



GUIDELINES FOR WEIGHT-BASED DOSING AND INFUSION

Includes

Example dose
calculation reference

Preparation and administration
information for healthcare
professionals



elaprase[®]
(idursulfase)

Please click [here](#) for full Prescribing Information, including Boxed Warning, and see Important Safety Information on pages 19–20.

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Boxed warning, indication and usage

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Indication and usage

ELAPRASE is indicated for patients with Hunter syndrome (mucopolysaccharidosis II, MPS II).¹

ELAPRASE has been shown to improve walking capacity in patients 5 years and older.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 less than 16 months of age.¹

Recommended dose of ELAPRASE

The recommended dosage regimen of ELAPRASE is 0.5 mg per kg of body weight, administered once weekly as an intravenous (IV) infusion.¹

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.

Importance of weight-based dosing

Hunter syndrome is caused by a deficiency in the activity of the lysosomal enzyme iduronate-2-sulfatase (I2S).¹ In a healthy individual, every cell in the body, except red blood cells, expresses the I2S enzyme.²

ELAPRASE is a purified form of the I2S enzyme, designed to replace the deficient or malfunctioning I2S enzyme in Hunter syndrome patients.¹

The recommended dose of ELAPRASE is dependent on the body weight of the Hunter syndrome patient.¹

It is therefore important to weigh patients before each infusion to ensure correct dosing.

Dose calculation

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Calculating the required volume and number of vials¹

1

Example calculation:



$$21 \text{ kg} \times 0.5 \text{ mg/kg} = 10.5 \text{ mg}$$

Recommended dose of ELAPRASE is 0.5 mg/kg patient body weight administered once weekly as an IV infusion

Dose of ELAPRASE required:
Patient body weight (kg) x 0.5 mg/kg of ELAPRASE

2



$$10.5 \text{ mg} \div 2 \text{ mg/mL} = 5.25 \text{ mL}$$

ELAPRASE is provided at a concentration of 2 mg/mL

Total mL volume of ELAPRASE required:
Dose of ELAPRASE ÷ 2 mg/mL

3



$$5.25 \text{ mL} \div 3 \text{ mL/vial} = 1.75 \text{ vials}$$

One vial of ELAPRASE contains 3 mL

Number of ELAPRASE vials required:
Total mL volume of ELAPRASE ÷ 3 mL/vial

4



Withdraw
5.25 mL
ELAPRASE

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

5



Dispose of
unused product

Any unused product or waste material should be discarded and disposed of in accordance with local requirements

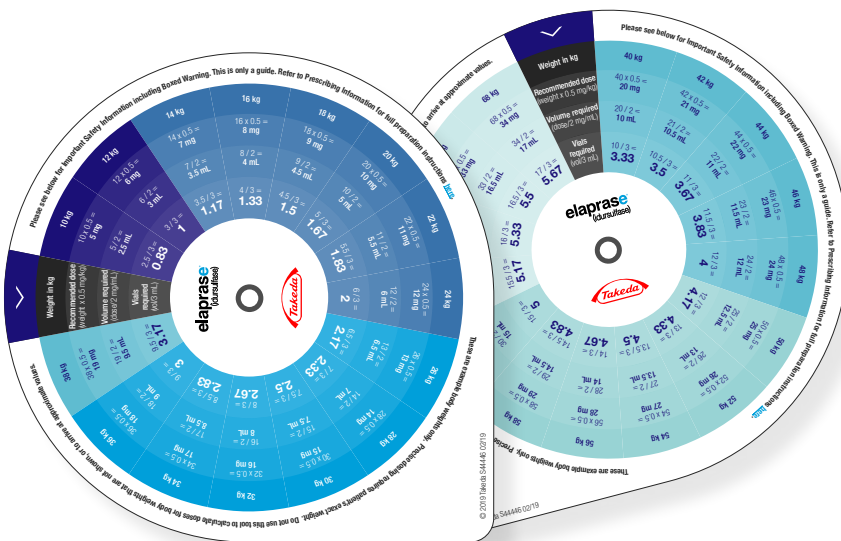


How to use the example dose calculation reference

The **example dose calculation reference**, located on pages 22–27 of this document, provides example calculations of the number of vials required to withdraw the recommended mL volume of ELAPRASE according to example patient weights.

