MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Pharmacy Medical Policy

Alglucerase (Ceredase® and Cerezyme®) for Gaucher Disease

Table of Contents

Policy Number: 317

BCBSA Reference Number: None

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Note: All requests for indications listed and not listed on the medical policy guidelines may be submitted to BCBSMA Pharmacy Operations by completing the Prior Authorization Form on the last page of this document. Physicians may also submit requests for exceptions via the web using Express PAth which can be found on the BCBSMA provider portal or directly on the web at https://provider.express-path.com.

This medication is not covered by the pharmacy benefit. It is covered by the Medical Benefit or as a Home Infusion Therapy.

Gaucher is an extremely complex disease that requires individualization of treatment for each patient. While the following guidelines apply to a large number of patients with Gaucher, because patients respond variably, individual tailoring may be required to optimize dosing.

We cover alglucerase therapy for Type 1 Gaucher disease:[1]

INITIAL DOSING FOR CHILDREN (<18 YEARS)

Children at highest risk: children with any of the following may likely require an initial dose of 60 U/kg every 2 weeks:

- Symptomatic disease, including abdominal or bone pain, fatigue, exertional limitation, weakness, or cachexia
- Growth failure[4]
- Any evidence of skeletal involvement, including radiographic evidence of Erlenmeyer flask deformity, necrosis, or destructive lesions
- Thrombocytopenia: platelets ≤ 60,000/mm3 , or documented abnormal bleeding episode
- Anemia: hemoglobin <2.5 g/dL below the lower limit of normal for age and sex

1-3 days	14.5-22.5 g/dl

2 months	9.0-14.0 g/dl
6-12 years	1.5-15.5. g/dl
12-18 years, male	13.0-16.0 g/dl
12-18 years, female	12.0-16.0 g/dl

- Impairment of quality of life due to Gaucher disease.[5]

Other children who may benefit from therapy: patients without any of the above may likely require an initial dose of 30-60 U/kg every 2 weeks.

INITIAL DOSING FOR ADULTS

Adults at highest risk: patients with any of the following may likely require an initial dose of 60 U/kg every 2 weeks:

- Symptomatic skeletal disease
  - Moderate to severe osteopenia
  - Chronic bone pain
  - Bone crises
  - Avascular necrosis
  - Pathologic fractures
  - Joint replacement
- Cardiopulmonary Gaucher disease, including pulmonary hypertension
- Thrombocytopenia: platelets ≤ 60,000/mm3 or documented abnormal bleeding episodes
- Anemia: hemoglobin ≤ 8.0 g/dL, or documented symptoms due to anemia, or transfusion dependency
- Significant liver disease
  - Severe hepatomegaly (volume >2.5x normal by MR or CT)
  - Hepatic infarcts
  - Esophageal varices
  - Portal hypertension
  - Hepatitis due to Gaucher
- Significant splenic disease
  - Severe splenomegaly (volume >15x normal by MR or CT)
  - Splenic pain and discomfort
  - Splenic infarcts
- Significant renal disease due to Gaucher
- Any concomitant medical condition which may be exacerbated by Gaucher disease.[6]

Other adults who may benefit from therapy: the following patients for whom it may be acceptable to begin an initial dose of 30 U/kg or less every 2 weeks:

Adults who have at least a minimal level of disease severity:
Any one of the following:

- Skeletal disease beyond mild osteopenia and Erlenmeyer flask deformity
- Hemoglobin ≤ 11.5 g/dL (women) or ≤ 12.5 g/dL (men) or ≤ 1.0g/dL or more below the lower limit of normal for age and sex
- Platelets ≤ 120,000/mm3
- Liver volume ≥ 1.25 times normal by MR (or CT)
- Spleen volume ≥ 5 times normal by MR (or CT)
- Any of the following symptoms due to Gaucher disease, which impair quality of life.[5]
  - Hepatic, cardiac, pulmonary, and renal function not impaired by Gaucher disease
  - No evidence symptomatic skeletal disease (see above)
  - Minimal or no quality of life impairment from Gaucher
  - No detectable progression of Gaucher disease

- o Hemoglobin > 10.5 g/dL (women) or > 11.5 g/dL (men) or not more than > 2.0g/dL or more below the lower limit of normal for age and sex
- o Platelets > 60,000/mm3 on 3 determinations
- o Liver volume < 2.5 times normal by MR (or CT)
- o Spleen volume <1.5 times normal by MR (or CT).

