start Form with your physician
2. Your physician will fax the form to OnePath
3. A dedicated OnePath Patient Support Manager will be assigned to eligible patients

You can learn more about OnePath by visiting [www.OnePath.com](http://www.OnePath.com) or by calling toll-free **1-866-888-0660**, Monday through Friday, 8:30 a.m. to 8:00 p.m. Eastern Time.
Frequently asked questions about ELAPRASE® (idursulfase)

What is ELAPRASE?
ELAPRASE is the first and only enzyme replacement therapy (ERT) for Hunter syndrome available in the USA. It is designed to replace deficient/absent I2S enzyme activity in people with Hunter syndrome.\(^1,2\)

How can ELAPRASE help people with Hunter syndrome?
In a clinical study of patients with Hunter syndrome, aged 5–31 years, ELAPRASE was shown to significantly increase patients’ ability to walk further compared with those who received an infusion of non-active medicine. ELAPRASE was also shown to improve some other measures of activity such as GAG levels in the urine, and the size of the liver and spleen. The results of tests on one measure of lung capacity, known as the % predicted FVC, were not significant.\(^1\)

In a clinical study of patients aged younger than 5 years, similar improvements in urine GAG levels and spleen size were observed, but disease-related symptoms such as walking capacity were not assessed.

ELAPRASE has not been studied in patients younger than 16 months of age in clinical trials.\(^1\)

What are the common side effects of ELAPRASE?
In all clinical trials, the most common side effects requiring medical attention were hypersensitivity reactions, and included rash, hives, itching, flushing, fever, and headache.\(^1\)

How is ELAPRASE administered?
ELAPRASE is administered by intravenous infusion once a week. This means that ELAPRASE is diluted in a saline solution and is slowly delivered into a vein via a drip. The infusion can take up to 3 hours but there may be additional time for preparation and observation. Your healthcare provider can give you more details about what to expect and can help you plan ahead.\(^1\)

Where will I have to go to receive ELAPRASE?
To begin ELAPRASE therapy, you will have to go to a treatment center every week. Patients who tolerate the infusions well for several months may be able to instead receive infusions at home under the supervision of a healthcare professional.
For eligible patients enrolled in OnePath product support services, a Patient Support Manager can provide information about treatment center options near you. For more information about this service, see page 11 of this booklet. Discuss signing up for this service with your doctor.

Is ELAPRASE covered by my health insurance?
For eligible patients enrolled in OnePath product support services, a Patient Support Manager can help them review and understand their insurance coverage. For more information about this service, see page 11 of this booklet. Discuss signing up for this service with your doctor.

Who can I contact to ask any other questions I may have?
Your healthcare providers should always be your first source of information; ask them any questions you may have about your treatment plan.
If you are enrolled in OnePath, your Patient Support Manager can help answer product access and reimbursement questions.

Please see the accompanying full Prescribing Information, including the Boxed Warning.
Talk with your healthcare provider about ELAPRASE® (idursulfase)

To find out if ELAPRASE is right for you or your child, talk to your healthcare provider. Together you’ll come to a decision that’s best for you and your family.

The Hunter Outcome Survey collects information about Hunter syndrome and the long-term treatment effects of ELAPRASE outside of clinical trials. Talk to your doctor if you would like to participate in the Hunter Outcome Survey.¹

The information contained in this booklet, and provided by OnePath, is not meant to replace the care and advice you receive from healthcare providers.

To learn more about ELAPRASE therapy, visit www.elaprase.com.

To learn more about OnePath product support services, visit www.OnePath.com or call toll-free 1-866-888-0660, Monday through Friday, 8:30 a.m. to 8:00 p.m. Eastern Time.

References:

Please click here for full Prescribing Information, including the Boxed Warning.
ELAPRASE® (idursulfase) injection, for intravenous use

Initial U.S. Approval: 2006

WARNING: RISK OF ANAPHYLAXIS
See full prescribing information for complete boxed warning.
Life-threatening anaphylactic reactions, presenting as respiratory distress, hypoxia, hypotension, urticaria and/or angioedema of throat or tongue have occurred in some patients during and up to 24 hours after ELAPRASE infusions. Closely observe patients during and after ELAPRASE administration and be prepared to manage anaphylaxis. Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions, and require additional monitoring. (5.1, 5.3, 6)

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ELAPRASE safely and effectively. See full prescribing information for ELAPRASE.