HOW TO USE THE DOSING REFERENCE

Point to an example patient weight and read off the recommended dose, volume and number of vials from the dosing reference sector. The dosing reference is only a guide. See Prescribing Information [here](#) for full preparation instructions. The dosing reference provides example body weights only. Precise dosing requires patient's exact weight. Do not use this tool to calculate doses for body weights that are not shown, or to arrive at approximate values.



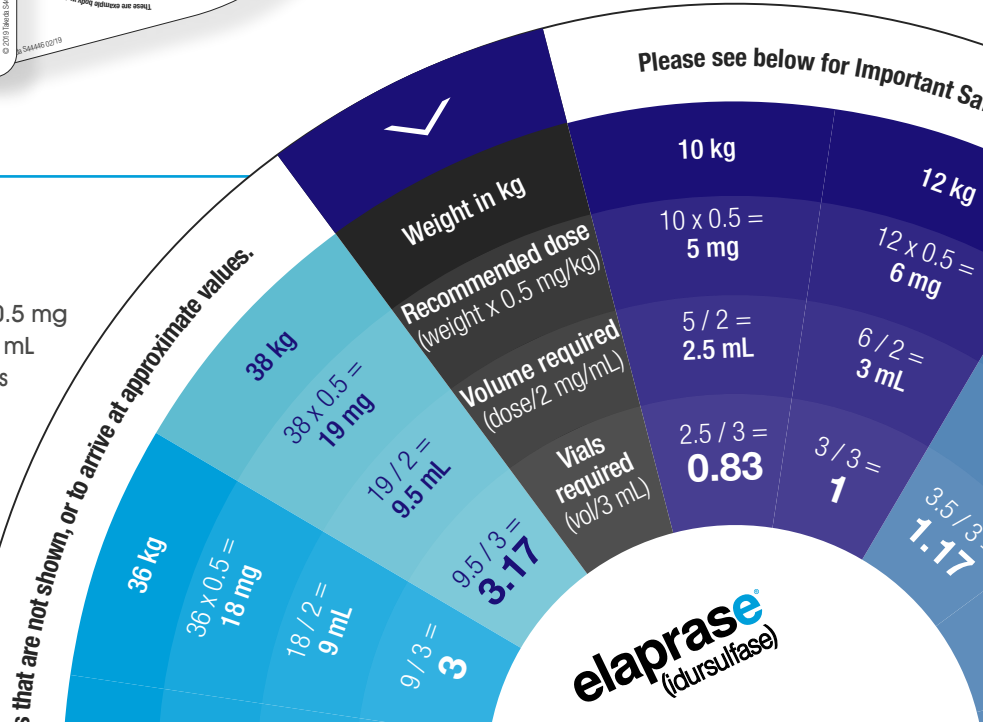
EXAMPLE CALCULATION

Patient weight: 21 kg
 Recommended dose: $21 \text{ kg} \times 0.5 \text{ mg/kg} = 10.5 \text{ mg}$
 Volume required: $10.5 \text{ mg} \div 2 \text{ mg/mL} = 5.25 \text{ mL}$
 Number of vials required: $5.25 \text{ mL} \div 3 \text{ mL/vials}$

= 1.75 vials

Withdraw a total volume of **5.25mL** from 2 vials

Any unused product or waste material should be discarded and disposed of in accordance with local requirements



Preparation

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Supplies for infusion

Required supplies for diluting ELAPRASE solution

- 100 mL bag of 0.9% Sodium Chloride Injection, USP.¹
- Low-protein-binding infusion set equipped with a low-protein-binding 0.2 micrometer (μm) in-line filter.¹
- ELAPRASE should not be infused with other products in the infusion tubing.¹

Additional infusion supplies*

- Blunt fill or filter needle to withdraw drug from vial(s).³
- 50 mL bag of 0.9% Sodium Chloride Injection, USP (flush infusate).³
- IV needle/catheter and insertion supplies.³
- Infusion control device.

*These additional infusion supplies are recommendations only. They should be reconciled with appropriate institution policies and procedures, other manufacturers' guidelines, required regulations, and medical judgment.

