Ontario

Ministry of Health
and Long-Term Care

Ontario Public Drug Programs
Exceptional Access Program
Zavesca (miglustat) – Niemann Pick Type C (NPC)
Reimbursement Guidelines

Version 2 – May 2011

The Ministry will consider requests for reimbursement of Zavesca (miglustat) for the treatment of Niemann Pick Type C (NPC).

Please note that patients must be eligible through the Ontario Drug Benefit (ODB) Program in order to receive coverage for this medication. Coverage is not retroactive and reimbursement may only be provided for medications dispensed after Exceptional Access Program (EAP) approval has been granted. In addition, the reimbursement criteria must always be met - even in cases where EAP approval is required to provide continued treatment that was previously supplied through a clinical trial, or paid for by other means (such as a third party payor).

Physicians may use the attached EAP request form to ensure that the necessary clinical information is provided, and to facilitate the review process. Please ensure that all relevant clinical information is provided on the request or by including copies of laboratory results. Requests should be faxed to EAP at (416) 327-7526 or toll free 1-866-811-9908.

Background on Ontario's Drug for Rare Diseases (DRDs) Evaluation Process for Public Drug Reimbursement

The Ontario Ministry of Health has moved forward to develop a funding framework for Drugs for Rare Diseases (DRDs). This approach recognizes that an innovative approach is required that considers the level of available clinical evidence, patient need, and the current funding gap.

In December 2007, Ontario Public Drug Programs (OPDP) established a working group comprised of clinical experts (including genetic medicine) and health economists to develop a new evaluation framework to review and evaluate DRDs for funding by the province.

The new approach is based on the "best available evidence", to assist us in predicting the potential benefit or lack of benefit of a drug treatment in specific groups of patients. This new approach will help identify groups of individuals that may potentially benefit from treatment with a particular drug, and where we may consider funding.

EAP Reimbursement Criteria:

Initial funding for Zavesca (miglustat) under the ODB program may be considered where the patient meets the following criteria:

- Diagnosis of Niemann Pick Type C (NPC) based on the following confirmatory results:
  - NPC 1 and 2 mutational analysis

If there are less than 2 disease associated/pathogenic mutations identified in the NPC 1 or NPC 2 genes, the following additional information is required:

- Lysosomal filipin staining in cultured fibroblasts **OR**
- Fibroblast cholesterol esterification studies

AND

- NPC Functional Disability Rating* of ≥ 5 and ≤ 10. (Score *of 11 or higher is not eligible for miglustat funding)*
  **See Appendix 1 for further details*

- No other life-threatening disease where prognosis is unlikely to be influenced by Substrate Reduction Therapy [SRT] (e.g. neuroblastoma, leukemia etc.)

- Treatment should be carried out in medical centres with expertise in the management of inherited metabolic disorders

- Dosage:

Adults and juveniles (12-17 years old)
200 mg three times a day

Pediatrics (under 12 years of age)
Please refer to the product monograph

- Higher doses will not be funded
- Requests for lower doses to be sent for clinical review by medical geneticist

According to the product monograph for Zavesca (miglustat) there is an 85% chance of diarrhea associated with therapy. Patients are recommended to follow a low carbohydrate diet to mitigate the risk of diarrhea.

Exclusion Criteria:

- Pregnant or lactating patients

If a patient falls under the following categories, the Ministry will NOT consider funding of Zavesca (miglustat) since it is unlikely that SRT therapy will benefit the patient in terms of disease stabilization.

- Patient's life expectancy less than 6 months irrespective of cause

Extension of funding will be considered where the patient meets the following criteria:

- Patient maintains a NPC Functional Disability Rating Score of ≤ 10. [If NPC Functional Disability Score is 11 or higher *that is sustained over 2 consecutive 6 month intervals,* the Ministry should consider withdrawal of funding of SRT therapy]
- Patient must NOT be bedridden where any physical activity brings on discomfort and symptoms which occur at rest AND not amenable to surgical/medical intervention
- No other life-threatening disease where prognosis is unlikely to be influenced by Substrate Reduction Therapy [SRT] (e.g. neuroblastoma, leukemia etc.)
- Patient has not developed a life-threatening complication to SRT not treatable by other therapeutic measures and is unlikely to benefit from further SRT
- Patient has adhered with prescribed dosing protocol for optimal management of the disease
- Patient has adhered to all safety and effectiveness monitoring of the treatment
- Treatment should be carried out in medical centres with expertise in the management of inherited metabolic disorders
- Dosage:

Adults and juveniles (12-17 years old)
200 mg three times a day

Pediatrics (under 12 years of age)
Please refer to the product monograph

- Higher doses will not be funded
- Requests for lower doses to be sent for clinical review by medical geneticist

Patients are recommended to follow a low carbohydrate diet to mitigate risk of diarrhea.

If all the above renewal criteria are not met, the patient may NOT be eligible for continued public funding.

Your feedback is welcomed. Please contact us at:
Ontario Public Drug Programs – Exceptional Access Program
5700 Yonge Street, 3rd Floor, Toronto ON M2M 4K5
Tel: 416-327-8109; Toll-free: 1 866-811-9893
Fax: 416 327-7526; Toll-free: 1 866 811-9908 (EAP requests)
E-mail: EAPFeedback.moh@ontario.ca
Web: www.health.gov.on.ca

***Appendix 1:**
Wraith J. et al. Molecular Genetics and Metabolism 98 (2009) 152-165.

NPC functional disability rating scale

Ambulation	Score	Language	Score
Normal	1	Normal	1
Autonomous ataxic gait	2	Mild dysarthria[d]	2
Outdoor assisted ambulation	3	Severe dysarthria[e]	3
Indoor assisted ambulation	4	Non-verbal communication	4
Wheelchair bound	5	Absence of communication	5
Manipulation	**Score**	**Swallowing**	**Score**
Normal	1	Normal	1
Slight dysmetria/dystonia[a]	2	Occasional dysphagia	2
Mild dysmetria/dystonia[b]	3	Daily dysphagia	3
Severe dysmetria/dystonia[c]	4	NG tube or gastric button feeding	4

Abbreviations: NG, nasogastric
[a] Autonomous manipulation
[b] Requires help for tasks but able to feed self
[c] Requires help for all activities
[d] Understandable
[e] Only comprehensible to certain family members