REEVALUATION OF DOSING
While individual patient follow-up varies according to disease severity, and depends on whether or not dose is changing, for the purposes of dose approval from BCBSMA annual follow-up is required. At yearly intervals, clinical data is submitted regarding progress on all previously abnormal findings. Depending on the degree of improvement, dosage may be increased, maintained or reduced. Severe bone disease or pulmonary hypertension are two manifestations that are particularly concerning, because damage from uncontrolled disease may not be reversible with these two manifestations.

We do not cover:

- Alglucerase therapy for patients who have Gaucher disease but do not have at least a minimal level of disease severity (see above), because treatment has not been proven to improve health outcome for patients without signs or symptoms of disease.[3]
- Alglucerase therapy for patients who have Type 2 or Type 3 Gaucher disease, because alglucerase therapy has not been proven to improve the nerve problems associated with these types of Gaucher disease.[3]

CPT Codes / HCPCS Codes / ICD-9 Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member. A draft of future ICD-10 Coding related to this document, as it might look today, is included below for your reference.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

There is no specific CPT code for this service.

HCPCS Codes

HCPCS codes:	Code Description
J0205	Injection, alglucerase, per 10 units
J1786	Injection, imiglucerase, 10 units

Diagnosis coding

ICD-9-CM diagnosis codes:	Code Description
272.7	Lipidoses

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
E75.22	Gaucher disease

Other Information
Preferred Home Infusion Therapy Network
Referring providers are encouraged to use these preferred Home Infusion providers to obtain these medications.

Preferred Home Infusion Therapy Provider Contact Information:
Accredo Health Group Phone: 1-877-988-0058 Website: www.accredo.com
Caremark, LLC. Phone: 1-866-846-3096 Website: www.caremark.com

Individual Consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be considered in light of current scientific literature. Physicians may send relevant clinical information for individual patients for consideration to:

Blue Cross Blue Shield of Massachusetts
Clinical Pharmacy Department
One Enterprise Drive
Quincy, MA 02171
Tel: 1-800-366-7778
Fax: 1-800-583-6289

Managed Care Authorization Instructions

- Prior authorization is required for all out patient sites of service
- For all outpatient sites of service, physicians may fax or mail the attached form to the address above
- For all outpatient sites of service, physicians may also submit authorization requests via the web using Express PAth which can be found on the BCBSMA provider portal or directly on the web at https://provider.express-path.com

PPO and Indemnity Authorization Instructions

- Prior authorization **is** required when this medication is processed under the home infusion therapy benefit.
- Prior authorization **is not** required when this medication is purchased by the physician and administered in the office in accordance with this medical policy.
- Physicians may also fax or mail the attached form to the address above.
- Physicians may also submit authorization requests via the web using Express PAth which can be found on the BCBSMA provider portal or directly on the web at https://provider.express-path.com

Policy History

Date	Action
7/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
1/2014	Updated ExpressPAth Language.
11/2011- 4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.

9/2009	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
10/2009	Updated to reflect UM requirements.
10/2008	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/2007	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/1991	New policy, effective 9/1991, describing covered and non-covered indications.

