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UNDERSTANDING ELAPRASE: DOCTOR DISCUSSIONS

What is ELAPRASE® (Idursulfase)?

ELAPRASE is a prescription medicine for patients with Hunter syndrome.

ELAPRASE has been shown to improve walking ability in patients 5 yrs and older.

In patients 16 months to 5 yrs 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 yrs and older.

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

IMPORTANT SAFETY INFORMATION

RISK OF SERIOUS ALLERGIC REACTIONS:

Some patients have experienced serious allergic reactions (including life-threatening anaphylactic reactions) during and up to 24 hours after treatment, regardless of how long they were taking ELAPRASE. Anaphylactic reactions are immediate and include breathing problems, low oxygen levels, low blood pressure, hives and/or swelling of the throat or tongue. If a patient (you or your child) has experienced an anaphylactic reaction, the patient may require an extended period of observation by the patient's healthcare team. If you or your child has breathing problems, a fever, or a respiratory illness, you or your child may be at risk of life-threatening worsening of those conditions due to allergic reactions from ELAPRASE. Your healthcare team should be advised of those conditions before treatment with ELAPRASE because the information may affect the timing of ELAPRASE treatment.

For Patients and Caregivers

Please see additional Important Safety Information on pages 12–13 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

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For more information, please visit www.ELAPRASE.com

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INTRODUCTION

What will we discuss

This guide aims to talk about Hunter syndrome and treatment with ELAPRASE. ELAPRASE (Idursulfase) is a prescription medicine for patients with Hunter syndrome. You can use this guide to discuss Hunter syndrome and ELAPRASE with your doctor, and to help you with any questions you may have about the disease and treatment.

Hunter syndrome is a rare progressive disease. You and your doctor will discuss Hunter syndrome, and will discuss ELAPRASE and why it may be suitable for you or your child.

This guide has been designed for you to take with you to your appointment with your doctor to discuss ELAPRASE. This guide has been created to help you take notes during the meeting, ask any questions you might have, and provide information to refer back to.

IMPORTANT SAFETY INFORMATION (CONTINUED)

You or your child should be closely watched during and after ELAPRASE treatment and you should confirm with your healthcare team in advance of treatment that it is prepared to manage serious allergic reactions, including anaphylactic reactions. **Tell your healthcare team immediately if any signs of an allergic reaction happen.** Those signs may include breathing problems, low blood pressure, rash, hives, itching, flushing, fever and/or headache.

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WHAT IS HUNTER SYNDROME?

- Hunter syndrome is a rare, life-long, progressive, genetic condition predominantly affecting boys
- Hunter syndrome is one of the lysosomal storage diseases in which long complex sugar molecules called glycosaminoglycans (GAGs) cannot be broken down and accumulate in cells in the body
- This build-up of GAGs is caused by missing or low levels of an enzyme called iduronate-2-sulfatase (I2S), which breaks down GAGs
- The build-up of GAGs occurs within cells throughout the body, affecting many different organs.

At this point, if you have any questions about Hunter syndrome, please ask your doctor. You may wish to discuss the specific symptoms of Hunter syndrome that you are experiencing.

Here is some space to jot down any questions or discussion points that you would like to bring up with your doctor, or make any notes:

IMPORTANT SAFETY INFORMATION (CONTINUED)

When serious allergic reactions happened during clinical trials, later ELAPRASE treatments were managed with allergy-controlling drugs before or during treatment, a slower rate of ELAPRASE treatment, and/or early discontinuation of treatment.

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WHAT IS ELAPRASE?

- ELAPRASE is a prescription medicine for patients with Hunter syndrome.
- ELAPRASE has been shown to improve walking ability in patients 5 years and older. In patients 16 months to 5 years old, ELAPRASE did not show improvement in disease-related symptoms or long term clinical results; however, treatment with ELAPRASE has reduced spleen size similarly to patients 5 years and older.
- It is not known if ELAPRASE is safe and effective in children under 16 months old.
- ELAPRASE is a type of enzyme replacement therapy (ERT) intended for Hunter syndrome patients who are unable to produce enough of the iduronate-2-sulfatase enzyme themselves.
- ELAPRASE is an "enzyme replacement therapy" because it is a formulation of the enzyme that is missing or low in people with Hunter syndrome. ELAPRASE is a purified form of the iduronate-2-sulfatase enzyme produced by recombinant DNA technology in a human cell line.
- The active substance in ELAPRASE is an enzyme that breaks down glycosaminoglycans (GAGs), which build up inside people with Hunter syndrome, causing the signs and symptoms of the condition. For example, the build-up of GAGs within organs such as the liver and spleen results in enlarged organ size.
- ELAPRASE may affect individuals differently and each person's experience with ELAPRASE will be unique.