ELAPRASE® (idursulfase) injection, for intravenous use

Initial U.S. Approval: 2006

WARNING: RISK OF ANAPHYLAXIS
See full prescribing information for complete boxed warning.
Life-threatening anaphylactic reactions, presenting as respiratory distress, hypoxia, hypotension, urticaria and/or angioedema of throat or tongue have occurred in some patients during and up to 24 hours after ELAPRASE infusions. Closely observe patients during and after ELAPRASE administration and be prepared to manage anaphylaxis. Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions, and require additional monitoring. (5.1, 5.3, 6)

INDICATIONS AND USAGE
ELAPRASE is a hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). ELAPRASE has been shown to improve walking capacity in patients 5 years and older. In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with ELAPRASE has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of ELAPRASE have not been established in pediatric patients less than 16 months of age (1).

The recommended dosage is 0.5 mg per kg of body weight administered once every week as an intravenous infusion (2).

FULL PRESCRIBING INFORMATION: CONTENTS*
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dose
2.2 Preparation Instructions
2.3 Administration Instructions
2.4 Storage and Stability
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions Including Anaphylaxis
5.2 Risk of Hypersensitivity, Serious Adverse Reactions, and Antibody Development in Hunter Syndrome Patients with Severe Genetic Mutations
5.3 Risk of Acute Respiratory Complications
5.4 Risk of Acute Cardiorespiratory Failure
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Immunogenicity
6.3 Postmarketing Experience
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
14.1 Clinical Trials in Patients 5 Years and Older
14.2 Clinical Trial in Patients 7 Years and Younger
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
1 INDICATIONS AND USAGE
ELAPRASE is indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). ELAPRASE has been shown to improve walking capacity in patients 5 years and older.

In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with ELAPRASE has reduced spleen volume similarly to that of adults and children 5 years of age and older.

The safety and efficacy of ELAPRASE have not been established in pediatric patients less than 16 months of age [see Use in Specific Populations (8.4)].

2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dose
The recommended dosage regimen of ELAPRASE is 0.5 mg per kg of body weight administered once weekly as an intravenous infusion.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

2.2 Preparation Instructions
Prepare and use ELAPRASE according to the following steps using aseptic technique:

a. Determine the total volume of ELAPRASE to be administered and the number of vials needed based on the patient’s weight and the recommended dose of 0.5 mg/kg. Patient’s weight (kg) x 0.5 mg per kg of ELAPRASE + 2 mg per mL = Total mL of ELAPRASE

b. Before withdrawing the ELAPRASE solution from the vial, visually inspect each vial for particulate matter and discoloration. The ELAPRASE solution should be clear to slightly opalescent and colorless. Do not use if the solution is discolored or if there is particulate matter in the solution. Do not shake the ELAPRASE solution.

c.Withdraw the calculated volume of ELAPRASE from the appropriate number of vials.

d. Add the calculated volume of ELAPRASE solution to a 100 mL bag of 0.9% Sodium Chloride Injection, USP for intravenous infusion.

e. Mix gently. Do not shake the solution.

2.3 Administration Instructions
Administer the diluted ELAPRASE solution to patients using a low-protein-binding infusion set equipped with a low-protein-binding 0.2 micrometer (μm) in-line filter. The total volume of infusion should be administered over a period of 3 hours, which may be gradually reduced to 1 hour if no hypersensitivity reactions are observed. Patients may require longer infusion times if hypersensitivity reactions occur; however, infusion times should not exceed 8 hours. The initial infusion rate should be 8 mL per hour for the first 15 minutes. If the infusion is well tolerated, the rate of infusion may be increased by 8 mL per hour increments every 15 minutes. The infusion rate should not exceed 100 mL per hour. The infusion rate may be slowed, temporarily stopped, or discontinued for that visit in the event of hypersensitivity reactions [see Warnings and Precautions (5.1), Adverse Reactions (6.1), and Use in Specific Populations (8.4)].

2.4 Storage and Stability
ELAPRASE does not contain preservatives; therefore, after dilution with saline, the infusion bags should be used immediately. If immediate use is not possible, the diluted solution should be stored refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours. Other than during infusion, do not store the diluted ELAPRASE solution at room temperature. Any unused product or waste material should be discarded and disposed of in accordance with local requirements.

