IMPORTANT REMINDER
This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Miglustat (Zavesca) is an oral medication that treats type 1 Gaucher disease, a rare genetic disorder affecting the skeleton, bone marrow, spleen, liver, and lungs.
Policy/Criteria

I. Most contracts require prior authorization approval of miglustat (Zavesca) prior to coverage. Miglustat (Zavesca) may be considered medically necessary when criterion A or B below is met:

A. A diagnosis of **type 1 Gaucher disease** when criteria 1 through 3 below are met:
   
   1. The diagnosis is confirmed by one of the following:
      
      a. Biochemical assay of glucocerebrosidase activity in white blood cells or skin fibroblasts is less than or equal to 30% of normal activity. (Note: laboratory normals may vary).
      
      OR
      
      b. Genotyping revealing two pathogenic mutations of the glucocerebrosidase gene.
      
   AND
   
   2. Clinically significant symptoms of the disease are present, such as malnutrition, growth retardation, anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.
   
   AND
   
   3. Enzyme replacement therapy (ERT) is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).
   
   OR

B. A diagnosis of **Niemann-Pick Disease type C**

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers miglustat (Zavesca) to be a self-administered medication.

B. When prior authorization is approved, miglustat (Zavesca) may be covered in quantities up to 300 mg per day (90 capsules per month).

C. Authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective. Documentation by chart notes of maintenance or improvement in disease must be provided. (This may include, but is not limited to hematologic indicis, reduction in spleen or liver volume, MRI of spine/femurs, normalized growth, reduced dependency on oxygen, quality of life, and/or plain films of skeleton).

III. Miglustat (Zavesca) is considered not medically necessary when used in combination with imiglucerase (Cerezyme), taliglucerase alfa (Elelyso), or velaglucerase alfa (VPRIV).
IV. Miglustat (Zavesca) is considered investigational when used for all other conditions including, but not limited to:

A. Combination use with eliglustat (Cerdelga)
B. Juvenile GM2 gangliosidosis
C. Mucopolysaccharidosis
D. Tay-Sachs disease
E. Cystic fibrosis

Position Summary

- Miglustat (Zavesca) is considered a substrate reduction therapy (SRT) and works by minimizing the amount of GL1 that a cell makes.
- Miglustat (Zavesca) is FDA approved for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy (ERT) is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access). [1]
- SRT with miglustat (Zavesca) should not be used in neuronopathic (type 2 or type 3) Gaucher disease and is generally only appropriate for mild systemic disease. [2]
- Treatment should be reserved for symptomatic children (including those with malnutrition, growth retardation, impaired psychomotor development, and/or fatigue), and for adults with symptomatic disease (e.g. platelet count < 60,000/mm³, liver volume > 2.5 times normal size, spleen volume > 15 times normal size, radiological evidence of skeletal disease). [2]
- Treatment goals include elimination or improvement in symptoms, prevention of irreversible complications, and improvement in the overall health and quality of life. [2]
- Enzyme replacement therapy (ERT) with imiglucerase (Cerezyme), taliglucerase alfa (Elelyso), or velaglucerase alfa (VPRIV) is considered the preferred treatment option for all patients with type 1 Gaucher disease requiring pharmacologic treatment. [3]
- The diagnosis of Gaucher disease is usually confirmed by identifying reduced glucocerebrosidase activity in peripheral leukocytes. Targeted DNA analysis to detect the most common mutations is an effective method for confirming the diagnosis. [2]
- There are no data showing miglustat (Zavesca) has better safety or efficacy than ERT with imiglucerase (Cerezyme) and the addition of miglustat (Zavesca) to ERT has not been shown to provide a substantial benefit over ERT alone. [4]
**Clinical Efficacy**

**Gaucher Disease**

- Miglustat (Zavesca) has only been studied in patients with mild-to-moderate symptomatic Gaucher disease. It has not been evaluated for efficacy in patients with severe disease (such as patients with skeletal manifestations, hemoglobin concentrations less than 9 mg/L, and/or platelet counts less than 50 x 10^9/L). [1,3,5]

- Two prospective, open-label, non-comparative trials described the safety and efficacy of miglustat (Zavesca) in patients with mild-to-moderate type 1 Gaucher disease. Over a period of 12 to 24 months, miglustat (Zavesca) therapy resulted in improvement in liver and spleen volume, increases in hemoglobin, and stable or improved platelet counts and bone involvement. [6,7]

**Niemann Pick Disease Type C**

- There is evidence which suggests that miglustat (Zavesca) in doses of 200 mg three times daily improves clinical markers for Niemann-Pick disease type C (NPC) and stabilizes neurological disease progression. Although the small numbers of patients studied and concomitant medications make the results uncertain, patients with NPC have few other treatment options. [8-10]

**Investigational Uses**

- A small study evaluate the use of miglustat (Zavesca) in the management of five patients with juvenile GM2 gangliosidosis. There was no clear benefit observed, but the study was small and did not include a comparator. Larger, well-designed randomized controlled trials are needed to establish the safety and efficacy of miglustat (Zavesca) in this condition. [11]

- One single-center, placebo-controlled study evaluated the use of miglustat (Zavesca) for improvement in Vineland Adaptive Behavior Scales in patients with mucopolysaccharidosis type III. No improvement or stabilization in behavior was seen in the miglustat (Zavesca) group. [12]

- A small study evaluated the use of miglustat (Zavesca) in the management of late-onset Tay-Sachs disease. Though the study had flaws that make the results uncertain, the study authors concluded that miglustat (Zavesca) did not lead to measurable benefits. [13]

- A small, single-center, double-blind, placebo-controlled study evaluated the use of miglustat (Zavesca) in 11 patients with cystic fibrosis. No statistically significant changes in total chloride secretion, sweat chloride value, or FEV1 were detected. Further study is required to assess any potential benefit of miglustat (Zavesca) in the condition. [14]
**Safety**
- Gastrointestinal effects, weight loss, and tremors are the most frequently reported adverse effects with miglustat (Zavesca). \[1\]
- Cases of peripheral neuropathy have been reported in patients treated with miglustat (Zavesca). All patients treated with miglustat (Zavesca) should undergo baseline and repeat neurological evaluations at approximately 6-month intervals. \[1\]
- Diarrhea (approximately 85%) and weight loss (up to 65%) were common in clinical studies of patients treated with miglustat (Zavesca). \[1\]
- According to the prescribing information, male patients should maintain reliable contraceptive methods while taking miglustat (Zavesca) as studies in the rat have shown that miglustat (Zavesca) adversely affects spermatogenesis and sperm parameters, thereby reducing fertility. \[1\]

**Cross References**

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<td>Cerdelga™, eliglustat, Medication Policy Manual, Policy dru370</td>
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<td>Cerezyme®, imiglucerase, VPRIV®, velaglucerase alfa, Elelyso™, taliglucerase alfa, Medication Policy Manual, Policy dru002</td>
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**Codes**

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**References**


