Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: ***Gucosylceramide Synthase Inhibitors (Cerdelga, Zavesca)***
DEPARTMENT: **Clinical Pharmacy Services- Utilization Management**
ORIGINAL DATE: ***June 2011 (as adopted from UPMC Health Plan)***

Last P & T Committee Approval Date: *February 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Zavesca (miglustat) and Cerdelga (eliglustat).

Zavesca (Miglustat) is an inhibitor of the enzyme glucosylceramide synthase, which is a glucosyl transferase enzyme responsible for the first step in the synthesis of most glycosphingolipids, and is indicated for the treatment of adult patients with mild to moderate Type I Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (due to constraints such as allergy, hypersensitivity, or poor venous

Cerdelga (Eliglustat) is an inhibitor of the enzyme glucosylceramide synthase, which is a glucosyl transferase enzyme responsible for the first step in synthsis of most glycosphingolipids, and is indicated for the treatment of adult patients with mild to moderate Type 1 Gaucher disease who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by and FDA-cleared test.

DEFINITIONS

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Type I Gaucher Disease – an inherited disease that is caused by a functional deficiency of glucocerebrosidase, the enzyme that mediates degradation of the glycosphingolipid glucosylceramide. The failure to degrade glucosylceramide results in the lysosomal storage of this lipid material within tissue macrophages leading to widespread pathology. Macrophages containing stored glucosylceramide are typically found in the liver, spleen, and bone marrow and occasionally in the lung, kidney, and intestine. Secondary hematologic consequences include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly. Skeletal complications include osteonecrosis and osteopenia with secondary pathological features. Enzyme replacement therapy is the standard of care for most patients who require treatment of type I Gaucher disease. Type I disease is distinguished from type 2 and type 3 diseases by the lack of the characteristic involvement in the central nervous system.

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.002 Pharmacy and Therapeutics Committee and RX.003-Prior Authorization Process.

The drugs, Zavesca (miglustat) and Cerdelga (eliglustat), are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all of the criteria listed below:

- Must be prescribed by or in consultation with a physician who specializes in the treatment of inherited metabolic disorders
- Must be age 18 years or older
- Must have a diagnosis of mild to moderate Type I Gaucher disease with any of the following:
    - Hepatomegaly
        - Defined as liver size 1.25 or more times normal. (Normal liver size is 2.5% of total body weight)
    - Splenomegaly
        - Defined as a splenic mass greater than normal. (Normal spleen size is 0.2% of total body weight).

    - Bone disease
        - Defined as having one of the following:
            - Avascular necrosis
            - Ernlenmeyer flask deformity
            - Lytic disease
            - Marrow infiltrations
            - Osteopenia
            - Osteosclerosis
            - Pathological fracture
            - Radiological evidence of joint deterioration
    - Bone marrow disease
        - Defined as having one of the following:
            - Anemia
            - Thrombocytopenia
- Must not have enzyme replacement therapy (ERT) as a therapeutic option (e.g. allergy/hypersensitivity to ERT, poor venous access, difficulties with infusion, etc.)
- In addition, the following applies to Cerdelga (eliglustat):
    - Must have chart documentation of FDA-cleared test confirming CYP2D6 extensive metabolizer (EMs), intermediate metabolizer (IM), or poor metabolizer (PMs).
    - Must not be on concomitant therapy with a CYP2D6 inhibitor (e.g. paroxetine) and a strong or moderate CYP3A inhibitor (e.g. ketoconazole) if a CYP2D6 EM or IM
    - Must not be on concomitant therapy with a strong CYP3A inhibitor (e.g. ketoconazole) if a CYP2D6 IM or PM
    - Must not be a CYP2D6 ultra-rapid metabolizer
    - Requests for doses above 84mg/day:
        - Must be a CYP2D6 EM or IM

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy and that the member is being monitored for neurologic side effects of the medication.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 1 year
Reauthorization	Same as initial

If the established criteria are not met, the request is referred to a Medical Director for review.

