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THIS IS A MODEL LETTER - PLEASE CUSTOMIZE FOR YOUR PATIENT

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[Date]

[Contact Name] [Insurance Company] [Street Address]
[City], [State] [Zip]

Patient Name: [Patient Name]
Subscriber ID#: [ID Number]
Group#: [Group Number]

Subject: Intent to Treat with Aldurazyme® (laronidase) Solution for intravenous infusion only

Dear [Contact Name]:

I am writing on behalf of my patient, {Patient Name} who has been diagnosed with Mucopolysaccharidosis I disease (MPS I) whom I plan to treat with Aldurazyme, an enzyme replacement therapy. 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.

Important Safety 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.

Anaphylaxis and severe allergic reactions have been observed in patients during or up to 3 hours after ALDURAZYME infusions. Some of these reactions were life-threatening and included respiratory failure, respiratory distress, stridor, tachypnea, bronchospasm, obstructive airways disorder, hypoxia, hypotension, bradycardia, and urticaria. 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. 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 post marketing 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. 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.

Patients with an acute febrile or respiratory illness at the time of ALDURAZYME infusion may be at greater risk for infusion reactions. Careful consideration should be given to the patient's clinical status prior to administration of ALDURAZYME and consider delaying ALDURAZYME infusion.

Sleep apnea is common in MPS I patients. Evaluation of airway patency should be considered prior to Initiation of treatment with ALDURAZYME. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an infusion reaction or extreme drowsiness/sleep induced by antihistamine use.

Caution should be exercised when administering ALDURAZYME to patients susceptible to fluid overload or patients with an 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 ALDURAZYME infusion, and some patients may require prolonged observation times that should be based on the individual needs of the patient, Because of the potential for infusion reactions, patients should receive antipyretics and/or antihistamines prior to infusion. If an infusion-related reaction occurs, regardless of pre-treatment, decreasing the infusion rate, temporarily stopping the infusion, or administering additional antipyretics and/or antihistamines may ameliorate the symptoms.

The most serious adverse reactions reported with ALDURAZYME treatment during clinical trials were anaphylactic and allergic reactions.

In a 26-week, placebo-controlled clinical trial in patients 6 years and older, the most commonly reported infusion reactions regardless of treatment group were flushing, pyrexia, headache, and rash. Flushing occurred in 5 patients (23%) receiving ALDURAZYME; the other reactions were less frequent. Less common infusion reactions included angioedema (including face edema), hypotension, paresthesia, feeling hot, hyperhidrosis, tachycardia, vomiting, back pain, and cough. Other reported adverse reactions included bronchospasm, dyspnea, urticaria, and pruritus. In the open-label, uncontrolled extension phase of this clinical trial, the infusion reactions were similar, but also included abdominal pain or discomfort and injection site reaction. Less commonly reported infusion reactions included nausea, diarrhea, feeling hot or cold, vomiting, pruritus, arthralgia and urticaria. Additional common adverse reactions included, back pain and musculoskeletal pain. In an open-label, uncontrolled clinical trial in patients 6 years and younger who received ALDURAZYME treatment for up to 52 weeks, the most commonly reported serious adverse events (regardless of relationship) in patients 6 years and younger, were otitis media (20%), and central venous catherization required for ALDURAZYME infusion (15%). The most commonly reported adverse reactions in patients 6 years and younger were infusion reactions reported in 35% (7 of 20) of patients and included pyrexia (30%), chills (20%), blood pressure increased (10%), tachycardia (10%), and oxygen saturation decreased (10%). Other commonly reported infusion reactions occurring in ≥5% of patients were pallor, tremor, respiratory distress, wheezing, crepitations (pulmonary), pruritus, and rash.

In post marketing experience with ALDURAZYME, severe and serious infusion reactions have been reported, some of which were life-threatening, including anaphylactic shock. Adverse reactions resulting in death reported in the post marketing setting with ALDURAZYME treatment included cardio-respiratory arrest, respiratory failure, cardiac failure, and pneumonia. These events have been reported in MPS I patients with significant underlying disease. Additional common adverse reactions included erythema and cyanosis. There have been a small number of reports of extravasation in patients treated with ALDURAZYME. There have been no reports of tissue necrosis associated with extravasation. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

In clinical trials, 99 of 102 patients (97%) treated with ALDURAZYME were positive for IgG antibodies to ALDURAZYME. In the 2 trials of patients 6 years and older, 9 patients who experienced severe infusion reactions were tested for ALDURAZYME-specific IgE antibodies and complement activation. One of the nine patients had an anaphylactic reaction consisting of urticaria and airway obstruction and tested positive for both ALDURAZYME-specific IgE binding antibodies and complement activation. In the post marketing setting, approximately 1% of patients experienced severe or serious infusion- allergic reactions and tested positive for IgE. Of these IgE-positive patients, some have discontinued treatment, but some have been successfully re-challenged. The clinical significance of antibodies to ALDURAZYME, including the potential for product neutralization, is not known.

Adverse events should be reported promptly to Genzyme Medical Information at 800-745-4447, option 2 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Please see enclosed full Prescribing Information including Boxed Warning

Documentation Enclosed
The attached *Statement of Medical Necessity* contains information pertaining to **[**Patient Name**]**'s clinical history, diagnosis and signs and symptoms - demonstrating that the use of Aldurazyme is medically indicated for treatment of **[**his/her**]** MPS I disease. Initially, my prescribed dosing regimen will be
[ ] mg per kilogram administered **[ ]** per week.

Action Requested
Please send verification of **[**Patient Name**]**'s insurance coverage for enzyme replacement therapy with Aldurazyme as soon as possible. If you have any questions pertaining to **[**Patient Name**]**'s clinical history and/or my treatment plan, please call me at **[**Phone Number**]**.

Thank you for your immediate attention to this request. Sincerely,

[Physician Name**]**

Enclosure: Statement of Medical Necessity
Cc: **[**Patient Name/Legal Guardian**]**