3 DOSAGE FORMS AND STRENGTHS
Injection: 6 mg/3 mL (2 mg/mL) in single-use vials

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions Including Anaphylaxis
Serious hypersensitivity reactions, including anaphylaxis, have occurred during and up to 24 hours after ELAPRASE infusions. Anaphylaxis, presenting as respiratory distress, hypoxia, hypotension, urticaria and/or angioedema of throat or tongue have been reported to occur during and after ELAPRASE infusions, regardless of duration of the course of treatment. Closely observe patients during and after ELAPRASE administration and be prepared to manage anaphylaxis.

Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions, and require additional monitoring [see Warnings and Precautions (5.1, 5.2) and Adverse Reactions (6)].

Due to the potential for severe reactions, appropriate medical support should be readily available when ELAPRASE is administered. Observe patients closely for an appropriate period of time after administration of ELAPRASE, taking into account the time to onset of anaphylaxis seen in premarketing clinical trials and postmarketing reports. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur.

5.2 Risk of Hypersensitivity, Serious Acute Anaphylactic Reactions and Antibody Development in Hunter Syndrome Patients with Severe Genetic Mutations
In the clinical trial of Hunter syndrome patients aged 7 years and younger, patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations experienced a higher incidence of hypersensitivity reactions, serious adverse reactions, and anti-idursulfase antibody development than Hunter syndrome patients with missense mutations. Eleven of 15 (73%) patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations and five of 12 (42%) patients with missense mutations experienced hypersensitivity reactions. Nine of 15 (60%) patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations and two of 12 (17%) patients with missense mutations had serious adverse reactions. All 15 patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations developed anti-idursulfase (ELAPRASE) antibodies, compared to only 3 patients with missense mutations (Table 2). Thirteen patients with these mutations developed neutralizing antibodies, which interfere with ELAPRASE uptake into the cell or ELAPRASE enzyme activity, compared to only one patient with missense mutation [see Warnings and Precautions (5.1), Adverse Reactions (6.1, 6.2), and Use in Specific Populations (8.4)].

5.3 Risk of Acute Respiratory Complications
Patients with compromised respiratory function or acute febrile or respiratory illness at the time of ELAPRASE infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Careful consideration should be given to the patient’s clinical status prior to administration of ELAPRASE and consider delaying the ELAPRASE infusion. One patient with a tracheostomy, severe airway disease, and acute febrile illness experienced respiratory distress, hypoxia, cyanosis, and seizure with a loss of consciousness during ELAPRASE infusion.
5.4 Risk of Acute Cardiorespiratory Failure
Caution should be exercised when administering ELAPRASE to patients susceptible to fluid overload, or patients with acute underlying respiratory illness or compromised cardiac and/or respiratory function for whom fluid restriction is indicated. These patients may be at risk of serious exacerbation of their cardiac or respiratory status during infusions. Appropriate medical support and monitoring measures should be readily available during ELAPRASE infusion, and some patients may require prolonged observation times that should be based on the individual needs of the patient [see Adverse Reactions (6.1, 6.3)].

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The following serious adverse reactions are described below and elsewhere in the labeling:
- Hypersensitivity Reactions Including Anaphylaxis [see Warnings and Precautions (5.1)]

In clinical trials, the most common adverse reactions (>10%) following ELAPRASE treatment were hypoxia episodes. Other notable serious adverse reactions that occurred in the ELAPRASE-treated patients but not in the placebo-treated patients included one case each of: cardiac arrhythmia, pulmonary embolism, cyanosis, respiratory failure, infection, and arthralgia.

Clinical Trials in Patients 5 Years and Older
A 53-week, double-blind, placebo-controlled clinical trial of ELAPRASE was conducted in 96 male patients with Hunter syndrome, ages 5-31 years old. Of the 96 patients, 83% were White, non-Hispanic. Patients were randomized to three treatment groups, each with 32 patients: ELAPRASE 0.5 mg/kg once weekly, ELAPRASE 0.5 mg/kg every other week, or placebo. Hypersensitivity reactions were reported in 69% (22 of 32) of patients who received once-weekly treatment during infusions. Rates in the extension trial were hypoxic episodes. Other notable serious adverse reactions that occurred in the ELAPRASE-treated patients but not in the placebo-treated patients included one case each of: cardiac arrhythmia, pulmonary embolism, cyanosis, respiratory failure, infection, and arthralgia.

