MEDICAL MUTUAL®

Drug Policy

Policy:	**Gaucher Disease Oral Agents** **Cerdelga (eliglustat)** **miglustat (generic)** **Zavesca (miglustat)** **Yargesa (miglustat capsules)**	**Annual Review Date:** **12/19/2024** **Last Revised Date:** **12/19/2024**

OVERVIEW

Miglustat (Zavesca) is an oral treatment approved for adult patients with mild to moderate type I Gaucher disease if enzyme replacement therapy (Cerezyme, Elelyso, Vpriv) is not a therapeutic option (for example, allergy, hypersensitivity or poor venous access). Miglustat works by inhibiting the enzyme that makes glucosphingolipid. Miglustat's role in decreasing the rate of glycosphingolipid biosynthesis allows a reduction of the substance to a level which can be cleared by the remaining activity of the naturally occurring defective enzyme. Eliglustat (Cerdelga) is an oral glucosylceramide synthase inhibitor indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.

Gaucher disease is an autosomal recessive lipid storage disorder characterized by a deficiency of glucocerebrosidase. Decreased glucocerebrosidase activity leads to accumulation of glucocerebroside within cell lysosomes in the liver, spleen, bone marrow and bone. Gaucher disease is classified into three clinical types:

Type I Gaucher disease, known as non-neuronopathic because there is no central nervous system involvement, is the most common form and occurs at any age, predominantly in individuals of Ashkenazi Jewish descent. The disease involves visceral organs (e.g., liver, spleen), bone marrow and bone.

Types II and III Gaucher disease, known as neuronopathic, are very rare forms with neurological involvement in addition to other organs affected by type I Gaucher disease. Type II Gaucher disease typically begins during the first year of life and is characterized as a rapidly progressive form (referred to as acute neuronopathic disease), whereas type III is typically a slowly progressive form that appears in early childhood (referred to as chronic neuronopahic disease).

POLICY STATEMENT

This policy involves the use of Cerdelga, generic miglustat, and Zavesca. Prior authorization is recommended for pharmacy benefit coverage of Cerdelga, generic miglustat, and Zavesca. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Cerdelga, generic miglustat, and Zavesca as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Cerdelga, generic miglustat, and Zavesca be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cerdelga, generic miglustat, Yargesa and Zavesca is recommended in those who meet the following criteria:

1. **Type I Gaucher Disease in Adults**

   Criteria. *Patient must meet the following criteria*

   A. Member must be 18 years of age or older; AND
   B. Cerdelga, Yargesa, generic miglustat, or Zavesca is prescribed by or in consultation with a geneticist, an endocrinologist, metabolic disorder sub-specialist, or a physician who specializes in the treatment of Gaucher Disease; AND
   C. Diagnosis of Type I Gaucher Disease established by ***at least one*** of the following:
      a. White blood cell or skin fibroblast glucocerebrosidase activity ≤ 30% of normal; OR
      b. Mutation of two glucocerebrosidase genome alleles; AND
   D. ***At least one*** of the following is met:
      a. Hemoglobin ≥ 1.0 g/dL below lower limit of normal for age and sex (≤ 11.5 g/dL for females, ≤ 12.5 g/dL for males); OR
      b. Platelet count ≤ 120,000/mm3; OR
      c. Clinically significant hepatomegaly (liver ≥ 1.25 times normal size established by magnetic resonance imaging [MRI] or computed tomography [CT]); OR
      d. Clinically significant splenomegaly (spleen ≥ 5 times normal size established by magnetic resonance imaging [MRI] or computed tomography [CT]); OR
      e. Skeletal involvement (e.g. Erlenmeyer flask deformity, osteopenia, pathological fracture, radiological evidence of joint deterioration, avascular necrosis)
   E. If request is for Cerdelga, member has had an FDA-cleared test showing the member's CYP2D6 metabolizer status [documentation required]
   F. If request is for Brand Zavesca or Cerdegla, one of the following is met:
      a. The member has tried and failed generic miglustat
      b. The prescribing physician attests that the request for Brand Zavesca or Cerdelga is due to a difference in formulation or inactive ingredients (e.g. preservatives) which has or would result in a significant allergy or serious adverse reaction

2. **Patient has been started on Cerdelga, generic miglustat, or Zavesca**

   Criteria. Approve for an indication or condition addressed as an approval in this document and if the drug continues to provide clinical benefit for the patient (e.g. improvement in symptoms, platelet count, or decrease in liver or spleen size) and the requested medication continues to be prescribed by or in consultation with a geneticist, endocrinologist, metabolic disorder sub-specialist, or a physician who specializes in the treatment of Gaucher Disease.

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Drug Policy

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cerdelga, generic miglustat, and Zavesca have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Type II Gaucher Disease.** Based upon our findings, the Company has determined enzyme replacement therapy and substrate reduction therapy have not been accepted in the medical community as the standard or appropriate means of treatment for type II Gaucher disease.

2. **Type III Gaucher Disease.** Based upon our findings, the Company has determined that enzyme replacement therapy and substrate reduction therapy have not been accepted in the medical community in the United States as the standard or appropriate means of treatment for type III Gaucher disease

3. **Coadminstration with another enzyme replacement therapy for Gaucher disease such as Cerdelga, Cerezyme, Elelyso, generic miglustat, Vpriv, and Zavesca**.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

DOSING:

Cerdelga (eliglustat) capsules. The recommended dosage of Cerdelga is 84 mg twice daily in CYP2D6 extensive metabolizers (EMs) and intermediate metabolizers (IMs). The recommended dosage in CYP2D6 poor metabolizers (PMs) is 84 mg once daily; appropriate adverse event monitoring is recommended.

Zavesca (miglustat) capsules**.** The recommended dose is one 100 mg capsule administered orally three times a day at regular intervals. If a dose is missed, the next Zavesca capsule should be taken at the next scheduled time. It may be necessary to reduce the dose to one 100 mg capsule once or twice a day in some patients due to adverse reactions, such as tremor or diarrhea.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Zavesca [prescribing information]. San Francisco, CA: Actelion Pharmaceuticals US, Inc.; November 2017.
2. Cerdelga [prescribing information]. Cambridge, MA: Genzyme Corporation. July 2021.
3. National Gaucher Foundation. Gaucher disease types 2 and 3. National gaucher foundation. Available at: http://www.gaucherdisease.org/about-gaucher-disease/what-is/type-2-3/?gclid=CLeP0pzE4s8CFQEGaQodIm0IIw. Accessed on 18 October 2017.
4. Andersson HC, Charrow J, Kaplan P et al. Individualization of long-term enzyme replacement therapy for Gaucher disease. Genet Med. 2005 Feb;7(2):105-10. Review. Erratum in: Genet Med. 2005 Sep;7(7):514.
5. Hughes D, Hahn S, and TePas E. Gaucher Disease: Treatment. UpToDate. Available at: https://www.uptodate.com/contents/gaucher-disease-treatment?source=search_result&search=gaucher&selectedTitle=2~60#H4. Accessed on 18 October 2017.
6. Miglustat. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 2 November 2018. Accessed on 16 December 2018.
7. Eliglustat. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 5 November 2018. Accessed on 16 December 2018.