REFERENCES

1. Zavesca [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US Inc; 2010.
2. Pastores GM, Weinreb NJ, Aerts NJ et al. Therapeutic goals in the treatment of Gaucher Disease. *Semin Hematol* 2004;41 (suppl 5):4-14
3. Charrow J. Enzyme replacement for Gaucher Disease. Expert Opin Biol Ther 2009;9(1):121-131
4. Grabowski GA. Lysosomal storage disease 1: phenotype, diagnosis, and treatment of Gaucher's disease. Lancet 2008;372:1263-71
5. Cox T, Lachmann R, Hollak C, et al. Noval oral treatment of Gaucher's disease with Nbutyldeoxynojirimycin (OGT 918) to decrease substrate biosynthesis. Lancet 2000;355:1481-85
6. Heitner R, Elstein D, Aerts J, et al. Low-dose N-butyldeoxynojirimycin (OGT 918) for type I Gaucher disease. Blood Cells, Molecules and Diseases 2002;28(2):127-133
7. Cox TM, Aerts FG, Andria G, et al. The role of iminosugar N-butyldeoxynojirimycin (miglustat) in the management of type I (non-neuropathic) Gaucher disease: a position statement. J Inherit Metab Dis 2003;26:513-526
8. Pastores GM, Elstein D, Hrebicek M, et al. Effect of miglustat on bone disease in adults with type I Gaucher disease: a pooled analysis of three multinational, open-label studies. Clin Ther 2007;29:1645-1654
9. Pastores GM, Barnett NL, Kolodny EH, et al. An open-label, non-comparative study of miglustat in type I Gaucher Disease: efficacy and tolerability over 24 months of treatment. Clin Ther 2005;27:1215-1227
10. Giraldo P, Latre P, Alfonso P,et al. Short-term effect of miglustat in every day clinical use in treatment-naïve or previously treated patients with type Gaucher's disease. Haematologica 2006;91:703-706
11. Cerdelga [prescribing information]. Cambridge, MA: Genzyme a Sanofi company; August 2014.
12. Cox TM, Drelichman G, Cravo R, et al. ENCORE: A randomized, controlled, open-label, noninferiority study comparing eliglustat to imiglucerase in Gaucher disease type 1 patients on enzyme replacement therapy who have reached therapeutic goals. Mol Genet Metab. 2014; 111 (2): S33. Abstract 49 [abstract].
13. Cox TM, Drelichman G, Cravo R, et al. ENCORE: A multi-national, randomized, controlled, open-label, non-inferiority study comparing eliglustat with imiglucerase in Gaucher disease type 1 patients on enzyme replacement therapy who have reached therapeutic goals. Presented at lysosomal disease network 10th annual WORLD symposium, San Diego, CA, USA, February 11-13, 2014. Poster 49 [poster presentation].
14. Ross, L, Peterschmitt MJ, Puga A, et al. Eliglustat safety profile based on pooled analysis of four trials in Gaucher Disease Type 1. Mol Genet Metab. 2014; 111 (2):S90. Abstract 206 [abstract]
15. Ross, L, Peterschmitt MJ, Puga A, et al. Eliglustat adverse event data from a pooled analysis of four trials in Gaucher Disease Type 1. Presented at lysosomal disease network 10th annual WORLD symposium, San Diego, CA, USA, February 11-13, 2014. Poster 206 [poster presentation].

16. Shankar S, Lukina E, Amato D, et al. ENGAGE: A phase 3 randomized, double-blind, placebocontrolled
study of the efficacy and safety of eliglustat in adults with Gaucher disease type 1: 9
month results. Presented at 55th annual meeting of the American Society of Hematology, New Orleans, LA, USA, December 7-10, 2013. [poster presentation].
17. Shankar S, Lukina E, Amato D, et al. ENGAGE: A phase 3 randomized, double-blind, placebocontrolled, multi-center study to investigate the efficacy and safety of eliglustat in adults with Gaucher disease type 1: 9 month results. Blood. 2013; 122 (21): Abstract 2275 [abstract].

RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual review	*02/17, 02/18*