Table 1 summarizes the adverse reactions that occurred in at least 9% of patients (≥3 patients) in the ELAPRASE 0.5 mg/kg once weekly group and with a higher incidence than in the placebo group.

Table 1. Adverse Reactions That Occurred in the Placebo-Controlled Trial in At Least 9% of Patients in the ELAPRASE 0.5 mg/kg Once Weekly Group and with a Higher Incidence than in the Placebo Group (5 Years and Older)

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reaction</th>
<th>ELAPRASE (0.5 mg/kg weekly)</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N=32 n (%)</td>
<td>N=32 n (%)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>Diarrhea</td>
<td>3 (9%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>Musculoskeletal Pain</td>
<td>4 (13%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td>9 (28%)</td>
<td>8 (25%)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Cough</td>
<td>3 (9%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Pruritus</td>
<td>8 (25%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>5 (16%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Additional adverse reactions that occurred in at least 9% of patients (≥3 patients) in the ELAPRASE 0.5 mg/kg every other week group and with a higher incidence than in the placebo group included: rash (19%), flushing (16%), fatigue (13%), tachycardia (9%), and chills (9%).

Extension Trial
An open-label extension trial was conducted in patients who completed the placebo-controlled trial. Ninety-four of the 96 patients who were enrolled in the placebo-controlled trial consented to participate in the extension trial. All 94 patients received ELAPRASE 0.5 mg/kg once weekly for 24 months. No new serious adverse reactions were reported. Approximately half (53%) of patients experienced hypersensitivity reactions during the 24-month extension trial. In addition to the adverse reactions listed in Table 1, common hypersensitivity reactions occurring in at least 5% of patients (≥5 patients) in the extension trial included: rash (23%), pyrexia (9%), flushing (7%), erythema (7%), nausea (5%), dizziness (5%), vomiting (5%), and hypotension (5%).

Clinical Trial in Patients 7 Years and Younger
A 53-week, open-label, single-arm, safety trial of once weekly ELAPRASE 0.5 mg/kg treatment was conducted in patients with Hunter syndrome, ages 16 months to 4 years old (n=20) and ages 5 to 7.5 years old (n=8) at enrollment. Patients experienced similar adverse reactions as those observed in clinical trials in patients 5 years and older, with the most common adverse reactions following ELAPRASE treatment being hypersensitivity reactions (57%). A higher incidence of the following common hypersensitivity reactions were reported in this younger age group: pyrexia (36%), rash (32%), and vomiting (14%). The most common serious adverse reactions occurring in at least 10% of patients (≥3 patients) included: bronchopneumonia/pneumonia (18%), ear infection (11%), and pyrexia (11%). Twenty-seven patients had results of genotype analysis: 15 patients had complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations and 12 patients had missense mutations.

Safety results demonstrated that patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations are more likely to experience hypersensitivity reactions and have serious adverse reactions following ELAPRASE administration, compared to patients with missense mutations. Table 2 summarizes these findings.

Table 2. Impact of Antibody Status and Genetic Mutations on Occurrence of Serious Adverse Reactions and Hypersensitivity in Patients 7 Years and Younger Treated with ELAPRASE

<table>
<thead>
<tr>
<th>Antibody Status Reported (patients)</th>
<th>Antibody status</th>
<th>Antibody Status</th>
<th>Antibody Status</th>
<th>Antibody Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Antibody Status Reported (patients)</td>
<td>28</td>
<td>19</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Serious Adverse Reactions* (patients)</td>
<td>13</td>
<td>11</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Hypersensitivity (patients)</td>
<td>16</td>
<td>12</td>
<td>4</td>
<td>10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients with genotype data</th>
<th>Antibody status</th>
<th>Antibody status</th>
<th>Antibody status</th>
<th>Antibody status</th>
<th>Antibody status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Antibody status Reported (patients)</td>
<td>27</td>
<td>20</td>
<td>7</td>
<td>20</td>
<td>15</td>
</tr>
</tbody>
</table>

* Serious adverse reactions included: bronchopneumonia/pneumonia, ear infection, and pyrexia [see Adverse Reactions (6.1)].

