elaprase® (idursulfase)

DISCUSSING ELAPRASE: YOUR NEW PATIENT AND CAREGIVER GUIDE

ELAPRASE Indications and Usage

ELAPRASE® (Idursulfase) 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.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF ANAPHYLAXIS

Life-threatening anaphylactic reactions have occurred in some patients 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.

For Healthcare Professionals

Please see additional Important Safety Information on pages 18–19 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

For more information,
please visit www.ELAPRASE.com/HCP

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Please see Important Safety Information on **pages 18–19** and **CLICK HERE** to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

INTRODUCTION

This guide has been designed for healthcare professionals (HCPs) to use before an initial ELAPRASE discussion with caregivers or, in some cases, patients. Whilst every discussion will be different, this guide aims to help facilitate conversations with families new to ELAPRASE treatment.

The topics covered provide an introduction to ELAPRASE and answer initial questions about Hunter syndrome that may be relevant to new patients and their caregivers.

If your patient and their caregiver are Spanish-speaking, materials are available in Spanish to aid their understanding.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Hypersensitivity Reactions Including Anaphylaxis: Ensure that personnel administering product are adequately trained in cardiopulmonary resuscitative measures, and have ready access to emergency medical services (EMS).

If anaphylactic or other acute reactions occur, immediately discontinue the infusion of ELAPRASE and initiate appropriate medical treatment. 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. When severe reactions have occurred during clinical trials, subsequent infusions were managed with antihistamine and/or corticosteroids prior to or during infusions, a slower rate of ELAPRASE infusion, and/or early discontinuation of the ELAPRASE infusion.

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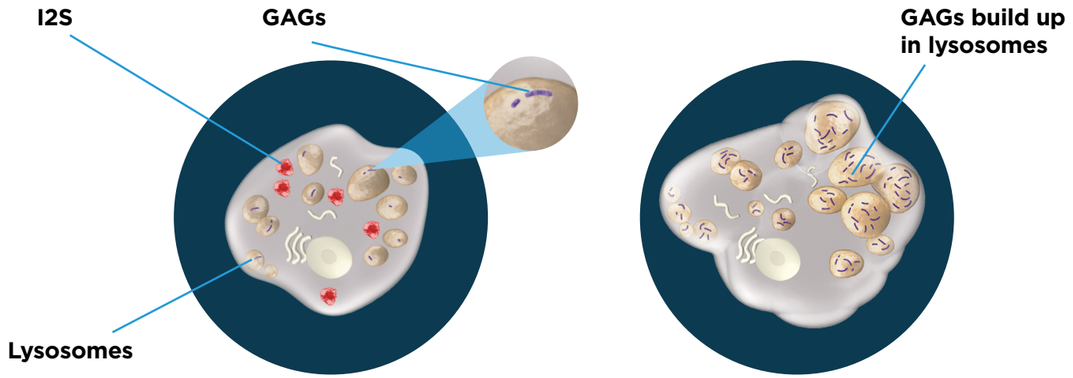
HUNTER SYNDROME OVERVIEW

- Hunter syndrome, also called mucopolysaccharidosis II (MPS II), is a rare, progressive, genetic condition predominantly affecting boys.[1]
- Hunter syndrome is one of the lysosomal storage diseases, in which glycosaminoglycans (GAGs) accumulate abnormally in the body over time.[1]
- This build up of GAGs is caused by a deficiency of the enzyme iduronate-2-sulfatase (I2S). Normally this enzyme would break down the GAGs, preventing them from building up in the cells.[1]

This diagram shows how cells are affected by Hunter syndrome compared with a healthy cell:



HEALTHY CELL

Healthy cells contain the enzyme (I2S) that breaks down GAGs in the lysosomes.[2]

HUNTER SYNDROME-AFFECTED CELL

Hunter syndrome cells have deficient I2S activity. GAGs are not broken down and accumulate in lysosomes, causing them and the cell to swell.[2]

IMPORTANT SAFETY INFORMATION (CONTINUED)

Risk of Hypersensitivity, Serious Adverse Reactions, and Antibody Development in Hunter Syndrome Patients with Severe Genetic Mutations: Hunter syndrome patients aged 7 years and younger 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.

