



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.

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Coverage Policy Number 6015

Subject **Agalsidase Beta (Fabrazyme™)**

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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 ©2009 CIGNA

Coverage Policy

CIGNA covers agalsidase beta (Fabrazyme™) as medically necessary for the treatment of Fabry disease.

FDA Approved Indications

Fabrazyme is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

FDA Recommended Dosing

The recommended dose of Fabrazyme is 1 mg/kg body weight given every two weeks as an IV infusion. Patients should receive antipyretics prior to infusion.

Drug Availability

Fabrazyme is supplied as a sterile, nonpyrogenic, white to off-white lyophilized cake or powder. Fabrazyme 35 mg vials are supplied in single-use, clear Type I glass 20 mL (cc) vials. Fabrazyme 5 mg vials are supplied in single-use, clear Type I glass 5 mL (cc) vials.

General Background

Disease Overview

Fabry disease is an X-linked genetic disorder of glycosphingolipid metabolism. It is caused by a deficient lysosomal activity of α -galactosidase A (also known as ceramide trihexosidase). Deficiency of α -galactosidase A results in a progressive accumulation of glycosphingolipids, primarily GL-3 (globotriacylceramide-3) in body tissues such as: the vascular endothelial lysosomes of the kidneys, skin, heart and brain. Over time, the accumulation of GL-3 in the microvasculature of the kidneys, heart and brain may lead to renal impairment, cardiac disease, stroke, and premature death.

Clinical diagnosis of Fabry disease is based upon some (or all) of the following: family history, history of childhood fevers in association with pain in the extremities, the characteristic skin lesions (angiokeratomas), the characteristic "whorled" corneal opacity, and the presence of lipid-laden cells in urinary sediment or biopsied tissues. In males, diagnosis is confirmed biochemically by demonstration of very low or undetectable α -galactosyl hydrolase (α -GAL) activities in plasma, serum, leukocytes, tears, or biopsied tissue, using an assay with a synthetic substrate of α -GAL and with N-acetylgalactosamine in the reaction mixture to inhibit α -N-acetylgalactosaminidase (alpha-galactosidase B) activity.

It is important to recognize that although most patients with classical Fabry disease are male, females can also have classical Fabry disease. The majority of female heterozygotes (with or without manifestations) have below normal levels of α -GAL activity and the characteristic "whorled" corneal opacity. However, absence of these clinical indicators does not preclude Fabry carrier status, since some female heterozygotes have tissue-specific normal α -GAL activity. In Fabry kindreds with a known mutation, mutation analysis can identify female heterozygotes. In families for whom a specific mutation is not documented, linkage analysis can be performed to establish carrier status. Atypical variants can be identified by low α -GAL activity. These patients may be diagnosed after the onset of cardiac or renal manifestations. Hemizygotes can be identified parentally by assaying for an XY karyotype and deficient α -GAL activity in chorionic villi (obtained in the ninth to tenth week of pregnancy) or in cultured amniotic cells obtained through amniocentesis (at 15 weeks of pregnancy). Heterozygotes can be identified parentally if the family mutation is known.

Pharmacology

Agalsidase beta reduces globotriacylceramide (GL-3) deposition in the capillary endothelium of the kidney, heart and skin. It is a recombinant form of the defective enzyme, α -galactosidase, and is intended to provide an exogenous source of α -galactosidase in Fabry disease patients.

Clinical Efficacy

Agalsidase plasma profiles were studied at 0.3, 1 and 3mg/kg in 15 patients with Fabry disease. The area under the plasma concentration-time curve and clearance did not increase in proportion with increasing doses, showing that the enzyme follows nonlinear pharmacokinetics. The half-life was dose independent ranging from 45–102 minutes.

FDA approval of Fabrazyme was based on a randomized, double-blind, placebo-controlled, multinational multicenter study of 58 Fabry patients who were naïve to enzyme replacement therapy. The primary efficacy endpoint of GL-3 inclusion in renal interstitial capillary endothelial cells was assessed by light microscopy and was graded on an inclusion severity score ranging from 0 (normal or near normal) to 3 (severe inclusions). Of the 58 patients, 20 of 29 (69%) treated with agalsidase beta had a GL-3 score of 0 (zero), compared to 0 of 29 in the placebo group. Also, reductions of GL-3 inclusions to normal or near normal levels were also noted in the capillary endothelium of the kidney, heart and skin. The reduction of GL-3 inclusions in the heart occurred in 21 of 29 with drug and one of 29 patients on placebo and in skin, 29 of 29 with drug, and one of 29 patients on placebo in the five months of the controlled study. In the open-label extension study (six months), all 58 patients participated. At the end of the six months in the open-label study, all the patients achieved a GL-3 inclusion score of 0 in the capillary endothelium.

Adverse Reactions

Life-threatening anaphylactic and severe allergic reactions have been observed in patients during Fabrazyme infusions. Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion. Interventions have included cardiopulmonary resuscitation, oxygen

supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, epinephrine, and IV corticosteroids. In clinical trials and postmarketing safety experience with Fabrazyme, approximately 1% of patients developed anaphylactic or severe allergic reactions during Fabrazyme infusion. If anaphylactic or severe allergic reactions occur, immediately discontinue the administration of Fabrazyme and initiate necessary emergency treatment. Because of the potential for severe allergic reactions, appropriate medical support measures should be readily available when Fabrazyme is administered. The risks and benefits of re-administering Fabrazyme following an anaphylactic or severe allergic reaction should be considered. Extreme care should be exercised, with appropriate medical support measures readily available, if the decision is made to re-administer the product.

Other common adverse effects associated with agalsidase beta are infusion reactions. Tachycardia, hypertension, chest pain/tightness, dyspnea, fever, chills/rigors, abdominal pain, puritus, urticaria, nausea and vomiting are some of the side effects associated with the infusion. Other reported adverse events include stroke, pain, ataxia, bradycardia, cardiac arrhythmia, cardiac arrest and nephrotic syndrome.

Coding/Billing Information

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

Covered when medically necessary:

HCPCS Codes	Description
J0180	Injection, agalsidase, 1 mg

ICD-9-CM Diagnosis Codes	Description
272.7	Lipidoses

References

1. Fabrazyme. Diagnosis – classical Fabry disease. Accessed September 25, 2009. Available at http://www.fabrazyme.com/hcp/disease/fz_us_hc_ds_diagnose.asp
2. Fabrazyme. St. Louis (MO): Facts and Comparisons, 2007. Available from: <http://online.factsandcomparisons.com/>
3. Genzyme Corporation. Fabrazyme® package insert. Cambridge, MA: Genzyme Corporation, January 2009.
4. McEvoy GK, ed. AHFS 2009 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2009.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	10/15/2008	6015	Aglasidase Beta (Fabrazyme™)

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