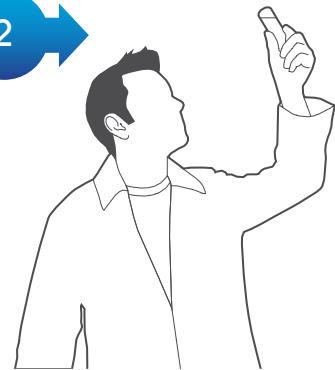
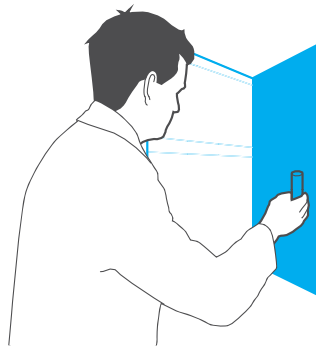


Preparation Instructions

Remove the required number of vials (refer to instructions on page 8) from the refrigerator to allow them to reach room temperature.¹

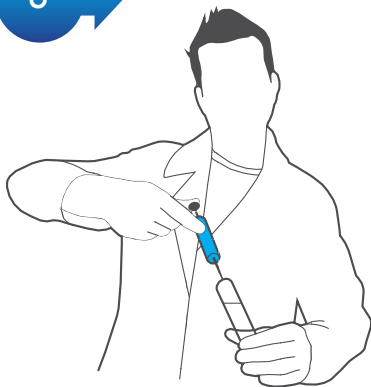
After dilution of ELAPRASE with saline, the infusion bags should be used immediately.¹

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.



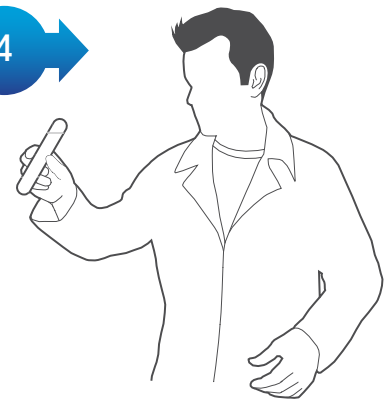
Before withdrawing the ELAPRASE solution from the vial, visually inspect each vial for particulate matter and discoloration:

- The ELAPRASE solution should be clear to slightly opalescent and colorless.¹
- Do not use if the solution is discolored or if there is particulate matter in the solution.¹
- Do not shake the ELAPRASE solution.¹



Withdraw the calculated volume of ELAPRASE from the appropriate number of vials and add to a 100 mL bag of 0.9% Sodium Chloride Injection, USP for IV infusion – using aseptic technique:¹

1. Remove the cap from a stock bag containing 100 mL of 0.9% Sodium Chloride Injection, USP.
2. Wipe the exposed rubber seal injection port with an alcohol swab and allow to dry.³
3. Remove the flip-off cap from the ELAPRASE vial(s).³
4. Wipe the exposed rubber seal(s) of the vial(s) with alcohol swabs and allow to dry.³
5. Using sterile syringe(s), withdraw the calculated volume of ELAPRASE from the appropriate number of vials.¹
6. Add the contents of the syringe(s) to the bag containing 100 mL of 0.9% Sodium Chloride Injection, USP.^{1,3}
7. Label the ELAPRASE solution with the patient name, product name, dose, discard date, and time, or per institution policy.³



Mix gently. Do not shake the solution.¹

- ELAPRASE does not contain preservatives; therefore, after dilution with saline, the infusion bags should be used immediately.¹
- If immediate use is not possible, see [Storage and stability](#) on page 15.

These preparation instructions are recommendations only. They should be reconciled with appropriate institution policies and procedures, other manufacturers' guidelines, required regulations, and medical judgment.

Administration and storage

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Administration instructions

ELAPRASE is intended for IV use only.¹

Prepare the diluted ELAPRASE solution according to the [Preparation instructions](#) on pages 11–12.

Obtain or assess IV access and prime/backprime the tubing based on the individual patient.³

Spike the 100 mL bag of 0.9% Sodium Chloride Injection, USP, containing ELAPRASE with the filtered IV administration set (a low-protein-binding infusion set equipped with a low-protein-binding 0.2 μm in-line filter) and prime according to the set manufacturer's recommendations.^{1,3}



- Once the tubing is primed, connect the ELAPRASE drug solution to the primary line's injection/access port.³
- ELAPRASE should not be infused with other products in the infusion tubing.¹

Start the infusion control device to regulate the flow of the ELAPRASE solution at the prescribed rate.³

- 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.¹
- Patients may require longer infusion times if hypersensitivity reactions occur; however, infusion times should not exceed 8 hours.¹
- The initial infusion rate should be 8 mL per hour for the first 15 minutes.¹
- If the infusion is well tolerated, the rate of infusion may be increased by 8 mL per hour increments every 15 minutes.¹
- The infusion rate should not exceed 100 mL per hour.¹
- The infusion rate may be slowed, temporarily stopped, or discontinued for that visit in the event of hypersensitivity reactions.¹
- ELAPRASE should not be infused with other products in the infusion tubing.¹

Infuse the ELAPRASE solution.