At this point, if you would like your doctor to repeat anything they have said or explained, please ask them to do so.

Here are some questions you may have about ELAPRASE and may want to ask your doctor:

> ***What are the side effects of ELAPRASE?***
>
> ***Is ELAPRASE a new medication?***
>
> ***How can ELAPRASE help manage Hunter syndrome?***
>
> ***How does ELAPRASE affect individuals differently?***

IMPORTANT SAFETY INFORMATION (CONTINUED)

Children with serious genetic mutations may be at risk for allergic reactions, serious side effects and antibody development. In a clinical study of children 7 years and younger, patients with certain types of genetic mutations experienced a higher number of allergic reactions, serious side effects, and development of an immune response to treatment. This immune response may interfere with the effectiveness of ELAPRASE. Talk to your healthcare team about whether you or your child may be at risk.

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HOW IS ELAPRASE ADMINISTERED?

- ELAPRASE is a weekly infusion administered intravenously by a healthcare professional.
- To receive ELAPRASE, you will go to a treatment center every week for an infusion that can last up to 3 hours; a longer infusion time may be required if hypersensitivity reactions occur. This time may be gradually reduced to 1 hour if no hypersensitivity reactions occur. There may also be additional time needed for preparation and observation.
- The dose of ELAPRASE depends on your weight, so you will be regularly weighed to calculate the best dose of ELAPRASE for you.
- Patients will be closely monitored during the infusion and for a period of time afterwards. Patients should notify their healthcare team immediately if any symptoms of an allergic reaction occur.

At this point, if you would like your doctor to repeat anything they have said or explained, please ask them to do so.

Here are some questions that you may like to ask your doctor:

> ***What can I do during infusions?***
>
> ***Where is the infusion center that I should go to?***
>
> ***Who will give me the infusion?***
>
> ***What should I bring to my first infusion?***
>
> ***Who can come along with me to my infusions?***

IMPORTANT SAFETY INFORMATION (CONTINUED)

If you or your child has breathing problems, other respiratory illness, heart problems, or susceptibility to fluid overload, you or your child may be at higher risk of fluid overload during ELAPRASE treatment. Your healthcare team should be advised of those problems before treatment and you should confirm with your healthcare team in advance of treatment that it is appropriately trained to watch for signs of fluid overload and provide the necessary medical support. Patients at risk for fluid overload may require longer observation time.

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MULTIDISCIPLINARY TEAM

Your pediatrician may work alongside many specialists to diagnose and manage Hunter syndrome. These can include:

- Geneticists
- Rheumatologists
- Neurologists
- Cardiologists
- Physiotherapists
- Speech therapists
- Specialist nurses
- Otorhinolaryngologists
- Orthopedic surgeons
- Ophthalmologists
- Pneumologists
- Anesthesiologists
- Psychologists
- Social workers

Here are some questions that you may wish to ask your doctor:

> ***Why might I see these specialists?***
>
> ***What kind of tests and assessments will be conducted?***

Here is some space for you to make notes:

IMPORTANT SAFETY INFORMATION (CONTINUED)

What are possible side effects of ELAPRASE? The most common side effects of ELAPRASE include:

- In patients aged 5 and older:
  - Headache
  - Itching
  - Muscle and bone pain
  - Hives
  - Diarrhea
  - Cough
- In patients aged 7 years or younger:
  - Fever
  - Rash
  - Vomiting
  - Hives

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RESOURCES

Websites

ELAPRASE website (www.ELAPRASE.com): more information about ELAPRASE, clinical trials, and other resources.

MPS Society (www.MPSSociety.org): Hunter syndrome is one of a group of lysosomal storage diseases known as mucopolysaccharidoses, and this website has resources, support, and ways to connect with other patients.

ELAPRASE emails

Stay up to date with ELAPRASE news and updates by signing up to receive occasional emails: **www.ELAPRASE.com/stay-updated**

These resources are not intended to replace the care and advice you should receive from your doctor.

When researching Hunter syndrome, it is important to remember that every patient's experience is unique.

It may feel overwhelming looking at all the resources and information, so try to remember that it is important to take breaks and take care of yourself.

