



# CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date ..... 1/15/2011  
Next Review Date ..... 1/15/2012  
Coverage Policy Number ..... 1006

Subject **Laronidase (Aldurazyme®)**

## Table of Contents

Coverage Policy .....	1
General Background .....	2
Coding/Billing Information .....	3
References .....	3

## Hyperlink to Related Coverage Policies

Stem-Cell Transplant for Inherited  
Metabolic Disorders

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

CIGNA covers laronidase (Aldurazyme®) as medically necessary for individuals with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for individuals with the Scheie form who have moderate to severe symptoms.

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to laronidase (Aldurazyme®) therapy.

## FDA Approved Indications

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.

## **FDA Recommended Dosing**

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.

## **Black Box 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.**

## **Drug Availability**

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

## **General Background**

### **Disease Overview**

MPS I is an autosomal recessive lysosomal storage disease caused by a deficiency of L-iduronidase ( $\alpha$ -L-iduronidase). Reduced or absent L-iduronidase activity blocks the degradation of the glycosaminoglycan substrates dermatan sulfate and heparan sulfate and leads to accumulation of these substrates throughout the body, resulting in clinical manifestations that may include inhibited growth, developmental delay, impaired vision (e.g. corneal clouding), hearing loss, impaired cardiac and pulmonary function, hepatosplenomegaly, skeletal deformities, and mental dysfunction. Many patients afflicted with Hurler's or Hurler-Scheie syndrome die within the first or the second or third decade of life, respectively, while those diagnosed with Scheie's syndrome may survive well into adulthood. Previously, management of MPS I consisted principally of supportive care and treatment of complications. In severely affected patients, bone marrow or hematopoietic cell transplantation is sometimes performed.

### **Pharmacology**

Mucopolysaccharide storage disorders are caused by the deficiency of specific lysosomal enzymes required for the catabolism of glycosaminoglycans (GAG). MPS I is characterized by the deficiency of  $\alpha$ -L-iduronidase, a lysosomal hydrolase which catalyzes the hydrolysis of terminal  $\alpha$ -L-iduronic acid residues of dermatan sulfate and heparan sulfate. Reduced or absent  $\alpha$ -L-iduronidase activity results in the accumulation of the GAG substrates, dermatan sulfate and heparan sulfate, throughout the body and leads to widespread cellular, tissue, and organ dysfunction.

The rationale of Aldurazyme therapy in MPS I is to provide exogenous enzyme for uptake into lysosomes and increase the catabolism of GAG. Aldurazyme uptake by cells into lysosomes is most likely mediated by the mannose-6-phosphate-terminated oligosaccharide chains of laronidase binding to specific mannose-6-phosphate receptors. Because many proteins in the blood are restricted from entry into the central nervous system (CNS) by the blood brain barrier, effects of intravenously administered Aldurazyme on cells within the CNS cannot be inferred from activity in sites outside the CNS. The ability of Aldurazyme to cross the blood brain barrier has not been evaluated in animal models or in clinical studies.

### **Clinical Efficacy**

Safety and efficacy of laronidase were evaluated in a placebo-controlled clinical trial in 45 patients with MPS I who had a baseline forced vital capacity (FVC) of 77% or less of the predicted normal value. Improvement in pulmonary function, as measured by percent of predicted normal FVC, was observed in patients receiving laronidase compared with those receiving placebo. After 26 weeks, the median change from baseline in percent of predicted FVC was 1 or -1% in patients receiving laronidase or placebo, respectively; the median difference in percent of predicted FVC between the laronidase and placebo groups was 2% (95% confidence interval of 0.4-7). Walking capacity, as measured by distance walked in 6 minutes, increased over baseline in patients receiving laronidase and decreased in those receiving placebo; however, the difference in median walking distance between the laronidase and placebo groups was not statistically significant. In addition, decreases in urinary glycosaminoglycan concentrations and liver size were observed in patients receiving laronidase

compared with placebo; however, urinary glycosaminoglycan concentrations were not restored to normal values during the trial.

In an open-label extension of the trial in which all patients received laronidase therapy for 36 weeks following the double-blind period, improvements in FVC and walking capacity were observed in patients who received the drug after having received placebo during the double-blind period; maintenance of mean FVC and additional increases in mean walking distance were observed in patients who continued receiving laronidase after the double-blind period.

### 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..

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## Coding/Billing Information

**Note: Note:** This list of codes may not be all-inclusive.

**Covered when medically necessary:**

HCPSC Codes	Description
J1931	Injection, laronidase, 0.1 mg

ICD-9-CM Diagnosis Codes	Description
277.5	Mucopolysaccharidosis

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## References

1. BioMarin Pharmaceutical Inc. Aldurazyme<sup>®</sup> (laronidase) prescribing information. Novato, CA: BioMarin Pharmaceutical Inc. May 2010.
2. McEvoy GK, ed. AHFS 2010 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2010.

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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA's subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.