After the ELAPRASE solution has been infused, remove the ELAPRASE drug bag from the IV administration set and replace with the bag containing 50 mL of 0.9% sodium chloride injection, USP. Flush through the volume of drug remaining in the IV tubing to ensure full dosing.³

These administration guidelines are recommendations only. They should be reconciled with appropriate institution policies and procedures, other manufacturers' guidelines, required regulations, and medical judgment.

Storage and stability

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.¹ Do not use ELAPRASE after the expiration date on the vial.¹

- ELAPRASE does not contain preservatives; therefore, after dilution with saline, the diluted solution should be used immediately.¹
- 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.¹

- Other than during infusion, do not store the diluted ELAPRASE solution at room temperature.¹
- Any unused product or waste material should be discarded and disposed of in accordance with applicable requirements.¹

Hypersensitivity reactions, including anaphylaxis

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Management of hypersensitivity reactions, including anaphylaxis

If anaphylactic or other acute reactions occur, immediately discontinue the infusion of ELAPRASE and initiate appropriate medical treatment.¹

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.¹

In postmarketing reports, patients receiving ELAPRASE experienced

anaphylactic reactions up to several years after initiating treatment. Some patients were reported to have repeated anaphylactic events over a two- to four-month time period. Anaphylactic reactions have been managed by discontinuing treatment, using a slower infusion rate, premedication, or treatment with antihistamines, inhaled beta-adrenergic agonists, corticosteroids, oxygen, and vasopressors.¹

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.¹

Safety



Important Safety Information¹

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.

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

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.

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.

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.

Important Safety Information¹

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 ($\geq 9\%$) 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 ($\geq 10\%$) 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 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 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%) of 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 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 1-800-828-2088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Please click [here](#) for full Prescribing Information, including Boxed Warning.



References

1. Shire. ELAPRASE Prescribing Information.
2. Martin R *et al.* Pediatrics 2008; 121(2): e377–386.
3. Lilley LL *et al.* Pharmacology and the Nursing Process (7th ed.) Missouri: Elsevier, 2014.



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Do not use this tool to calculate doses for body weights that are not shown, or to arrive at approximate values.

These are example body weights only. Precise dosing requires patient's exact weight.


Weight in kg

Recommended dose
(weight x 0.5 mg/kg)

Volume required
(dose/2 mg/mL)

Vials required
(vol/3 mL)

elaprase
(idursulfase)



Weight in kg	Recommended dose (weight x 0.5 mg/kg)	Volume required (dose/2 mg/mL)	Vials required (vol/3 mL)
10 kg	10 x 0.5 = 5 mg	5 / 2 = 2.5 mL	2.5 / 3 = 0.83
12 kg	12 x 0.5 = 6 mg	6 / 2 = 3 mL	3 / 3 = 1
14 kg	14 x 0.5 = 7 mg	7 / 2 = 3.5 mL	3.5 / 3 = 1.17
16 kg	16 x 0.5 = 8 mg	8 / 2 = 4 mL	4 / 3 = 1.33
18 kg	18 x 0.5 = 9 mg	9 / 2 = 4.5 mL	4.5 / 3 = 1.5
20 kg	20 x 0.5 = 10 mg	10 / 2 = 5 mL	5 / 3 = 1.67
22 kg	22 x 0.5 = 11 mg	11 / 2 = 5.5 mL	5.5 / 3 = 1.83
24 kg	24 x 0.5 = 12 mg	12 / 2 = 6 mL	6 / 3 = 2
26 kg	26 x 0.5 = 13 mg	13 / 2 = 6.5 mL	6.5 / 3 = 2.17
28 kg	28 x 0.5 = 14 mg	14 / 2 = 7 mL	7 / 3 = 2.33
30 kg	30 x 0.5 = 15 mg	15 / 2 = 7.5 mL	7.5 / 3 = 2.5
32 kg	32 x 0.5 = 16 mg	16 / 2 = 8 mL	8 / 3 = 2.67
34 kg	34 x 0.5 = 17 mg	17 / 2 = 8.5 mL	8.5 / 3 = 2.83
36 kg	36 x 0.5 = 18 mg	18 / 2 = 9 mL	9 / 3 = 3
38 kg	38 x 0.5 = 19 mg	19 / 2 = 9.5 mL	9.5 / 3 = 3.17

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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.