At the end of your appointment, your doctor may ask you if you have any further questions. If you can't think of anything, look back through this guide to see if there is anything else you would like to ask.

Alternatively, you could use this as an opportunity to summarize what you have learned and repeat this back to your doctor. They can then clarify any points that were unclear and you may feel more confident that you have understood everything.

IMPORTANT SAFETY INFORMATION (CONTINUED)

The most common side effects needing medical attention were allergic reactions, and included rash, hives, itching, flushing, fever, and headache. **Tell your healthcare team immediately if any signs of an allergic reaction happen.** These are not all the possible side effects of ELAPRASE.

Please see additional Important Safety Information on pages 12–13 and CLICK HERE to see accompanying Full Prescribing Information, including Boxed WARNING for Risk of Anaphylaxis.

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FREQUENTLY ASKED QUESTIONS

Here are some frequently asked questions:

1. Who gets Hunter syndrome?

Hunter syndrome is a rare disease primarily affecting boys. It is a genetic condition, meaning that it is inherited.

2. What is ELAPRASE?

ELAPRASE is a prescription medicine for patients with Hunter syndrome. ELAPRASE has been shown to improve walking ability in patients 5 years and older. 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. It is not known if ELAPRASE is safe and effective in children under 16 months old. It is a type of enzyme replacement therapy intended for Hunter syndrome patients who are unable to produce enough of the iduronate-2-sulfatase enzyme themselves.

3. How does 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 percentage predicted forced vital capacity (FVC), were not significant.

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.

IMPORTANT SAFETY INFORMATION (CONTINUED)

RISK OF SERIOUS ALLERGIC REACTIONS:

Some patients have experienced serious allergic reactions (including life-threatening anaphylactic reactions) during and up to 24 hours after treatment, regardless of how long they were taking ELAPRASE. Anaphylactic reactions are immediate and include breathing problems, low oxygen levels, low blood pressure, hives and/or swelling of the throat or tongue. If a patient (you or your child) has experienced an anaphylactic reaction, the patient may require an extended period of observation by the patient's healthcare team. If you or your child has breathing problems, a fever, or a respiratory illness, you or your child may be at risk of life-threatening worsening of those conditions due to allergic reactions from ELAPRASE. Your healthcare team should be advised of those conditions before treatment with ELAPRASE because the information may affect the timing of ELAPRASE treatment.

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FREQUENTLY ASKED QUESTIONS (CONTINUED)

4. 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. Inform your healthcare provider immediately if you notice any of these symptoms beginning.

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.

Please **CLICK HERE** for the Full Prescribing Information for more about ELAPRASE's risk and safety profile.

5. How will I receive my treatment with ELAPRASE?

ELAPRASE is administered intravenously by a trained healthcare professional, such as a nurse, in a treatment center.

Initial infusions may be administered over a period of approximately 3 hours; this time may be gradually reduced to 1 hour if no hypersensitivity reactions occur. There may also be additional time needed for preparation and observation. Your healthcare provider can give you more details about what to expect and can help you plan ahead.

To learn more about ELAPRASE and see more FAQs, visit www.ELAPRASE.com

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What is ELAPRASE® (Idursulfase)?

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You or your child should be closely watched during and after ELAPRASE treatment and you should confirm with your healthcare team in advance of treatment that it is prepared to manage serious allergic reactions, including anaphylactic reactions. **Tell your healthcare team immediately if any signs of an allergic reaction happen.** Those signs may include breathing problems, low blood pressure, rash, hives, itching, flushing, fever and/or headache.

When serious allergic reactions happened during clinical trials, later ELAPRASE treatments were managed with allergy-controlling drugs before or during treatment, a slower rate of ELAPRASE treatment, and/or early discontinuation of treatment.

Children with serious genetic mutations may be at risk for allergic reactions, serious side effects and antibody development. In a clinical study of children 7 years and younger, patients with certain types of genetic mutations experienced a higher number of allergic reactions, serious side effects, and development of an immune response to treatment. This immune response may interfere with the effectiveness of ELAPRASE. Talk to your healthcare team about whether you or your child may be at risk.

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Important Safety Information (continued)

If you or your child has breathing problems, other respiratory illness, heart problems, or susceptibility to fluid overload, you or your child may be at higher risk of fluid overload during ELAPRASE treatment. Your healthcare team should be advised of those problems before treatment and you should confirm with your healthcare team in advance of treatment that it is appropriately trained to watch for signs of fluid overload and provide the necessary medical support. Patients at risk for fluid overload may require longer observation time.