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ELAPRASE AS AN ERT

- ELAPRASE is the only FDA-approved enzyme replacement therapy (ERT) for MPS II.[2]
- ELAPRASE is a formulation of idursulfase: a purified form of human I2S, which is the enzyme that is missing or defective in patients with Hunter syndrome.[2]
- ELAPRASE is a hydrolytic GAG-specific enzyme and works by substituting the missing or defective I2S enzyme in people with Hunter syndrome, helping to break down the GAGs that can accumulate in the lysosomes of a variety of cells.[2]
- ELAPRASE is designed to be comparable to the naturally occurring enzyme and is produced by recombinant DNA technology in a human cell line.[2]

IMPORTANT SAFETY INFORMATION (CONTINUED)

Risk of Acute Respiratory Complications: Patients with compromised respiratory function or acute febrile or respiratory illness 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.

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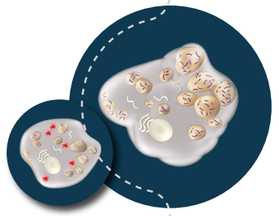
ELAPRASE MECHANISM OF ACTION

- ELAPRASE is internalized by cells in the body, specifically targeted to lysosomes where GAGs accumulate.[2]
- ELAPRASE can then break down the accumulated GAGs within some areas of the body.[2]

ELAPRASE mechanism of action

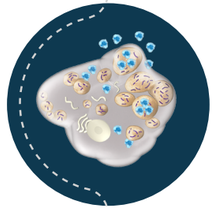
1



HEALTHY CELL VS. HUNTER SYNDROME -AFFECTED CELL

Hunter syndrome patients have insufficient I2S enzyme activity. This means GAGs build up in cells, causing cellular and organ damage.[2]

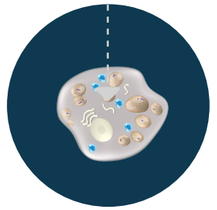
2



HOW ELAPRASE WORKS

ELAPRASE is an ERT. It is absorbed into cells where it breaks down GAGs, like the naturally occurring I2S.[2]

3



ELAPRASE-TREATED CELL

ELAPRASE is intended to reduce the levels of GAGs in tissues. Decreases in urinary GAG levels are observed following treatment with ELAPRASE. The responsiveness of urinary GAG levels to dosage alterations of ELAPRASE is unknown, and the relationship of urinary GAG levels to other measures of clinical response has not been established.[2]

Illustration only. Not intended to imply clinical significance.

In the body, some systems are less accessible to systemic drugs than others. A limitation of ELAPRASE is that it is not able to cross the blood–brain barrier, meaning it does not treat cognitive symptoms.[1]

Please see Important Safety Information on pages 18–19 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

15+ YEARS

ELAPRASE® (idursulfase) is a global brand with over 15 years of real-world experience

ELAPRASE is available in 77 countries* and has been FDA approved since 2006[2]

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HISTORY AND USAGE

1990–2000

Development of idursulfase, a purified form of the human I2S enzyme produced by recombinant DNA technology in a continuous human cell line.[2,3]

2001

Idursulfase ERT clinical trial program initiated, beginning with a Phase I/II trial.[4]

2006

ELAPRASE receives US Food and Drug Administration (FDA) approval for use in patients with MPS II aged 5 years or older, based on data from the pivotal clinical trial in MPS II patients aged 5–31 years.[2]

2014

US prescribing information updated to include information about the use of ELAPRASE in children 16 months to 5 years of age.[2]

In patients 16 months to 5 years old, ELAPRASE did not show improvement in disease-related symptoms or long-term clinical result; however, treatment with ELAPRASE has reduced spleen size similarly to patients 5 years and older.[2]

It is not known if ELAPRASE is safe and effective in children under 16 months old.[2]

2016

10 YEARS

ELAPRASE hits 10-year mark. As of July 2016, 1200 patients, from 134 clinics, in 33 countries had been enrolled in the Hunter Outcome Survey (HOS), making it the largest global source of data on Hunter syndrome.[5]

2021

15 YEARS

ELAPRASE celebrated 15 years of FDA approval.[2]

*Indication and risk Information may vary by country. Intended for US healthcare professionals only.