References

1. Gaucher Disease. Current Issues in Diagnosis and Treatment. *JAMA* 1996; 275:7 548-553.
2. van Weely S, van Leeuwen MB, Jansen IDC, et al. Clinical phenotype in relation to properties of mutant glucocerebrosidase in cultured fibroblasts. *Biochem Biophys Acta* 1991; 1096: 301-11.
3. Barton NW, Brady RO, Dambrosia JM, et al. Replacement Therapy for inherited enzyme deficiency: Macrophage-targeted glucocerebrosidase for Gaucher's disease. *NEJM* 1991; 324:1464-1470.
4. Fallet SH, Grace ME, Sibille A, et al. Enzyme Augmentation in Moderate to Life-Threatening Gaucher Disease. *Pediatric Research* 1992;31:5: 496-502.
5. Pastores GM, Sibille AR, Grawbowski GA. Enzyme Therapy in Gaucher Disease Type 1: Dosage Efficacy and Adverse Effects in 33 Patents Treated for 6-24 Months. Blood 82:2:408-416, 1993.
6. Verderese CL, Graham OC, Holder-McShane CA, et al. Gaucher's Disease: A Pilot Study of the Symptomatic Responses to Enzyme Replacement Therapy. *Journal of Neuroscience Nursing* 1993; 25:5: 296-301.
7. Zimran, A, Elstein D, Kannai R, et al. Low-dose Enzyme Replacement Therapy for Gaucher's Disease: Effects of Age, Sex, Genotype and Clinical Features on Response to Treatment. *The American Journal of Medicine* 1994; 97: 3-13.
8. Beutler E, Kay A, Saven A, et al. Enzyme Replacement Therapy for Gaucher Disease. Blood 1991;78:5 1183-1189.
9. Hollack CEM, Aerts JMFG, Goudsmit R, et al. Individualized low-dose alglucerase therapy for type 1 Gaucher's disease. *The Lancet* 1995; 345: 1474-1478.
10. ICGG Registry Update, August 1995. Dosage Regiments of Alglucerase in Gaucher Disease: A Comparison of the Rate and Extent of Clinical Response.
11. Barton NW, Brady RO, Dambrosia JM, et al. Dose-dependent responses to macrophage-targeted glucocerebrosidase in a child with Gaucher Disease. *The Journal of Pediatrics* 1992; 120:2: 227-280.
12. Cremin BJ, Davey H, Goldblatt J. Skeletal complications of type 1 Gaucher disease: The Magnetic resonance features. *Clinical Radiology* 41: 244-247, 1990
13. Rosenthal DJ, Doppelt SH, Mankin HJ, et al. Enzyme Replacement Therapy for Gaucher Disease: Skeletal Responses to Macrophage-targeted Glucocerebrosidase. *Pediatrics* 1995; 96:4: 629-636.
14. Zaizov R, Frisch A, Cohen I. Lower-dose, High-frequency Enzyme Replacement therapy in Children's Medical Center of Israel. *Seminars in Hematology* 1995;32:3:S1:33-38.
15. Migata M, Fukunaga Y, Ueda Tn, et al. Progression of bone disease without deterioration of hematological parameters in a child with Gaucher during low-dose glucocerebroside therapy. *J. Nippon on Med Sch* 1994;61:*6:*109-113.
16. International Collaborative Gaucher Group (ICGG) Gaucher Registry database
17. ICGG Registry Protocol. A Randomized Dose Frequency Study of Ceredase® For Untreated, Non-neurologic, Less Severely Affected Patients with Gaucher Disease.

Endnotes

1. 2/97Consensus Statement of the International Collaborative Gaucher Group U.S. Regional Coordinators
2. Revised 2/96 based on the American Journal of Medicine (Zimran, et al.) 1994 97:3-13.
3. Revised 5/96 to include the NIH Technology Assessment Conference Panel recommendations published in JAMA Feb. 21, 1996- Vol 275, no.7 page 548. Full text available at: http://text.nlm.nih.gov/nih/nih.html or by calling the NIH (301) 480-5144.
4. Growth failure, for this purpose, may be defined as either of the following:

A. Children who fall below the 5th percentile of the growth curve for age and sex (see Hamill PV et a. in *Physical Growth: National Center for Health Statistics percentiles.* Am J Clin Nutr 1979;32:607-29.)
B. Children who fall below the expectation for genetic potential based on mid-parental height, or demonstrate a decrease in growth velocity by crossing percentiles (see Tanner JM et al *in Standards for children's height at ages 2-9 years allowing for height of parents*. Arch Dis Child 1970;45:755-62.