6.2 Immunogenicity
Clinical Trials in Patients 5 Years and Older
As with all therapeutic proteins, there is potential for immunogenicity. In clinical trials in patients 5 years and older, 63 of the 84 patients treated with ELAPRASE 0.5 mg/kg once weekly or placebo for 53 weeks, followed by ELAPRASE 0.5 mg/kg once weekly in the extension trial, had immunogenicity data available.
ELAPRASE® (idursulfase) injection, for intravenous use

for analysis. Of the 63 patients, 32 (51%) patients tested positive for anti-idursulfase IgG antibodies (Ab) at least one time (Table 2). Of the 32 Ab-positive patients, 23 (72%) tested positive for Ab at three or more different time points (persistent Ab). The incidence of hypersensitivity reactions was higher in patients who tested positive for Ab who tested negative. Thirteen of 32 (41%) Ab-positive patients also tested positive for antibodies that neutralize idursulfase uptake into cells (uptake neutralizing antibodies, uptake NAb) or enzymatic activity (activity NAb) at least one time, and 8 (25%) of Ab-positive patients had persistent NAb. There was no clear relationship between the presence of either Ab or NAb and therapeutic response.

Clinical Trial in Patients 7 Years and Younger

In the clinical trial in patients 7 years and younger, 19 of 28 (68%) patients treated with ELAPRASE 0.5 mg/kg once weekly tested Ab-positive. Of the 19 Ab-positive patients, 16 (84%) tested positive for Ab at three or more different time points (persistent Ab). In addition, 15 of 19 (79%) Ab-positive patients tested positive for NAb with 14 of 15 (93%) in four or more positive tests of Ab. All 15 patients with complete gene deletion, large gene rearrangement, nonsense, frameshift, or splice site mutations tested positive for Ab (Table 2). Of these 15 patients, neutralizing antibodies were observed in 13 (87%) patients. The NAbs in these patients developed earlier (most reported to be positive at Week 9 rather than at Week 27, as reported in clinical trials in patients older than 5 years of age) and were associated with higher titers and greater in vitro neutralizing activity than in patients older than 5 years of age. The incidence of Ab was associated with reduced systemic idursulfase exposure [see Clinical Pharmacology (12.3)]. The immunogenicity data reflect the percentage of patients whose test results were positive for antibodies to idursulfase in specific assays, and are highly dependent on the sensitivity and specificity of these assays. The observed incidence of positive antibody in an assay may be influenced by several factors, including sample handling, timing of sample collection, concomitant medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to idursulfase with the incidence of antibodies to other products may be misleading.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of ELAPRASE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. In post-marketing experience, late-emergent symptoms and signs of anaphylactic reactions have occurred up to 24 hours after initial treatment and recovery from an initial anaphylactic reaction. In addition, patients experienced repeated anaphylactic events after 4.5 years of treatment. Treatment has been withdrawn [see Overdosage (10)]. Serious adverse reactions that resulted in death included cardiopulmonary arrest, respiratory failure, respiratory distress, cardiac failure, and pneumonia.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with ELAPRASE use in pregnant women. Available data from a small number of postmarketing cases with ELAPRASE use in pregnancy are insufficient to inform drug-associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes. In an animal reproduction study, no evidence of adverse effects on pre- and postnatal development was observed with twice weekly intravenous administration of idursulfase to pregnant rats from gestation day 6 through lactation day 19 at about 4 times the recommended human weekly dose of 0.5 mg/kg based on body surface area (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In a pre- and post-natal development study, idursulfase was administered to pregnant rats twice weekly, intravenously. From gestation day 6 through lactation day 19. No significant adverse effects on pre- and post-natal development of the offspring were observed at twice weekly intravenous doses up to 12.5 mg/kg (about 4 times the recommended human weekly dose of 0.5 mg/kg based on body surface area).

8.2 Lactation

Risk Summary

There are no data on the presence of idursulfase in human milk, the effects on the breastfed infant, or the effects on milk production. Idursulfase was excreted in breast milk of lactating rats (see Data). When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ELAPRASE and any potential adverse effects on the breastfed child from ELAPRASE or from the underlying maternal condition.