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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.

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

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For more information, contact Takeda at 1-800-828-2088, or by e-mail at medinfo.us@shire.com

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These are example body weights only. Precise dosing requires patient's exact weight.

Weight in kg

Recommended dose
(weight x 0.5 mg/kg)

Volume required
(dose/2 mg/mL)

Vials required
(vol/3 mL)

elaprase
(idursulfase)



Please see below for Important Safety Information including Boxed Warning. This is only a guide. Refer to Prescribing Information for full preparation instructions [here](#).

68 kg	$68 \times 0.5 = 34 \text{ mg}$	$34 / 2 = 17 \text{ mL}$	$17 / 3 = 5.67$	40 kg	$40 \times 0.5 = 20 \text{ mg}$	$20 / 2 = 10 \text{ mL}$	$10 / 3 = 3.33$
66 kg	$66 \times 0.5 = 33 \text{ mg}$	$33 / 2 = 16.5 \text{ mL}$	$16.5 / 3 = 5.5$	42 kg	$42 \times 0.5 = 21 \text{ mg}$	$21 / 2 = 10.5 \text{ mL}$	$10.5 / 3 = 3.5$
64 kg	$64 \times 0.5 = 32 \text{ mg}$	$32 / 2 = 16 \text{ mL}$	$16 / 3 = 5.33$	44 kg	$44 \times 0.5 = 22 \text{ mg}$	$22 / 2 = 11 \text{ mL}$	$11 / 3 = 3.67$
62 kg	$62 \times 0.5 = 31 \text{ mg}$	$31 / 2 = 15.5 \text{ mL}$	$15.5 / 3 = 5.17$	46 kg	$46 \times 0.5 = 23 \text{ mg}$	$23 / 2 = 11.5 \text{ mL}$	$11.5 / 3 = 3.83$
60 kg	$60 \times 0.5 = 30 \text{ mg}$	$30 / 2 = 15 \text{ mL}$	$15 / 3 = 5$	48 kg	$48 \times 0.5 = 24 \text{ mg}$	$24 / 2 = 12 \text{ mL}$	$12 / 3 = 4$
58 kg	$58 \times 0.5 = 29 \text{ mg}$	$29 / 2 = 14.5 \text{ mL}$	$14.5 / 3 = 4.83$	50 kg	$50 \times 0.5 = 25 \text{ mg}$	$25 / 2 = 12.5 \text{ mL}$	$12.5 / 3 = 4.17$
56 kg	$56 \times 0.5 = 28 \text{ mg}$	$28 / 2 = 14 \text{ mL}$	$14 / 3 = 4.67$	52 kg	$52 \times 0.5 = 26 \text{ mg}$	$26 / 2 = 13 \text{ mL}$	$13 / 3 = 4.33$
54 kg	$54 \times 0.5 = 27 \text{ mg}$	$27 / 2 = 13.5 \text{ mL}$	$13.5 / 3 = 4.5$	54 kg	$54 \times 0.5 = 27 \text{ mg}$	$27 / 2 = 13.5 \text{ mL}$	$13.5 / 3 = 4.5$

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.

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.

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-idurulfase 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.

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 ($\geq 9\%$) 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 ($\geq 10\%$) 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 5 years and older, 32 of 63 (51%) patients tested positive for anti-idurulfase 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 those who tested negative.

Thirteen of 32 (41%) Ab-positive patients also tested positive for antibodies that neutralize idurulfase uptake into cells (neutralizing antibodies, NAb) or enzymatic activity 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.

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, 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 1-800-828-2088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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elaprased[®]

(idursulfase)

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The recommended dosage regimen of ELAPRASE[®] is **0.5 mg per kg of body weight** administered once weekly as an intravenous infusion.

Please see below for Important Safety Information including Boxed Warning. This is only a guide. See Prescribing Information [here](#) for full preparation instructions.

These are example body weights only. Precise dosing requires patient's exact weight. Do not use this tool to calculate doses for body weights that are not shown, or to arrive at approximate values.



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Indications and Usage

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