



What is MPS I?

MPS I (Mucopolysaccharidosis I, also known as Hurler, Hurler-Scheie, and Scheie Syndromes) is a progressive lysosomal storage disorder that is debilitating and commonly fatal.

MPS I is caused by a deficiency of an enzyme called alpha-L-iduronidase. This enzyme is required for the breakdown of certain substances in the body commonly referred to as 'GAG' (glycosaminoglycans). As more and more GAG builds up in a person's body, almost all organs may be irreversibly damaged. Clinical manifestations of the disease may include respiratory and cardiovascular complications, gastrointestinal symptoms, joint stiffness and restricted movement, loss of vision and hearing, and in the most severe form of the disease, delayed or regressed mental development. The incidence of MPS I is estimated at about 1 in 100,000 live births.

Early Diagnosis Vital in Aiding Long Term Outcome

Individuals diagnosed with MPS I have historically been classified into one of three categories (with much overlap), depending upon the severity of their symptoms and rate of disease progression: Hurler Syndrome, the most severe form, Hurler-Scheie Syndrome, the intermediate form, and Scheie Syndrome, the least severe form. While individuals with the Hurler form of MPS I are usually diagnosed by one to five years of age, those with a less severe form of the disorder may be under diagnosed as other more prevalent diseases are considered and ruled out. Since MPS I is a progressive disorder, people living with the disease typically get worse over time and experience severe disabilities and possibly early death—factors underscoring the importance of early diagnosis.



Aldurazyme[®] the First and Only Treatment for MPS I

Historically, treatment for MPS I has been limited primarily to palliative care and in select circumstances, bone marrow transplantation (BMT). BMT may be a potential treatment option for the severest forms of the disease, but its broad application may be limited by the risks associated with the procedure and difficulty finding appropriate donors. Aldurazyme (Laronidase), an enzyme replacement therapy (ERT), is the first drug treatment for MPS I and targets the underlying cause of the disorder by replacing the missing enzyme patients are naturally lacking. Aldurazyme was developed as part of a joint venture

between BioMarin Pharmaceutical and Genzyme Corporation and is approved in the United States, European Union and additional countries around the world for the treatment of MPS I.

Please see reverse for full indication and important safety information.

Resources

www.aldurazyme.com

www.bmrn.com

www.genzyme.com

Aldurazyme[®] is a registered trademark of BioMarin/Genzyme LLC. Aldurazyme has received orphan drug status in both the United States and European Union.

Indication and Fair Balance Statements for Physicians

ALDURAZYME® (laronidase) 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.

Life-threatening anaphylactic reactions have been observed in some patients during or up to three 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 intravenous corticosteroids.

In clinical trials 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 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.

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.

Patients should receive antipyretics and/or antihistamines prior to infusion. If an infusion reaction occurs, regardless of pre-treatment, decreasing the infusion rate, temporarily stopping the infusion, and/or administration of additional antipyretics and/or antihistamines may ameliorate the symptoms.

The most common adverse reactions associated with ALDURAZYME treatment in the clinical studies were upper respiratory tract infection, rash, and injection site reaction. The most common adverse reactions requiring intervention were infusion-related reactions involving flushing, fever, headache, and rash.

In postmarketing experience with ALDURAZYME, severe and serious infusion-related reactions have been reported, some of which were life-threatening. The most frequently reported adverse reactions included chills, vomiting, nausea, arthralgia, diarrhea, tachycardia, abdominal pain, blood pressure increased, and oxygen saturation decreased.

Approximately 91% of patients treated with ALDURAZYME in clinical studies were positive for antibodies to laronidase. The clinical significance of antibodies to ALDURAZYME is not known, including the potential for product neutralization. Adverse events should be reported promptly to Genzyme Medical Information at 800-745-4447, option 2. ALDURAZYME is available by prescription only.

To learn more, please see the full prescribing information (PDF) including boxed warning, visit www.ALDURAZYME.com or contact Genzyme at 1-800-745-4447.