

**Regence BlueCross BlueShield of Oregon • Regence BlueShield
Regence BlueCross BlueShield of Utah • Regence BlueShield of Idaho
Independent licensees of the Blue Cross and Blue Shield Association**

Medication Policy Manual

Policy No: dru109

Topic: Zavesca[®], miglustat

Date of Origin: June 18, 2004

Revised/Effective Date: January 9, 2009

Next Review Date: January 2010

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 prior to coverage. Miglustat may be considered medically necessary in patients with Type 1 Gaucher disease.

- II. Administration, Quantity Limitations, and Authorization Period
 - A. Regence considers miglustat to be a self-administered medication.
 - B. When prior authorization is approved, miglustat may be covered in quantities up to 300 mg per day.
 - C. Authorization shall be renewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

- III. Miglustat is considered investigational when used in combination with imiglucerase (Cerezyme[®]) or when it is used for all other conditions including, but not limited to, Niemann-Pick C disease.

Position Statement

- Miglustat 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 constraints such as allergy, hypersensitivity, or poor venous access).^[7]
- ERT with imiglucerase is considered the first line treatment option for all patients with Type 1 Gaucher disease requiring pharmacologic treatment.^[8]
- There are no data showing miglustat has better safety or efficacy than enzyme replacement therapy with imiglucerase (Cerezyme[®]).^[3-14]
- There is no useful evidence of additional clinical benefit using concomitant combination therapy of imiglucerase and miglustat. However, miglustat may be an effective maintenance therapy in patients with Type 1 Gaucher disease after initial stabilization with imiglucerase.^[3-7, 9, 18]

Clinical Efficacy

- Miglustat has only been studied in patients with mild-to-moderate symptomatic Gaucher disease.^[3-9] 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 $50 \times 10^9/L$).
- Two prospective, open-label, non-comparative trials described the safety and efficacy of miglustat in patients with mild-to-moderate type 1 Gaucher's disease. Over a period of 12 to 24 months, miglustat therapy resulted in improvement in liver and spleen volume, increases in hemoglobin, and stable or improved platelet counts and bone involvement.^[16,17]
- There is preliminary evidence that miglustat in doses of 200 mg three times daily improves clinical markers for Niemann-Pick disease type C (NPC), but the small numbers of patients and confounding with concomitant medications make the results uncertain. More study is needed to establish the long-term benefit of miglustat.^[15, 19]

Safety

- Gastrointestinal effects, weight loss, and tremors are the most frequently reported adverse effects with miglustat.^[7]
- Cases of peripheral neuropathy have been reported in patients treated with miglustat. All patients undergoing miglustat treatment should undergo baseline and repeat neurological evaluations at approximately 6-month intervals.^[7]
- Diarrhea and weight loss were common in clinical studies of patients treated with miglustat, approximately 85% and up to 65% of treated patients, respectively, reporting these conditions.^[7]
- Male patients should maintain reliable contraceptive methods while taking miglustat. Studies in rats have shown that miglustat adversely affects spermatogenesis and sperm parameters, thereby reducing fertility.^[7]

References

1. Cox T et al. "Novel oral treatment of Gaucher's disease with N-butyldeoxynojirimycin (OGT 918) to decrease substrate biosynthesis." *Lancet* 2000;355:1481-5.

2. Heitner R et al. "Low-dose N-butyldeoxynojirimycin (OGT 918) for type 1 Gaucher disease." *Blood Cells Mol Dis* 2002;28(2):127-33.
3. FDA medical review: http://www.fda.gov/cder/foi/nda/2003/21-348_Zavesca_Medr_P3.pdf
4. http://www.fda.gov/cder/foi/nda/2003/21-348_Zavesca_Medr_P4.pdf
5. http://www.fda.gov/cder/foi/nda/2003/21-348_Zavesca_Medr_P5.pdf
6. http://www.fda.gov/cder/foi/nda/2003/21-348_Zavesca_Medr_P6.pdf
7. Zavesca [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; February 2008
8. Cox TM et al for the Advisory Council to the European Working Group on Gaucher Disease. "The role of the iminosugar n-butyldeoxynojirimycin (miglustat) in the management of type I (non-neuronopathic) Gaucher disease: A position statement." *J Inherit Metab Dis* 2003;(26):513-26.
9. Elstein D et al. "A randomized study of OGT 918 as an oral therapy in patients previous treated with enzyme replacement type 1 gaucher disease." Presented at the Fifth Workshop of the European Working Group on Gaucher Disease, Prague, May 1-4, 2002.
10. Weinreb NJ et al. "Effectiveness of enzyme replacement therapy in 1028 patients with type I Gaucher disease after 2 to 5 years of treatment; a report from the Gaucher Registry." *Am J Med* 113:112-9.
11. Barton NW et al. "Replacement therapy for inherited enzyme deficiency--macrophage-targeted glucocerebrosidase for Gaucher disease. N Engl J Med 1991;324:14 NW et al. Replacement therapy for inherited enzyme deficiency--macrophage-targeted glucocerebrosidase for Gaucher disease." *N Engl J Med* 1991;324:1464-70.
12. Grabowski GA et al. "Enzyme therapy in type 1 Gaucher disease: comparative efficacy of mannose-terminated glucocerebrosidase from natural and recombinant sources." *Ann Intern Med* 1995;122:33-9.
13. Zimran A et al. "Low dose enzyme replacement therapy for Gaucher's disease: effects of age, sex, genotype, and clinical features on response to treatment." *Am J Med* 97:3-13.
14. Hollak CEM et al. "Individualized low-dose alglucerase therapy for type 1 Gaucher disease." *Lancet* 1995;345:1474-8.
15. Lachmann RH et al. "Treatment with miglustat reverses the lipid-trafficking defect in Niemann-Pick disease type C." *Neurobiol Dis* 2004;16:654-8.
16. Giraldo P, Latre P, Alfonso P, Acedo A, Alonso D, Barez A, et. al. Short-term effect of miglustat in every day clinical use in treatment-naive or previously treated patients with type 1 Gaucher's disease. *Haematologica*. 2006 May;91(5):703-6.

17. Pastores GM, Barnett NL, Kolodny EH. An open-label, noncomparative study of miglustat in type I Gaucher disease: efficacy and tolerability over 24 months of treatment. *Clin Ther.* 2005 Aug;27(8):1215-27.
18. Elstein D, Dweck A, Attias D, et al. Oral maintenance clinical trial with miglustat for type I Gaucher disease: switch from or combination with intravenous enzyme replacement. *Blood.* 2007 Oct 1;110(7):2296-301.
19. Patterson MC, Vecchio D, Prady H, Abel L, Wraith JE. Miglustat for treatment of Niemann-Pick C disease: a randomised controlled study. *Lancet Neurol.* 2007 Sep;6(9):765-72.

Cross References
Cerezyme [®] , imiglucerase dru002

Codes	Number	Description
N/A		