Please see Important Safety Information on pages 18–19 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

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TREATMENT WITH ELAPRASE

- Due to the progressive nature of the disease, doctors are advised to consider treatment as soon as possible.[1]
- ELAPRASE is administered as an intravenous infusion at a recommended dose of 0.5 mg per kg of body weight given once a week.[2]
- To receive ELAPRASE, patients will go to a treatment center every week for an infusion that can last 3 hours; patients may require longer infusion times if hypersensitivity reactions occur. The infusion time may be gradually reduced to 1 hour if no hypersensitivity reactions occur. Additional time for preparation and observation may be required.[2]
- With each infusion, patients are closely monitored to determine how they are responding to treatment with ELAPRASE. If ELAPRASE is well tolerated, the infusion time may be reduced gradually at the discretion of the administering HCP.[2]
- Treatment may be lifelong but this is at the HCP, patient, and family's discretion.
- Patients may be eligible for home infusions, under the supervision of an HCP, at the consideration of their doctor.

To access the ELAPRASE Dosing Calculator or download the ELAPRASE Dosing and Infusion Guide, visit ELAPRASE.com/HCP/dosing-and-administration

IMPORTANT SAFETY INFORMATION (CONTINUED)

Adverse Reactions: In clinical trials, the most frequent serious adverse reactions following ELAPRASE treatment 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.

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STORAGE AND STABILITY

Store ELAPRASE vials in the carton at 36°F to 46°F (2°C to 8°C) to protect from light.[2]

Do not freeze or shake. Do not use ELAPRASE after the expiration date on the vial.[2]

ELAPRASE does not contain preservatives; therefore, after dilution with saline, the diluted solution should be used immediately.[2]

If immediate use is not possible, the diluted solution should be stored refrigerated at 36°F to 46°F (2°C to 8°C) for up to 24 hours.[2]

Other than during infusion, do not store the diluted ELAPRASE solution at room temperature.[2]

ELAPRASE vials are single use. Any unused product or waste material should be discarded and disposed of in accordance with applicable requirements.[2]

Home infusion patients and caregivers should discuss complete storage and handling conditions with their doctor.

For more information on storage and stability, CLICK HERE for the Full Prescribing Information and please visit www.ELAPRASE.com/HCP/dosing-and-administration/storage-and-stability

IMPORTANT SAFETY INFORMATION (CONTINUED)

The most common adverse reactions occurring in at least three patients (≥9%) aged five years and older were headache, pruritus, musculoskeletal pain, urticaria, diarrhea, and cough. The most common adverse reactions occurring in at least three patients (≥10%) aged seven years and younger were pyrexia, rash, vomiting, and urticaria. In all clinical trials, the most common adverse reactions requiring medical intervention were hypersensitivity reactions, and included rash, urticaria, pruritus, flushing, pyrexia, and headache.

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ELAPRASE SAFETY AND EFFICACY

- The safety and efficacy of ELAPRASE were evaluated in a 53-week, randomized, double-blind, placebo-controlled clinical trial of 96 patients with Hunter syndrome, aged 5 to 31 years old.[2]
- ELAPRASE was shown to improve walking capacity and reduce spleen size in patients aged 5 years and older.[2]
- In patients aged 16 months to 5 years, no data are available to demonstrate improvement in disease-related symptoms or long-term clinical outcomes; however, treatment with ELAPRASE has reduced spleen volume similarly to the effect seen in patients aged 5 years and older.[2]
- Patients receiving ELAPRASE treatment will be monitored closely for any adverse reactions, including life-threatening anaphylactic reactions.[2]
- Due to the potential for severe reactions, appropriate medical support should be readily available when ELAPRASE is administered. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur.[2]
- The safety and efficacy of ELAPRASE have not yet been established for patients less than 16 months of age.[2]

Advise the patient or their caregiver that while it may not be possible to predict how they will respond to ELAPRASE, the HCP administering the infusion will be ready to respond appropriately in case of an adverse reaction.