Data

Idursulfase was excreted in breast milk of lactating rats at a concentration higher (4- to 5-fold) than the maximum blood concentration, when administered as a single intravenous dose up to 2.5 mg/kg. The concentration of drug in animal milk does not necessarily predict the concentration of drug in human milk.

8.4 Pediatric Use

Clinical trials with ELAPRASE were conducted in 96 patients with Hunter syndrome, ages 5 to 31 years old, with the majority of the patients in the pediatric age group (median age 15 years old). In addition, an open-label, uncontrolled clinical trial was conducted in 28 patients with Hunter syndrome, ages 16 months to 7.5 years old. Patients 16 months to 5 years of age demonstrated reduction in splenic volume that was similar to that of adults and children 5 years and older. However, there are no data to support improvement in disease-related symptoms or long term clinical outcome in patients 16 months to 5 years of age [see Clinical Studies (14)]. The safety and effectiveness of ELAPRASE have not been established in pediatric patients less than 16 months of age.

8.5 Geriatric Use

Clinical studies of ELAPRASE did not include patients older than 31 years of age. It is not known whether older patients respond differently from younger patients.

10 OVERDOSAGE

One patient with Hunter syndrome, who received ELAPRASE at twice the recommended dosage for one and a half years, experienced two anaphylactic reactions over a 3-month period 4.5 years after initiating ELAPRASE treatment.

11 DESCRIPTION

ELAPRASE is a formulation of idursulfase, a purified form of human iduronate-2-sulfatase, a lysosomal enzyme. Idursulfase is produced by recombinant DNA technology in a human cell line. Idursulfase is an enzyme that hydrolyzes the 2-sulfate esters of terminal iduronate sulfate residues from the glycosaminoglycans dermatan sulfate and heparan sulfate in the lysosomes of various cell types. Idursulfase is a 525-amino acid glycoprotein with a molecular weight of approximately 75 kiliograms. The enzyme contains eight asparagine-linked glycosylation sites occupied by complex oligosaccharide structures. The enzyme activity of idursulfase is dependent on the post-translational modification of a specific cysteine to formylglycine. Idursulfase has a specific activity ranging from 46 to 74 units/mg of protein (one unit is defined as the amount of enzyme required to hydrolyze 1 micromole of heparin disaccharide substrate per hour under the specified assay conditions).

ELAPRASE is administered as an intravenous infusion and supplied as a sterile, nonpyrogenic clear to slightly opalescent, colorless solution that must be diluted prior to administration in 0.9% Sodium Chloride Injection, USP. Each vial contains an extractable volume of 3 mL with an idursulfase concentration of 2 mg/mL at a pH of approximately 6. Each vial contains 6 mg idursulfase, sodium chloride (24 mg), sodium phosphate monobasic monohydrate (6.75 mg), sodium phosphate dibasic heptahydrate (2.97 mg), and polysorbate 20 (0.66 mg). ELAPRASE does not contain preservatives. Each vial is for single use only.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Hunter syndrome (Mucopolysaccharidosis II, MPS II) is an X-linked recessive disease caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. This enzyme cleaves the terminal 2-sulfate moieties from the glycosaminoglycans (GAG) dermatan sulfate and heparan sulfate. Due to the missing or defective iduronate-2-sulfatase enzyme in patients with Hunter syndrome, GAG progressively accumulate in the lysosomes of a variety of cells, leading to cellular engorgement, organomegaly, tissue destruction, and organ system dysfunction.

ELAPRASE is intended to provide exogenous enzyme for uptake into cellular lysosomes. Mannose-6-phosphate (M6P) residues on the oligosaccharide chains allow binding of the enzyme to the M6P receptors on the cell surface, leading to
ELAPRASE® (idursulfase) injection, for intravenous use
cellular internalization of the enzyme, targeting to intracellular lysosomes and subsequent catabolism of accumulated GAG.

12.2 Pharmacodynamics
Decreases in urinary GAG levels were observed following treatment with ELAPRASE. The responsiveness of urinary GAG to dosage alterations of ELAPRASE is unknown, and the relationship of urinary GAG to other measures of clinical response has not been established. Patients who tested positive for anti-idursulfase antibodies (Ab) experienced a less pronounced decrease in urinary GAG levels [see Adverse Reactions (6.2) and Clinical Studies (14.1, 14.2)].

