RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	miglustat
Policy Number:	RxA.570
Drug(s) Applied:	Zavesca®
Original Policy Date:	01/01/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Miglustat (Zavesca®) is a glucosylceramide synthase inhibitor. Miglustat 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
miglustat (Zavesca®)	GD1	100 mg PO TID	300 mg/day

Dosage Forms

- Capsules: 100 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 mild to moderate 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 or older;
3. Member is having following disease manifestations (e.g., anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly);
4. Failure of two 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 600 mg/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, reduced or stabilized spleen or liver volume, decreased bone pain, improvement in fatigue, constipation, and peripheral neuropathy;
3. Zavesca® is prescribed as monotherapy;
4. If request is for a dose increase, new dose does not exceed 600 mg/day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cerezyme (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 (taliglucerase alfa)	60 units/kg IV every other week	Individualized
VPRIV (velaglucerase alfa)	60 units/kg IV every other week	Individualized

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- 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 Zavesca®.
- Type 1 Gaucher disease is caused by a functional deficiency of glucocerebrosidase, the enzyme that mediates the degradation of the glycosphingolipid glucosylceramide. Miglustat functions as a competitive and reversible inhibitor of the enzyme glucosylceramide synthase, the initial enzyme in a series of reactions which results in the synthesis of most glycosphingolipids.
- Zavesca® helps reduce the rate of glycosphingolipid biosynthesis so that the amount of glycosphingolipid substrate is reduced to a level which allows the residual activity of the deficient glucocerebrosidase enzyme to be more effective (substrate reduction therapy). In vitro and in vivo studies have shown that miglustat can reduce the synthesis of glucosylceramide based glycosphingolipids.

References

1. Zavesca® Prescribing Information. San Francisco, CA: Actelion Pharmaceuticals US, Inc.; November 2017. Available at https://www.zavesca.com. Accessed October 6, 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. Accessed October 06, 2020
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 October 06, 2020.
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 October 06, 2020.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	01/01/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to All lines of business. 2. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized	10/06/2020	12/07/2020

by RxAdvance…". 3. Approval duration was updated (HIM removed and 12 month duration) 4. Appendix B: Pre table phrase was updated to *"Below are suggested therapeutic alternatives.."* 5. Updated verbiage from "symptomatic" to "disease manifestations" when describing improvement in clinical criteria. 6. Added symptoms to criteria in continued therapy criteria when describing disease improvement. 7. Appendix D was updated. 8. References were updated.		