What are possible side effects of ELAPRASE?

The most common side effects of ELAPRASE include:

- In patients aged 5 and older:
  - Headache
  - Itching
  - Muscle and bone pain
  - Hives
  - Diarrhea
  - Cough
- In patients aged 7 years or younger:
  - Fever
  - Rash
  - Vomiting
  - Hives

The most common side effects needing medical attention were allergic reactions, and included rash, hives, itching, flushing, fever, and headache. **Tell your healthcare team immediately if any signs of an allergic reaction happen**. These are not all the possible side effects of ELAPRASE.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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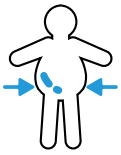
GLOSSARY

This is a collection of words or phrases that you may hear your doctor frequently mention or you may see during your research into Hunter syndrome:

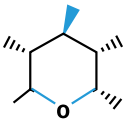


Abdominal distension – Swelling or enlargement of the abdomen. This can occur in patients with Hunter syndrome due to the enlargement of the liver or spleen.

Enzyme replacement therapy (ERT) – Treatment that works by replacing the missing or deficient enzyme in a disease. ELAPRASE is an ERT and is intended to replace the iduronate-2-sulfatase enzyme in patients with Hunter syndrome.

Glycosaminoglycans (pronounced gli-ko-sah-mee-no-gli-cans) (GAGs) – Long sugar molecules that are a component of connective tissue in the body. GAGs may also be referred to as mucopolysaccharides and build-up in patients with Hunter syndrome.

Hepatomegaly – An enlarged liver. The liver in patients with Hunter syndrome can swell due to the build-up of the long sugar molecules that the body cannot break down.



Iduronate-2-sulfatase (I2S) – This is the name of the enzyme that is missing or deficient in people with Hunter syndrome. ELAPRASE contains a purified form of this enzyme, which is intended to break down the long complex sugar molecules.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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GLOSSARY (CONTINUED)

Infusion – A therapy that requires administration of a drug through a needle or catheter. ELAPRASE is administered by an infusion.

Mucopolysaccharide – A long complex sugar molecule found in the body.

Mucopolysaccharidosis (pronounced mew-ko-pol-ee-sak-ah-ride-o-sis) (MPS) II – An alternative name for Hunter syndrome. Hunter syndrome is one type of a collection of diseases called mucopolysaccharidoses, which all involve the accumulation of long sugar molecules that cannot be broken down.

Multidisciplinary team – As Hunter syndrome can affect multiple organs of the body, it may require multiple specialists to help manage the disease.

Splenomegaly – An enlarged spleen. The spleen in patients with Hunter syndrome can swell due to the build-up of the long sugar molecules that the body cannot break down.

If you're unsure of the meaning of any words or phrases that your doctor uses, please ask them to explain them to you. If you would rather look these up after your meeting, here is some space to note them down:

IMPORTANT SAFETY INFORMATION (CONTINUED)

Children with serious genetic mutations may be at risk for allergic reactions, serious side effects and antibody development. In a clinical study of children 7 years and younger, patients with certain types of genetic mutations experienced a higher number of allergic reactions, serious side effects, and development of an immune response to treatment. This immune response may interfere with the effectiveness of ELAPRASE. Talk to your healthcare team about whether you or your child may be at risk.

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1. Wraith JE *et al. Eur J Pediatr.* 2008; 167: 267–277. 2. ELAPRASE Prescribing Information. 3. Scarpa M *et al. Orphanet J Rare Dis.* 2011; 6(72): 1–18. 4. Burton BK, Guiglian R. *Eur J Pediatr.* 2012; 171: 631–639. 5. Martin R *et al. Pediatr.* 2008; 121(2): e377–386. 6. Cambridge Dictionary. Distension. Available at: https://dictionary.cambridge.org/dictionary/english/distension. Accessed March 2022. 7. NORD. Mucopolysaccharidosis Type II. Available at: https://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-ii-2/. Accessed March 2022. 8. NINDS NIH. Mucopolysaccharidoses Fact Sheet. Available at: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Mucopolysaccharidoses-Fact-Sheet. Accessed March 2022. 9. Healthline. What Is Infusion Therapy and When Is It Needed? Available at: https://www.healthline.com/health/infusiontherapy#conditions-used-for. Accessed March 2022.

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