12.3 Pharmacokinetics

Clinical Trials in Patients 5 Years and Older
The pharmacokinetic characteristics of idursulfase were evaluated in 59 patients with Hunter syndrome. The serum concentration of idursulfase was quantified using an antigen-specific ELISA assay. The area under the concentration-time curve (AUC) increased in a greater than dose proportional manner as the dose increased from 0.15 mg/kg to 1.5 mg/kg following a single 1-hour infusion of ELAPRASE. The pharmacokinetic parameters at the recommended dose regimen (0.5 mg/kg ELAPRASE administered weekly as a 3-hour infusion) were determined at Week 1 and Week 27 in 10 patients 7.7 to 27 years of age (Table 3). There were no apparent differences in PK parameter values between Week 1 and Week 27 regardless of the antibody status in these patients.

Table 3. Pharmacokinetic Parameters in Patients 7.7 to 27 Years of Age

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Week 1 Mean (SD)</th>
<th>Week 27 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (mcg/mL)</td>
<td>1.5 (0.9)</td>
<td>1.1 (0.3)</td>
</tr>
<tr>
<td>AUC (min•mcg/mL)</td>
<td>206 (87)</td>
<td>169 (55)</td>
</tr>
<tr>
<td>t_{1/2} (min)</td>
<td>44 (19)</td>
<td>48 (21)</td>
</tr>
<tr>
<td>CL (mL/min/kg)</td>
<td>3.0 (1.2)</td>
<td>3.4 (1.0)</td>
</tr>
<tr>
<td>V_{ss} (mL/kg)</td>
<td>213 (82)</td>
<td>254 (87)</td>
</tr>
</tbody>
</table>

Clinical Trial in Patients 7 Years and Younger
Idursulfase pharmacokinetics was evaluated in 27 patients with Hunter syndrome 16 months to 7.5 years of age who received ELAPRASE 0.5 mg/kg once weekly as a 3-hour infusion. The presence of anti-idursulfase antibody (Ab) was associated with a reduced systemic exposure of idursulfase. Eight of the 18 Ab-positive patients had no measurable idursulfase concentrations. An additional 9 Ab-positive patients decreased C_{max}, AUC, and t_{1/2} at Week 27 compared to Week 1 (Table 4). Idursulfase pharmacokinetics was similar between Week 1 and Week 27 in Ab-negative patients (Table 4).

Table 4. Pharmacokinetic Parameters in Patients 16 months to 7.5 Years of Age

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Week 1 Mean (SD)</th>
<th>Week 27 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (mcg/mL)</td>
<td>1.33 (0.817)</td>
<td>1.40 (0.389)</td>
</tr>
<tr>
<td>AUC (min•mcg/mL)</td>
<td>224 (76.9)</td>
<td>281 (81.8)</td>
</tr>
<tr>
<td>t_{1/2} (min)</td>
<td>160 (69)</td>
<td>134 (19)</td>
</tr>
<tr>
<td>CL (mL/min/kg)</td>
<td>2.4 (0.7)</td>
<td>2.0 (0.8)</td>
</tr>
<tr>
<td>V_{ss} (mL/kg)</td>
<td>394 (423)</td>
<td>272 (112)</td>
</tr>
</tbody>
</table>

* Positive anti-idursulfase antibody (Ab) is defined as having at least one serum specimen with measurable antibody during study duration.
† Eight of 18 patients with positive Ab had no measurable concentrations at Week 27.
# N=26
$ N=9

Table 5. Clinical Trial Results

<table>
<thead>
<tr>
<th></th>
<th>ELAPRASE Weekly n=32*</th>
<th>Placebo n=32*</th>
<th>ELAPRASE Once Weekly – Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Change†</td>
<td>Baseline</td>
<td>Change†</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Age (years)</td>
<td>7.4 ± 3.7</td>
<td>7.5 ± 3.3</td>
<td>7.5 ± 3.3</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>Change†</td>
<td>Baseline</td>
<td>Change†</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>FVC (% of predicted)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>Change†</td>
<td>Baseline</td>
<td>Change†</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Results from the 6-Minute Walk Test (Meters)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Results from the Forced Vital Capacity Test (% of Predicted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

