Clinical Policy: Eliglustat (Cerdelga)

Reference Number: PA.CP.PHAR.153
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

Description
Eliglustat (Cerdelga®) is a glucosylceramide synthase inhibitor.

FDA Approved Indication(s)
Cerdelga is indicated for the long-term treatment of adult patients with type 1 Gaucher disease (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.

Limitation(s) of use:
- CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect.
- A specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Cerdelga is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Type 1 Gaucher Disease (must meets all):

1. Diagnosis of Type 1 Gaucher disease (GD1) confirmed by one of the following:
   a. Enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) activity;
   b. DNA testing;
2. Age ≥ 18 years;
3. Member is symptomatic (e.g., anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly);
4. Positive for one of the following CYP2D6 genotypes as detected by an FDA-cleared test:
   a. Extensive metabolizer (EM);
   b. Intermediate metabolizer (IM);
   c. Poor metabolizer (PM);
5. Cerdelga is prescribed as monotherapy;
6. Dose does not exceed:
   a. CYP2D6 EMs and IMs: 168 mg per day (2 capsules per day);
   b. CYP2D6 PMs: 84 mg per day (1 capsule per day).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Type 1 Gaucher Disease (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Cerdelga is prescribed as monotherapy;
4. If request is for a dose increase, new dose does not exceed:
   a. CYP2D6 EMs and IMs: 168 mg per day (2 capsules per day);
   b. CYP2D6 PMs: 84 mg per day (1 capsule per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EM: extensive metabolizer
FDA: Food and Drug Administration
GD1: type 1 Gaucher disease
IM: intermediate metabolizer
PM: poor metabolizer

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): For EMs – taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor; moderate or severe hepatic impairment; mild hepatic impairment taking a strong or moderate CYP2D6 inhibitor. For IMs – taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor; taking a strong CYP3A inhibitor; any degree of hepatic impairment. PMs – taking a strong CYP3A inhibitor; any degree of hepatic impairment.
- Boxed Warning(s): none reported.

Appendix D: General Information

- GD1 is a heterogeneous disorder which involves the visceral organs, bone marrow, and bone in almost all affected patients. Common conditions resulting from GD1 include anemia, thrombocytopenia, hepatomegaly, splenomegaly, and bone disease. Therefore, hemoglobin level, platelet count, liver volume, spleen volume, and bone pain are clinical parameters that can indicate therapeutic response to GD1 therapies. In some clinical trials, stability has been defined as the following thresholds of change from baseline: hemoglobin level < 1.5 g/dL decrease, platelet count < 25% decrease, liver volume < 20% increase, and spleen volume < 25% increase.
- There is currently insufficient evidence that supports the combination use of enzyme replacement therapy with Cerdelga.

- A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Type 1 Gaucher Disease	CYP2D6 EM, IM: 84 mg PO BID CYP2D6 PM: 84 mg PO QD	CYP2D6 EM, IM: 168 mg/day CYP2D6 PM: 84 mg/day

V. Product Availability

Capsule: 84 mg

VI. References

1. Cerdelga Prescribing Information. Waterford, Ireland: Genzyme Ireland, Ltd.; August 2018. Available at http://www.cerdelga.com. Accessed February 27, 2019.
2. Charrow J, Andersson HC, Kaplan P. Enzyme replacement therapy and monitoring for children with type 1 Gaucher disease: consensus recommendations. J Pediatr. 2004; 144: 112-20.
3. Hollak, CEM, Weinreb NJ. The attenuated/late onset lysosomal storage disorders: therapeutic goals and indications for enzyme replacement treatment in Gaucher and Fabry disease. Best Pract Res Clin Endocrinol Metab. 2015; 29: 205-218.
4. Pastores GM, Weinreb NJ, Aerts H, et al. Therapeutic goals in the treatment of Gaucher disease. Semin Hematol. 2004; 41(suppl 5): 4-14.
5. Andersson HC, Charrow J, Kaplan P, et al. Individualization of long-term enzyme replacement therapy for Gaucher disease. Genet Med. 2005; 7(2): 105-110.
6. Balwani M, Burrow TA, Charrow J, et al. Recommendations for the use of eliglustat in the treatment of adults with Gaucher disease type 1 in the United States. Molecular Genetics and Metabolism. 2016; 117(2): 95-103.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: no significant changes from previously approved policy; added age limit where relevant; added requirement for documentation that the member is symptomatic; removed requirement for prior trial of intravenous therapeutic alternatives; requirement of Cerdelga monotherapy; changed approval durations from length of benefit to 6 months initial/12 months reauthorization; references reviewed and updated.		
2Q 2019 annual review: references reviewed and updated.	04/19	