Clinical Policy: Miglustat (Zavesca)

Reference Number: CP.PHAR.164
Effective Date: 02/2016
Last Review Date: 02/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for miglustat (Zavesca®).

Policy/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 Type 1 Gaucher Disease (GD1) confirmed by one of the following:
   a. Enzyme assay demonstrating a deficiency in beta-glucocerebrosidase activity;
   b. DNA testing;
2. Member has failed at least two enzyme replacement therapies (i.e., Cerezyme [imiglucerase], Elelyso [taliglucerase alfa], VPRIV [velaglucerase alfa]) or is unable to take enzyme replacement therapies due to one of the following:
   a. Allergy or hypersensitivity;
   b. Poor venous access;
3. Zavesca is prescribed as monotherapy;
4. Prescribed daily dose of Zavesca does not exceed 300 mg;
5. Member does not have severe renal impairment (i.e., CrCl <30 mL/min/1.73 m^2).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Zavesca is prescribed as monotherapy;
4. Prescribed daily dose of Zavesca does not exceed 300 mg;
5. Member has none of the following reasons to discontinue Zavesca therapy:
   a. Severe renal impairment (i.e., CrCl <30 mL/min/1.73 m^2);
   b. Unresolved hand tremors despite dose reduction.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background
Description/Mechanism of Action:
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.

Formulations:
Zavesca (miglustat): Capsules for oral use
- 100 mg/capsule

FDA Approved Indications:
Zavesca is a glucosylceramide synthase inhibitor/oral capsule formulation indicated as monotherapy for the treatment of:
- Adult patients with mild to moderate Type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	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.	12/16	02/17

Reviews, Revisions, and Approvals	Date	Approval Date
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.		

References

1. Zavesca prescribing information. Irvine, CA: Actelion Pharmaceuticals US, Inc.; February 2016. Available at https://www.zavesca.com/pdf/ZAVESCA-Full-Prescribing-Information.pdf. Accessed December 21, 2016.
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.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs , and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.