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

ALDURAZYME (laronidase)
Solution for intravenous infusion only
Initial U.S. Approval: 2003

WARNING: RISK OF ANAPHYLAXIS.
See full prescribing information for complete boxed warning.
Life-threatening anaphylactic reactions have been observed in some patients during ALDURAZYME infusions. Therefore, appropriate medical support should be readily available when ALDURAZYME is administered. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.

----------RECENT MAJOR CHANGES----------
Dosage and Administration (2) (8/2009)

----------INDICATIONS AND USAGE----------
ALDURAZYME is indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with Scheie form have not been established. ALDURAZYME has been shown to improve pulmonary function and walking capacity. ALDURAZYME has not been evaluated for effects on the central nervous system manifestations of the disorder (1).

----------DOSAGE AND ADMINISTRATION----------
- 0.58 mg/kg of body weight administered once weekly as an intravenous (IV) infusion (2).

----------DOSAGE FORMS AND STRENGTHS----------
Solution for IV infusion: 2.9 mg/5 mL vial (3).

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
- Life-threatening anaphylactic reactions have been observed in some patients during or up to 3 hours after infusion. Patients with an acute illness at the time of infusion may be at greater risk for infusion-related reactions. Appropriate medical support should be available when ALDURAZYME is administered. If anaphylactic or other severe allergic reactions occur, immediately discontinue the infusion and initiate appropriate treatment, which may include ventilatory support, treatment with inhaled beta-adrenergic agonists, epinephrine, and IV corticosteroids (5.1).
- Pretreatment with antipyretics and/or antihistamines is recommended prior to the infusion to reduce the risk of infusion-related allergic reactions. If infusion-related reactions occur, decreasing the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines may ameliorate the symptoms (5.1).

----------ADVERSE REACTIONS----------
The most frequently occurring adverse reactions occurring in at least 10% of patients 6 years and older are rash, upper respiratory tract infection, injection site reaction, hyperreflexia, paresthesia, and vein disorder. The most commonly reported adverse reactions occurring in at least 10% of patients less than 6 years of age were pyrexia, chills, increased blood pressure, tachycardia, and decreased oxygen saturation (6).

To report SUSPECTED ADVERSE REACTIONS, contact: Genzyme at 1-800-745-4447, or FDA at 1-800-FDA-1088 or go to www.fda.gov/medwatch

----------USE IN SPECIFIC POPULATIONS----------
A registry for pregnant women is available. Pregnant women with MPS I should be encouraged to enroll in the MPS I Registry. For more information, visit www.MPSIregistry.com or call (800) 745-4447 (8.1).

See 17 for PATIENT COUNSELING INFORMATION.
Revised: May/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF ANAPHYLAXIS
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dose
2.2 Instructions for Use
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Anaphylaxis and Allergic Reactions
6 ADVERSE REACTIONS
6.1 Adverse Reactions in Clinical Studies
6.2 Immunogenicity
6.3 Postmarketing Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
14.1 Clinical Studies in Patients 6 Years and Older
14.2 Clinical Studies in Patients 6 Years and Younger
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the Full Prescribing Information are not listed

FULL PRESCRIBING INFORMATION

WARNING: RISK OF ANAPHYLAXIS.

Life-threatening anaphylactic reactions have been observed in some patients during ALDURAZYME® infusions. Therefore, appropriate medical support should be readily available when ALDURAZYME is administered. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.

1 INDICATIONS AND USAGE

ALDURAZYME is indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with the Scheie form have not been established.

ALDURAZYME has been shown to improve pulmonary function and walking capacity. ALDURAZYME has not been evaluated for effects on the central nervous system manifestations of the disorder.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose

The recommended dosage regimen of ALDURAZYME is 0.58 mg/kg of body weight administered once weekly as an intravenous (IV) infusion. Pretreatment with antipyretics and/or antihistamines is recommended 60 minutes prior to the start of the infusion [*see Warnings and Precautions (5)*].

2.2 Instructions for Use

Prepare and use ALDURAZYME according to the following steps.

1. Each vial of ALDURAZYME provides 2.9 milligrams (mg) of laronidase in 5.0 milliliters (mL) of solution and is intended for single use only. Do not use the vial more than one time. The concentrated solution for infusion must be diluted in 0.9% Sodium Chloride Injection, USP using aseptic techniques. Prepare ALDURAZYME using PVC containers and administer with a PVC infusion set equipped with an in-line, low protein binding 0.2 micrometer (µm) filter. There is no information on the compatibility of diluted ALDURAZYME with glass containers.
2. The total volume of the infusion is determined by the patient's body weight. Patients with a body weight of 20 kg or less should receive a total volume of 100 mL. Patients with a body weight greater than 20 kg should receive a total volume of 250 mL. Determine the number of vials to be diluted based on the individual patient's weight and the recommended dose of 0.58 mg/kg, using the following equation:

   Patient's weight (kg) x 1 mL/kg of ALDURAZYME = Total # mL of ALDURAZYME, then
   Total # of mL of ALDURAZYME ÷ 5 mL per Vial = Total # of Vials.
3. Round up to the nearest whole vial. Remove the required number of vials from the refrigerator to allow them to reach room temperature. Do not heat or microwave vials.
4. Before withdrawing the ALDURAZYME from the vial, visually inspect each vial for particulate matter and discoloration. The ALDURAZYME solution should be clear to slightly opalescent and colorless to pale yellow. A few translucent particles may be present. Do not use if the solution is discolored or if there is particulate matter in the solution.
5. Withdraw and discard a volume of the 0.9% Sodium Chloride Injection, USP from the infusion bag, equal to the volume of ALDURAZYME concentrate to be added.