Infusions will take place in an infusion center or hospital under close supervision and a medical professional will be on hand to manage any adverse reactions, if they arise.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Immunogenicity: In clinical trials in patients aged 5 years and older, 32 of 63 (51%) patients tested positive for anti-idursulfase IgG antibodies (Ab) at least one time. Of the 32 Ab-positive patients, 23 of 32 (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 than in those who tested negative.

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Notable serious adverse reactions that have occurred in ELAPRASE-treated patients

ELAPRASE clinical trials	Safety profile
Pivotal trial (N=32) ELAPRASE (idursulfase) was studied in a pivotal trial involving Hunter syndrome patients aged 5 years and older. Adverse reactions (≥9%) occurring in the ELAPRASE group with a higher incidence than the placebo group **(5 years and older)** included:[2]	**Headache** (28%) **Pruritus** (25%) **Urticaria** (16%) **Musculoskeletal pain** (13%) **Diarrhea** (9%) **Cough** (9%)
Extension trial (N=94) In addition to frequently experienced adverse reactions in the ELAPRASE once-weekly group in the pivotal trial, common hypersensitivity reactions occurring in at least five patients (≥5%) in the extension trial included:[2]	**Rash** (23%) **Pyrexia** (9%) **Flushing** (7%) **Erythema** (7%) **Nausea** (5%) **Dizziness** (5%) **Vomiting** (5%) **Hypotension** (5%)
Under 7s trial (N=28) Patients aged 16 months to 7.5 years experienced similar adverse reactions to those observed in clinical trials in patients aged ≥5 years. The most common adverse reactions following ELAPRASE treatment were hypersensitivity reactions (57%).[2]	A higher incidence of the following common hypersensitivity reactions was reported in this younger age group:[2] **Pyrexia** (36%) **Rash** (32%) **Vomiting** (14%) The most common serious adverse reactions occurring in at least three patients (≥10%) included:[2] **Bronchopneumonia/pneumonia** (18%) **Ear infection** (11%) **Pyrexia** (11%)

IMPORTANT SAFETY INFORMATION (CONTINUED)

Thirteen of 32 (41%) Ab-positive patients also tested positive for antibodies that neutralize idursulfase uptake into cells (neutralizing antibodies, NAb) or enzymatic activity at least one time, and 8 (25%) Ab-positive patients had persistent NAb. There was no clear relationship between the presence of either Ab or NAb and therapeutic response.

In the clinical trial in patients aged 7 years and younger, 19 of 28 (68%) patients treated with ELAPRASE 0.5 mg/kg once weekly tested Ab-positive, with 16 of 19 (84%) having persistent Ab. In addition, 15 of 19 (79%) Ab-positive patients tested positive for NAb, with 14 of 15 (93%) having persistent NAb.

Please see additional Important Safety Information on pages 18–19 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

FREQUENTLY ASKED QUESTIONS

1. What are the side effects of ELAPRASE?

Allergic reactions, including life-threatening anaphylaxis, have occurred in some patients treated with ELAPRASE. Anaphylactic reactions include breathing problems, low oxygen levels, low blood pressure, hives, and/or swelling of the throat or tongue.[2]

In clinical trials, the most common side effects occurring in at least three patients aged 5 years or older were headache, itching, muscle and bone pain, hives, diarrhea, and cough. Among patients aged 7 years or younger, the most common adverse reactions occurring in at least three patients were fever, rash, vomiting, and hives.[2] Please see **pages 18–19** for Important Safety Information.

