Clinical Policy: Miglustat (Zavesca)

Reference Number: CP.PHAR.164
Effective Date: 02.01.16
Last Review Date: 05.19
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®) 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® 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 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;
3. Member is symptomatic (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 300 mg/day (3 capsules/day).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit 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/day (3 capsules/day).

Approval duration: 12 months

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

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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

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 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

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

- 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.

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. Accessed February 27, 2019.
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 CP.PHAR.48. Policy converted to new template.	01.16	02.16
Removed age restriction. DNA testing added to diagnostic methods. Max dose added. Severe renal impairment as a restriction is added to initial and continuation criteria per the PI. Hand tremors added to the continuation criteria per the PI. Positive response to therapy added. Continuation approval period extended to 12 months. Background section converted to new template.	12.16	02.17
Added age restriction. Added requirement for presence of symptoms. Removed severe renal impairment (not a CI or BBW) and reasons to discontinue per new safety strategy. Added examples of what can constitute a positive response to therapy. Added appendix B.	08.24.17	11.17
2Q 2018 annual review: no significant changes from previously approved corporate policy; policies combined for Medicaid and Commercial lines of business; added HIM; Commercial: added specific examples of response to therapy for reauthorization; added age limit, requirement of Zavesca monotherapy; changed approval durations from length of benefit to 6 months initial/12 months reauthorization; 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

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members 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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.