6. Slowly withdraw the calculated volume of ALDURAZYME from the appropriate number of vials using caution to avoid excessive agitation. Do not use a filter needle, as this may cause agitation. Agitation may denature ALDURAZYME, rendering it biologically inactive.
7. Slowly add the ALDURAZYME solution to the 0.9% Sodium Chloride Injection, USP using care to avoid agitation of the solutions. Do not use a filter needle.
8. Gently rotate the infusion bag to ensure proper distribution of ALDURAZYME. Do not shake the solution.
9. The entire infusion volume (100 mL for patients weighing 20 kg or less and 250 mL for patients weighing greater than 20 kg) should be delivered over approximately 3 to 4 hours. The initial infusion rate of 10 µg/kg/hr may be incrementally increased every 15 minutes during the first hour, as tolerated, until a maximum infusion rate of 200 µg/kg/hr is reached. The maximum rate is then maintained for the remainder of the infusion (2-3 hours), as outlined in *Tables 1 and 2*.

Table 1: Incremental Rates for 100 mL ALDURAZYME® Infusion (For use with Patients Weighing 20 kg or Less)

Infusion Rate	Criteria for Increasing Infusion Rate
2 mL/hr x 15 minutes (10 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
4 mL/hr x 15 minutes (20 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
8 mL/hr x 15 minutes (50 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
16 mL/hr x 15 minutes (100 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
32 mL/hr x ~3 hours (200 µg/kg/hr)	For the remainder of the infusion.

Table 2: Incremental Rates for 250 mL ALDURAZYME® Infusion (For use with Patients Weighing Greater than 20 kg)

Infusion Rate	Criteria for Increasing Infusion Rate
5 mL/hr x 15 minutes (10 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
10 mL/hr x 15 minutes (20 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
20 mL/hr x 15 minutes (50 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
40 mL/hr x 15 minutes (100 µg/kg/hr)	Obtain vital signs, if stable then increase the rate to…
80 mL/hr x ~3 hours (200 µg/kg/hr)	For the remainder of the infusion.

ALDURAZYME must not be administered with other medicinal products in the same infusion. The compatibility of ALDURAZYME in solution with other products has not been evaluated.

3 DOSAGE FORMS AND STRENGTHS

ALDURAZYME is supplied as a sterile solution in single use clear Type I glass 5 mL vials (2.9 mg laronidase per 5 mL).

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis and Allergic Reactions [see *Boxed Warning*]

Life-threatening anaphylactic reactions have been observed in some patients during or up to 3 hours after ALDURAZYME infusions. Reactions have included respiratory failure, respiratory distress, stridor, tachypnea, bronchospasm, airway obstruction, hypoxia, hypotension, bradycardia, and urticaria. Interventions have included resuscitation, mechanical ventilatory support, emergency tracheotomy, hospitalization, and treatment with inhaled beta-adrenergic agonists, epinephrine, and IV corticosteroids.

In clinical studies and postmarketing safety experience with ALDURAZYME, approximately 1% of patients experienced severe or serious allergic reactions. In patients with MPS I, pre-existing upper airway obstruction may have contributed to the severity of some reactions. Due to the potential for severe allergic reactions, appropriate medical support should be readily available when ALDURAZYME is administered. Because of the potential for recurrent reactions, some patients who experience initial severe reactions may require prolonged observation.

Patients with an acute illness at the time of ALDURAZYME infusion may be at greater risk for infusion-related reactions. Careful consideration should be given to the patient's clinical status prior to administration of ALDURAZYME. One patient with acute bronchitis and hypoxia experienced increased tachypnea during the first ALDURAZYME infusion that resolved without intervention. The patient's respiratory symptoms returned within 30 minutes of completing the infusion and responded to bronchodilator therapy. Approximately 6 hours after the infusion, the patient experienced coughing, then respiratory arrest, and died.

Patients should receive antipyretics and/or antihistamines prior to infusion [*see Adverse Reactions (6); Dosage and Administration (2.1)*]. If an infusion-related reaction occurs, regardless of pre-treatment, decreasing the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines may ameliorate the symptoms [*see Adverse Reactions (6)*].

If anaphylactic or other severe allergic reactions occur, immediately discontinue the infusion of ALDURAZYME and initiate appropriate treatment. Caution should be exercised if epinephrine is being considered for use in patients with MPS I due to the increased prevalence of coronary artery disease in these patients.

The risks and benefits of re-administering ALDURAZYME following an anaphylactic or severe allergic reaction should be considered. Extreme care should be exercised, with appropriate resuscitation measures available, if the decision is made to re-administer the product.

6 ADVERSE REACTIONS

6.1 Adverse Reactions in Clinical Studies

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

The most serious adverse reactions reported with ALDURAZYME treatment during clinical studies were anaphylactic and allergic reactions [*see Boxed Warning and Warnings and Precautions (5)*]. Most adverse events reported in clinical studies were considered disease-related and unrelated to study drug. The most common adverse reactions were infusion-related reactions. The frequency of infusion-related reactions decreased over time with continued use of ALDURAZYME, and the majority of reactions were classified as being mild to moderate in severity. Most infusion-related reactions requiring intervention were ameliorated with slowing of the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines [*see Warnings and Precautions (5)*].

6.1.1 Clinical Studies in Patients 6 Years and Older

In a 26-week, double-blind, placebo-controlled clinical study (Study 1) of ALDURAZYME in 45 patients with MPS I, ages 6 to 43 years old, in which all patients were treated with antipyretics and antihistamines prior to the infusions, infusion-related reactions were reported in 32% (7 of 22) of ALDURAZYME treated patients. The most commonly reported infusion-related reactions were flushing, fever, headache, and rash. Flushing occurred in 5