Clinical Policy: Miglustat (Zavesca)

Reference Number: ERX.SPA.99
Effective Date: 10.01.16
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Miglustat (Zavesca®) 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 18 years;
3. Member is symptomatic (e.g., anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly);
4. Failure of at least 2 enzyme replacement therapies (i.e., Cerezyme®, Elelyso®, VPRIV®), 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. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by increased or stabilized platelet count or hemoglobin, reduced or stabilized spleen or liver volume, 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. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GD1: type 1 Gaucher disease

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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cerezyme (imiglucerase)	Individualize to each patient; initial dose ranges from 2.5 units/kg 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 (taliglucerase alfa)	Treatment-naïve patients: 60 units/kg IV every other week Patients switching from imiglucerase: Begin at the same unit/kg dose as the patient's previous imiglucerase dose; administer every other week	Individualized
VPRIV (velaglucerase alfa)	Patients naïve to enzyme replacement therapy: 60 units/kg IV every other week Patients being treated with stable imiglucerase dosages for GD1: Switch to VPRIV at previous imiglucerase dose 2 weeks after last imiglucerase dose	Individualized

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
GD1	100 mg PO TID	300 mg/day

VI. Product Availability

Capsule: 100 mg

VII. References

1. Zavesca Prescribing Information. Irvine, CA: Actelion Pharmaceuticals US, Inc.; November 2017. Available at https://www.zavesca.com/pdf/ZAVESCA-Full-Prescribing-Information.pdf. Accessed February 5, 2020.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from USS.SPMN.33 Lysosomal Storage Disorders and converted to new template. Replaced requirement for establishment of mild-moderate disease per CD-DS3 scoring system with requirement for attestation of mild-moderate disease. Removed all safety criteria. Modified approval duration to 6 months for initial and 12 months for re-auth.	08.16	09.16
Converted to new template. Initial: Added prescriber requirement and max dose criteria. Added DNA testing to diagnostic methods. Re-auth: Added max dose criteria and requirement for positive response to therapy.	06.17	08.17
4Q17 Annual Review Initial: Removed prescriber requirement. Added requirement for presence of symptoms. Removed subjective “mild to moderate” qualifier.	09.11.17	11.17
2Q 2018 annual review: No significant changes. References reviewed and updated.	02.26.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.27.19	05.19
2Q 2020 annual review: added specific examples of response to therapy for reauthorization; references reviewed and updated.	02.05.20	05.20

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.