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]

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ELAPRASE® (idursulfase): A treatment option for Hunter syndrome (MPS II)

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.[1,2] Together with your healthcare providers, you can decide if ELAPRASE is right for you or your child.

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.[1]

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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]

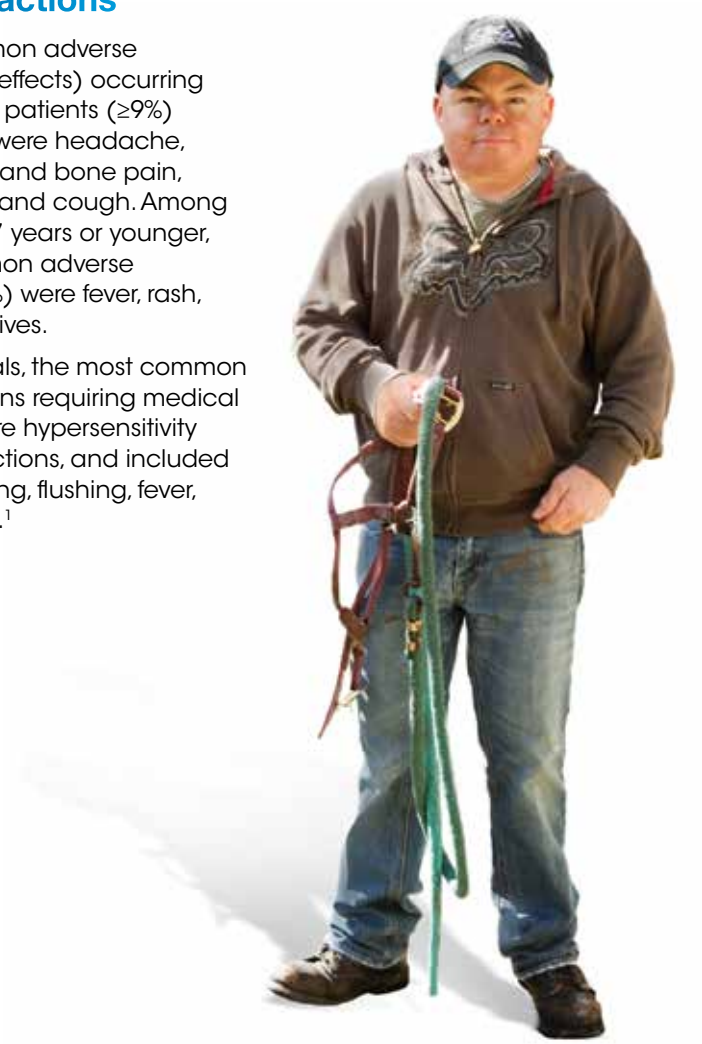
All patients in this trial were invited to receive weekly ELAPRASE treatment by participating in a 24-month extension study. In patients who were treated with ELAPRASE in the first study, improvements in the 6-MWT continued for a further 8 months.[1]

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]



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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).

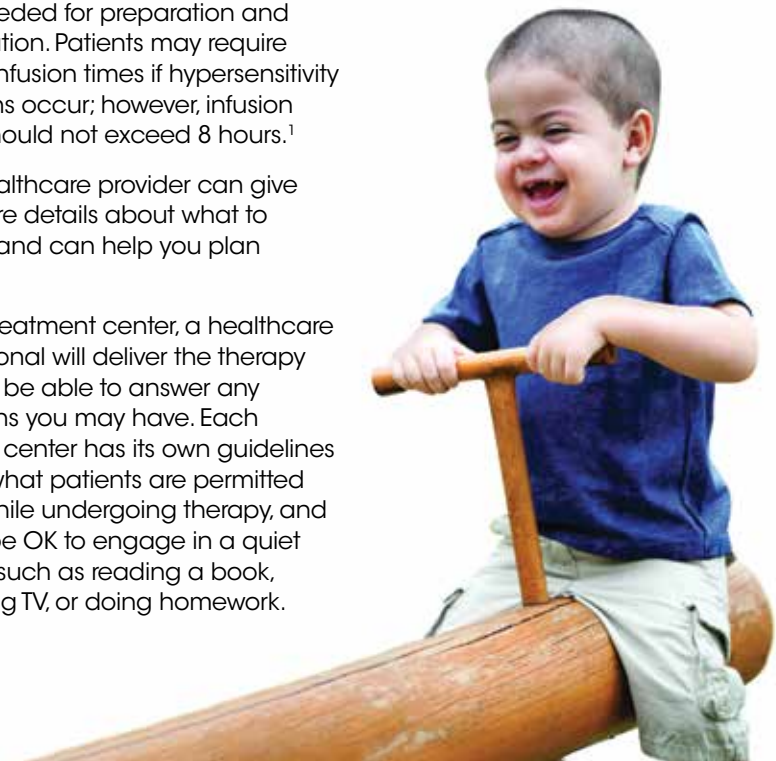
Typically, the infusion can take up to 3 hours, but there may be additional time needed for preparation and observation. Patients may require longer infusion times if hypersensitivity reactions occur; however, infusion times should not exceed 8 hours.[1]

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:

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

You can learn more about OnePath by visiting **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.

OnePath®
1-866-888-0660
www.OnePath.com

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.

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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:
1. Shire. ELAPRASE (idursulfase) Prescribing Information. June 2013. [US/ELA-00561]
2. OPDP Advisory Comments, MACMIS ID #14538, September 20, 2006. Data on File.
3. Martin R *et al.* Pediatrics 2008; 121(2): e377–386.

Please click here for full Prescribing Information, including the Boxed Warning.

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