

## **Clinical Policy: Miglustat (Zavesca)**

Reference Number: CP.PHAR.164

Effective Date: 02.01.16

Last Review Date: 02.25

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Miglustat (Zavesca<sup>®</sup>) is a glucosylceramide synthase inhibitor.

### **FDA Approved Indication(s)**

Zavesca is indicated as monotherapy for the treatment of adult patients with mild/moderate type 1 Gaucher disease (GD1) for whom enzyme replacement therapy is not a therapeutic option.

### **Policy/Criteria**

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

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Zavesca is **medically necessary** when the following criteria are met:

#### **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 in beta-glucocerebrosidase (glucosidase) activity;
  - b. DNA testing;
2. Age  $\geq$  18 years;
3. Member is symptomatic (e.g., anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly);
4. Failure of two enzyme replacement therapies (i.e., Cerezyme<sup>®</sup>, Elelyso<sup>®</sup>, VPRIV<sup>®</sup>), unless member is unable to take enzyme replacement therapies due to one of the following (a or b):
  - a. Allergy or hypersensitivity;
  - b. Poor venous access;
5. Zavesca is prescribed as monotherapy;
6. Dose does not exceed 300 mg (3 capsules) per day.

**Approval duration: 6 months**

##### **B. Niemann-Pick Disease Type C (must meet all):**

1. Diagnosis of NPC confirmed by one of the following (a or b):
  - a. Genetic analysis indicating mutation in both alleles of *NPC1* or *NPC2*;
  - b. Genetic analysis indicating mutation in one allele of *NPC1* or *NPC2* along with one of the following (i or ii):

- i. Positive filipin staining test result;
  - ii. Positive biomarker result (e.g., oxysterol, lyso-sphingolipid, bile acid);
2. Prescribed by or in consultation with a geneticist, neurologist, endocrinologist, or metabolic disease specialist;
3. Member presents with at least one neurological sign or symptom of the disease (*see Appendix D*);
4. Dose does not exceed 600 mg (6 capsules) per day.

**Approval duration: 6 months**

**C. Other diagnoses/indications (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy as evidenced by increased or stabilized platelet count or hemoglobin, reduced or stabilized spleen or liver volume, or decreased bone pain;
3. Zavesca is prescribed as monotherapy;
4. If request is for a dose increase, new dose does not exceed 300 mg (3 capsules) per day.

**Approval duration: 12 months**

**B. Niemann-Pick Disease Type C (must meet all):**

1. Member meets one of the following (a or b):

**CLINICAL POLICY****Miglustat**

- a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy as evidenced by an improvement or stabilization in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, sitting, or speech);
  3. If request is for a dose increase, new dose does not exceed 600 mg (6 capsules) per day.

**Approval duration: 12 months****C. Other diagnoses/indications (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information***Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

GD1: type 1 Gaucher disease

NPC: Niemann-Pick disease type C

**CLINICAL POLICY**

**Miglustat**

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| <b>Drug Name</b>                | <b>Dosing Regimen</b>   | <b>Dose Limit/<br/>Maximum Dose</b> |
|---------------------------------|---|-------------------------------------|
| Cerezyme<br>(imiglucerase)      | Individualize to each patient; initial dose ranges from 2.5 units/kg by IV infusion 3 times a week to 60 units/kg once every 2 weeks; disease severity may dictate treatment be initiated at relatively high dose or relatively frequent administration | Individualized                      |
| Elelyso<br>(taliglucerase alfa) | 60 units/kg IV every other week   | Individualized                      |
| VPRIV<br>(velaglucerase alfa)   | 60 units/kg IV every other week   | Individualized                      |

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

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 Zavesca.
- Examples of neurological signs or symptoms of NPC include hearing loss, vertical supranuclear gaze palsy, dysarthria, ataxia, dystonia, impaired ambulation, dysarthria, dysphagia, seizures, dementia

**V. Dosage and Administration**

| <b>Indication</b> | <b>Dosing Regimen</b> | <b>Maximum Dose</b> |
|-------------------|-----------------------|---------------------|
| GD1               | 100 mg PO TID         | 300 mg/day          |

**VI. Product Availability**

Capsule: 100 mg

**CLINICAL POLICY**  
**Miglustat**

**VII. References**

1. Zavesca Prescribing Information. Irvine, CA: Actelion Pharmaceuticals US, Inc.; August 2022. Available at <https://www.zavesca.com>. Accessed November 26, 2024.
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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.
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6. Gary SE, Ryan E, Steward AM, et al. Recent advances in the diagnosis and management of Gaucher disease. *Expert Rev Endocrinol Metab*. 2018 Mar;13(2):107–118.
7. Leonart LP, Fachi MM, Boger B, et al. A systematic review and meta-analyses of longitudinal studies on drug treatments for Gaucher disease. *Ann Pharmacother*. 2022;0(0). doi:10.1177/10600280221108443.
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9. Geberhiwot T, Moro Alessandro, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet Journal of Rare Diseases* 2018 April 6;13(1):50.
10. Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: An update. *Neurol Clin Pract*. 2017;7(6):499-511.

| Reviews, Revisions, and Approvals  | Date     | P&T Approval Date |
|--|----------|-------------------|
| 2Q 2020 annual review: no significant changes; references reviewed and updated.  | 02.05.20 | 05.20             |
| 2Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.   | 02.27.21 | 05.21             |
| 2Q 2022 annual review: no significant changes; removed the requirement for mild to moderate GD1 severity for coverage based on subjectivity of defining disease severity; references reviewed and updated. | 02.23.22 | 05.22             |
| Template changes applied to other diagnoses/indications and continued therapy section.   | 09.30.22 |                   |
| 2Q 2023 annual review: no significant changes; references reviewed and updated.  | 02.07.23 | 05.23             |
| 2Q 2024 annual review: no significant changes; references reviewed and updated.  | 01.09.24 | 05.24             |
| Added criteria for use in NPC.   | 11.26.24 | 02.25             |

## CLINICAL POLICY

### Miglustat

#### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**CLINICAL POLICY****Miglustat**

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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