

POLICY: Enzyme Replacement Therapy – Aldurazyme® (Iaronidase solution for intravenous infusion – Genzyme Corporation)

DATE REVIEWED: 04/15/2020

OVERVIEW

Aldurazyme is human α -L-iduronidase produced in Chinese hamster ovary cells via recombinant DNA technology.¹ Alpha-L-iduronidase catalyzes the hydrolysis of terminal α -L-iduronic acid from dermatan sulfate and heparin sulfate.

Aldurazyme is indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis type I and in patients with the Scheie form who have moderate to severe symptoms.¹ The risks and benefits of treating mildly affected patients with the Scheie form have not been established.

Disease Overview

Mucopolysaccharidosis type I (MPS I) is a rare autosomal recessive, lysosomal storage disease characterized by the deficiency of α -L-iduronidase.² Patients with MPS I are unable to degrade dermatan and heparin sulfate, resulting in the accumulation of glycosaminoglycans within lysosomes. Over time, the accumulation of glycosaminoglycans leads to progressive tissue damage,³ ultimately resulting in multiorgan dysfunction.^{2,3} Patients with MPS I commonly have a characteristic face, corneal clouding, cardiomyopathy, enlarged tongue, respiratory insufficiency, hepatosplenomegaly, hernias, dysostosis multiplex, joint stiffness, and cognitive impairment.^{4,5} MPS I is commonly classified as three separate entities, Hurler syndrome (severe form), Hurler-Scheie syndrome (intermediate form) and Scheie syndrome (mild form).^{2,4} However, this classification system is based on disease severity and age of onset, not on any biochemical differences between the three syndromes.⁵ All three forms of the disease are the result of the same enzymatic deficiency and represent varying degrees of severity along the disease continuum. The definitive diagnosis of MPS I is based on demonstrating deficient α -L-iduronidase activity in fibroblasts, leukocytes, plasma, or serum.^{2,3,5}

Specific treatments for MPS I include hematopoietic stem cell transplantation (HSCT) and enzyme replacement therapy.^{2,4,5} HSCT is indicated for the severe forms of MPS I, in children < 2 years of age who are cognitively intact.^{2,4} HSCT has been shown to preserve intellectual development, reverse some aspects of somatic disease and increase survival.^{2,4,5} Enzyme replacement therapy (Aldurazyme) does not cross the blood-brain barrier and is unlikely to improve cognitive or neurologic function.² Therefore, Aldurazyme is appropriate in children < 2 years of age who have already experienced cognitive decline, or who are cognitively intact with severe physical disease prior to HSCT to improve their health. Aldurazyme is also recommended in older patients with or without cognitive or neurologic decline.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Aldurazyme. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Aldurazyme as well as the monitoring required for adverse events and long-term efficacy, approval requires Aldurazyme to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Aldurazyme is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Mucopolysaccharidosis Type I (Hurler Syndrome, Hurler-Scheie Syndrome, and Scheie Syndrome). Approve for 1 year if the patient meets the following criteria (A and B):

- A) The diagnosis is established by one of the following (i or ii):
- i. Patient has a laboratory test demonstrating deficient α -L-iduronidase activity in leukocytes, fibroblasts, plasma, or serum; OR
 - ii. Patient has a molecular genetic test demonstrating α -L-iduronidase gene mutation; AND
- B) Aldurazyme is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

Dosing. Each dose must not exceed 0.58 mg/kg administered intravenously no more frequently than once weekly.¹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Aldurazyme has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Aldurazyme® solution for intravenous infusion [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc.; December 2019.
2. Muenzer J, Wraith JE, Clarke LA, et al. Mucopolysaccharidosis I: Management and treatment guidelines. *Pediatrics*. 2009;123:19-29.
3. Clarke LA, Atherton AM, Burton BK, et al. Mucopolysaccharidosis type I newborn screening: Best practices for diagnosis and management. *J Pediatr*. 2017;182:363-370.
4. Giugliani R, Federhen A, Munoz Rojas MV, et al. Mucopolysaccharidosis I, II, and VI: Brief review and guidelines for treatment. *Genet Mol Biol*. 2010;33:589-604.
5. Martins AM, Dualibi AP, Norato D, et al. Guidelines for the management of mucopolysaccharidosis type I. *J Pediatr*. 2009;155(Suppl 2):S32-S46.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	--	04/17/2019
Annual Revision	No criteria changes.	04/15/2020