* One patient in the placebo group and one patient in the ELAPRASE group died before Week 53; imputation was by last observation carried forward in the intent-to-treat analysis.
† Change, calculated as Week 53 minus Baseline
‡ Observed mean ± SE

Pharmacodynamic assessments included urinary GAG levels and changes in liver and spleen size. Urinary GAG levels were elevated in all patients at baseline. Following 53 weeks of treatment, mean urinary GAG levels were reduced in the ELAPRASE once weekly group, although GAG levels still remained above the upper limit of normal in half of the ELAPRASE-treated patients. Urinary GAG levels remained elevated and essentially unchanged in the placebo group. Sustained reductions in both liver and spleen volumes were observed in the ELAPRASE once weekly group through Week 53 compared to placebo. There were essentially no changes in liver and spleen volumes in the placebo group.
Extension Trial

Patients who participated in the placebo-controlled trial were eligible to continue treatment in an open-label extension trial. During the extension trial, all patients received ELAPRASE 0.5mg/kg once weekly for 24 months.

Patients who were treated with ELAPRASE once weekly and every other week in the placebo-controlled trial demonstrated improvement in distance walked in the 6-minute walk test for an additional 8 months of treatment in the extension trial. There was no change in mean % predicted FVC in all Hunter syndrome patients after 6 months of treatment in the extension trial; however, a slight decrease in mean % predicted FVC was demonstrated through to month 24 of the extension trial. The long-term effect of ELAPRASE on pulmonary function in Hunter syndrome patients is unclear.

There were no further reductions in mean urinary GAG levels in patients initially treated with ELAPRASE once weekly; however, the patients treated with ELAPRASE every other week during the placebo-controlled trial experienced further reductions in mean urinary GAG levels after changing to a more frequent dosing regimen during the extension trial. The persistence of reduced urinary GAG levels did not correlate with the long term effect demonstrated by the 6-minute walk test distance or % predicted FVC.

14.2 Clinical Trial in Patients 7 Years and Younger

A 53-week, open-label, multicenter, single-arm trial was conducted to assess the safety, pharmacokinetics, and pharmacodynamics of ELAPRASE 0.5 mg/kg once weekly in male Hunter syndrome patients aged 7 years and younger. Safety results demonstrated that patients with complete gene deletion or large gene rearrangement mutations are more likely to develop antibodies, including neutralizing antibodies, and to experience hypersensitivity reactions with ELAPRASE administration [see Adverse Reactions (6.1, 6.2)]. In patients who remained antibody negative, the pharmacokinetic profile, reduction in urinary GAG excretion levels, and reduction in spleen volume were similar to those of adults and children 5 years and older. In patients who were persistently antibody positive, the presence of anti-idursulfase antibody was associated with reduced systemic exposure of idursulfase and a less pronounced decrease in urinary GAG levels [see Clinical Pharmacology (12.2, 12.3)].

16 HOW SUPPLIED/STORAGE AND HANDLING

ELAPRASE is supplied as a sterile injection in a 5 mL Type I glass vial. The vials are closed with a butyl rubber stopper with fluororesin coating and an aluminum overseal with a blue flip-off plastic cap. Each carton contains a single vial NDC 54092-700-01

Store ELAPRASE vials in the carton at 2°C to 8°C (36°F to 46°F) to protect from light. Do not freeze or shake. Do not use ELAPRASE after the expiration date on the vial.

17 PATIENT COUNSELING INFORMATION

Information for Patients

Patients should be advised that life-threatening anaphylactic reactions have occurred in some patients during and up to 24 hours after ELAPRASE therapy. Patients who have experienced anaphylactic reactions may require prolonged observation. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions.

A Hunter Outcome Survey has been established in order to understand better the variability and progression of Hunter syndrome (MPS II) in the population as a whole, and to monitor and evaluate long-term treatment effects of ELAPRASE. Patients and their physicians are encouraged to participate in this program. For more information, call Shire Human Genetic Therapies, Inc. at 1-866-888-0660.

ELAPRASE is manufactured by:
Shire Human Genetic Therapies, Inc.
300 Shire Way
Lexington, MA 02421
US License Number 1593
Phone # 1-866-888-0660

ELAPRASE is a registered trademark of Shire Human Genetic Therapies, Inc.
S44652 11/18