5. Quality of life: The US Regional Coordinators of the International Gaucher Collaborative Group statement:
   A disease-specific quality of life (QOL) instrument has not yet been developed that quantifies the QOL burden from patients with Gaucher disease. Thus, the recommended approach is to assess and monitor a patient's physical and mental functional health and well-being by means of one of the more common and validated generic (non-disease-specific) instruments, such as the SF-36 (see Ware J et al. *in SF-36 health survey manual and interpretation guide*. Boston, MA: The Health Institute of New England Medical Center, 1993).
6. Concomitant conditions: Examples include patients with anemia which may jeopardize existing cardiovascular or cerebrovascular disease. Patients who have renal and/or hepatic disease unrelated to Gaucher disease may often experience more severe Gaucher symptoms, because Gaucher symptoms may be exacerbated by these concurrent conditions. The converse is also true, in that those with underlying renal and/or hepatic conditions may have symptoms that are additionally complicated by Gaucher disease. In general, patients with a serum creatinine > 2.0 mg/dL are considered to have renal dysfunction, and patients with an AST or ALT > 2x normal, are considered to have to have hepatic dysfunction (information provided by the US Regional Coordinators of the International Gaucher Collaborative Group)

Home Infusion Therapy
Prior Authorization Form

Please complete and fax with the physician's prescription to: (888) 641-5355. If the patient is a BCBSMA employee, please fax the form to: (617)246-4013.
FOR TPN THERAPY, USE MEDICAL POLICY #296 REQUEST FORM

Company name:		Contact Name:			
Phone #:		Provider #:			
Fax#		Address:			
Patient name:		Address:			
Patient ID#:		DOB: ____/____/__	Diagnosis:		
Prescribing Physician/address:	_____ _____ _____		Telephone:		
PCP name/address:	_____ _____ _____		Telephone:		

Is this fax number 'secure' for PHI receipt/transmission per HIPAA requirements? (circle one) Yes No

Place of Service ☐ **Home** ☐ **SNF** ☐ **MD office** ☐ **other (specify)**_____

Primary Therapy

Primary drug name: _____ Approximate duration: ____/____/____ to ____/____/____

Dose: _____

Frequency _____ Route of Administration: pump: Y N

Other Therapy

Other drug name: _____ Approximate duration: ____/____/____ to ____/____/____

Dose: _____

Frequency _____ Route of Administration: pump: Y N

☐If this is a "drug only" authorization request, indicate other services the nursing agency is providing:

_____

Nursing provided by: _____ Contact: _____

Phone: _____ Fax: _____

Request for 7 Day Coverage : Date of occurrence: _____ request dates:_____

Occurrence type: ☐ Hospitalization ☐ Death ☐ Change of Therapy

Physician signature:_____ **Date:**_____

OR Copy of prescription REQUIRED with this request

MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Outpatient Medical Prior Authorization Form
Please complete and fax to: (888) 641-5355
Please contact Pharmacy Operations with questions at (800) 366-7778
If the patient is a BCBSMA employee, please fax the form to: (617) 246-4013

Servicing Provider	**Name:** **NPI Number:**	**Requesting Provider**	**Name:** **NPI Number:**
Phone# **Fax#** **Contact Person:**		**Phone#** **Fax#** **Contact Person:**	
Patient Name:		**DOB___/___/___**	**Diagnosis:**
Patient BCBSMA ID#			

Is this fax number 'secure' for PHI receipt/transmission per HIPAA requirements? (circle one) Yes No

Drug/Therapy:
Drug Name:_____ Dates of Service:___/___/___ to ___/___/___

Dose:_____

Frequency:_____

Additional Clinical (including previous treatment failure):

Physician signature:_____ Date:_____