2. What will happen if there is a reaction to ELAPRASE?

If anaphylactic or other acute reactions occur, immediately discontinue the infusion of ELAPRASE and initiate appropriate medical treatment. When severe reactions have occurred during clinical trials, subsequent infusions were managed with antihistamine and/or corticosteroids prior to or during infusions, a slower rate of ELAPRASE infusion, and/or early discontinuation of the ELAPRASE infusion.[2]

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.[2]

3. How is ELAPRASE dosed?

ELAPRASE is administered at a dose of 0.5 mg/kg body weight every week, by intravenous infusion. The infusion period will last 3 hours, with a possible gradual reduction to 1 hour if no hypersensitivity reactions are observed. The dose of ELAPRASE depends on the patient's body weight; it is therefore important to weigh the patient before each treatment. Patients may require longer infusion times if hypersensitivity reactions occur; however, infusion times should not exceed 8 hours.[2]

IMPORTANT SAFETY INFORMATION (CONTINUED)

Postmarketing 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 anaphylaxis over a two to four month period, up to several years after initiating ELAPRASE treatment.

Serious adverse reactions that resulted in death included cardiorespiratory arrest, respiratory failure, respiratory distress, cardiac failure, and pneumonia.

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4. Is ELAPRASE a new medication?

No, ELAPRASE has been FDA-approved for use in the U.S. since 2006.[2] ELAPRASE has also received marketing authorization in many other countries. ELAPRASE has been approved in 77 other countries after receiving respective marketing authorizations and so is available to patients around the world. Indication and risk information may vary by country.

5. Why does the Prescribing Information say that "The safety and efficacy of ELAPRASE have not been established in pediatric patients less than 16 months of age"?

The clinical trials that studied ELAPRASE only included patients aged 16 months and older.[2]

6. When can patients start treatment with ELAPRASE?

Please advise the caregiver and patient how to proceed. You may wish to arrange a follow-up meeting with them to further explain treatment with ELAPRASE and the process involved in initiating treatment with ELAPRASE.

7. Where can I find more information on patient support?

When you prescribe ELAPRASE for your patient, Takeda Patient Support is here for them. Our support specialists can help with your patient's questions and concerns, and provide them with the information they need.

To learn more about Takeda Patient Support, click here

Please see Important Safety Information on pages 18–19 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

Takeda Patient Support
Your Source for Education and Access

Patient Support Services
— support for your patient throughout their treatment journey

*When you prescribe **ELAPRASE** for your patient, Takeda Patient Support is here for them. Our support specialists can help with your patient's questions and concerns and provide them with the information they need.*

For onboarding, access, and reimbursement assistance, some of our services may include:

- **Benefits investigation** to help determine your patient's insurance benefits and eligibility for certain services
- **Prior authorization (PA), reauthorization, and appeals information**
- **Enrolling your patient in the Takeda Patient Support Co-Pay Assistance Program** if they qualify*
- **Information about financial assistance options** for your patient, if they're eligible

Our additional services include:

- **Specialty pharmacy or site of care triage** and coordination
- **Directing your patient** to community support resources
- **Assistance** during life transitions like relocation, moving to college, or changing jobs, and insurance changes
- **Coordination** between your patient's specialty pharmacy and your site of care, even if they are traveling out of town or relocating

*To be eligible, the patient must be enrolled in Takeda Patient Support, and have commercial insurance. Other terms and conditions apply. Call for more details.

To get started, click here to visit our convenient online enrollment portal or Print & Fax our downloadable Start Form here.

We know living with Hunter syndrome looks different for everyone. We get to know your patient. We work to understand who they are, and we learn what's most important to them — so we can provide the support they need when it comes to their treatment.

Our support specialists are never more than a tap or a call away — **1-866-888-0660**, Monday through Friday, 8:30 am to 8:00 pm ET.

If English is not your preferred language, let your support specialist know. The team can communicate over the phone in a variety of languages — including Spanish, and more — using a translation service.

