Clinical Policy Title:	eliglustat
Policy Number:	RxA.062
Drug(s) Applied:	Cerdelga®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All line of business

Background

Eliglustat is a glucosylceramide synthase inhibitor. It 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 eliglustat to achieve a therapeutic effect.
- A specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
eliglustat (Cerdelga®)	Type 1 Gaucher Disease	CYP2D6 EM, IM: 84 mg PO BID CYP2D6 PM: 84 mg PO once daily	CYP2D6 EM, IM: 168 mg/day CYP2D6 PM: 84 mg/day

Dosage Forms

- Capsule: 84 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

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

1. Diagnosis of GD1 confirmed by one of the following (a or b):
   a. Enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) activity;
   b. DNA testing;
2. Member is 18 years of age or older;
3. Member is symptomatic (e.g., anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly);
4. Member is a CYP2D6 poor metabolizer, extensive metabolizer, or intermediate metabolizer confirmed by an FDA-cleared test;
5. Eliglustat 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
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by increased or stabilized platelet count or hemoglobin level, reduced or stabilized spleen or liver volume, and/or decreased bone pain;
3. Eliglustat 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
BID: Twice Daily
EM: Extensive Metabolizer
GD1: type 1 Gaucher Disease
FDA: Food and Drug Administration
IM: Intermediate Metabolizer
PM: Poor Metabolizer
PO: By Mouth

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; and
    - 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; and
    - Any degree of hepatic impairment.
  - For PMs:
    - Taking a strong CYP3A inhibitor; and

  - Any degree of hepatic impairment.

- Boxed Warning(s):
  - None

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

References

1. Cerdelga Prescribing Information. Waterford, Ireland: Genzyme Ireland, Ltd.; August 2018. Available at http://www.cerdelga.com. Accessed February 3, 2021.
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. Accessed February 3, 2021.
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. Accessed February 3, 2021.
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. Accessed February 3, 2021.
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. Accessed February 3, 2021.
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): 95-10 Accessed February 3, 2021.
7. Eliglustat. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, August 3. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed February 3, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy reviewed and updated. 1. Updated references. 2. Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, or documentation supports that member is currently receiving Cabometyx or Cometriq for a covered indication and has received this medication for at least 30 days.	04/29/2020	05/20/2020
Policy reviewed and updated. 1. Clinical policy title and lines of business updated. 2. Commercial approval duration updated. 3. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 4. References updated.	02/03/2021	03/09/2021