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RESOURCES

ELAPRASE.com/HCP has more information about ELAPRASE, clinical trials, and other resources.

The MPS Society (see mpssociety.org) is a patient organization providing support for families.

There are various social media community pages to help support patients and caregivers living with Hunter syndrome.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNING: RISK OF ANAPHYLAXIS

Life-threatening anaphylactic reactions have occurred in some patients 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.

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Hypersensitivity Reactions Including Anaphylaxis:

Ensure that personnel administering product are adequately trained in cardiopulmonary resuscitative measures, and have ready access to emergency medical services (EMS).

If anaphylactic or other acute reactions occur, immediately discontinue the infusion of ELAPRASE and initiate appropriate medical treatment. 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. When severe reactions have occurred during clinical trials, subsequent infusions were managed with antihistamine and/or corticosteroids prior to or during infusions, a slower rate of ELAPRASE infusion, and/or early discontinuation of the ELAPRASE infusion.

Risk of Hypersensitivity, Serious Adverse Reactions, and Antibody Development in Hunter Syndrome Patients with Severe Genetic Mutations:

Hunter syndrome patients aged 7 years and younger 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.

Risk of Acute Respiratory Complications:

Patients with compromised respiratory function or acute febrile or respiratory illness 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.

Important Safety Information (continued)

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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.

Adverse Reactions:

In clinical trials, the most frequent serious adverse reactions following ELAPRASE treatment 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.

The most common adverse reactions occurring in at least three patients (≥9%) aged five years and older were headache, pruritus, musculoskeletal pain, urticaria, diarrhea, and cough. The most common adverse reactions occurring in at least three patients (≥10%) aged seven years and younger were pyrexia, rash, vomiting, and urticaria. In all clinical trials, the most common adverse reactions requiring medical intervention were hypersensitivity reactions, and included rash, urticaria, pruritus, flushing, pyrexia, and headache.

Immunogenicity:

In clinical trials in patients aged 5 years and older, 32 of 63 (51%) patients tested positive for anti-idursulfase IgG antibodies (Ab) at least one time. Of the 32 Ab-positive patients, 23 of 32 (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 than in those who tested negative.

Thirteen of 32 (41%) Ab-positive patients also tested positive for antibodies that neutralize idursulfase uptake into cells (neutralizing antibodies, NAb) or enzymatic activity at least one time, and 8 (25%) Ab-positive patients had persistent NAb. There was no clear relationship between the presence of either Ab or NAb and therapeutic response.

In the clinical trial in patients aged 7 years and younger, 19 of 28 (68%) patients treated with ELAPRASE 0.5 mg/kg once weekly tested Ab-positive, with 16 of 19 (84%) having persistent Ab. In addition, 15 of 19 (79%) Ab-positive patients tested positive for NAb, with 14 of 15 (93%) having persistent NAb.

Postmarketing 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 anaphylaxis over a two to four month period, up to several years after initiating ELAPRASE treatment.

Serious adverse reactions that resulted in death included cardiorespiratory arrest, respiratory failure, respiratory distress, cardiac failure, and pneumonia.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda at 1-877-TAKEDA-7 or FDA at 1-866-FDA-1088 or www.fda.gov/medwatch

Please CLICK HERE for the Full Prescribing Information, including Boxed WARNING.

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elaprase® (idursulfase)

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ELAPRASE Indications and Usage

ELAPRASE® (Idursulfase) 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.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF ANAPHYLAXIS

Life-threatening anaphylactic reactions have occurred in some patients 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.

1. Wraith JE *et al. Eur J Pediatr*. 2008; 167: 267–277. 2. ELAPRASE Prescribing Information. 3. Whiteman DA *et al. Drug Des Devel Ther.* 2017; 11: 2467–2480. 4. Sohn YB *et al. Orphanet J Rare Dis*. 2013; 8: 42. 5. Burton BK *et al. J Inherit Metab Dis*. 2017; 40: 867–874.

Takeda