CANADIAN COORDINATING OFFICE FOR HEALTH TECHNOLOGY ASSESSMENT

OFFICE CANADIEN DE COORDINATION DE L'ÉVALUATION DES TECHNOLOGIES DE LA SANTÉ

CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

MIGLUSTAT
[Zavesca™ -- Actelion]

Description:
Miglustat (Zavesca™) is an oral competitive reversible inhibitor of glucosylceramide synthase, the key enzyme in glucosphingolipid synthesis. Miglustat is intended to reduce the rate of glucosylceramide synthesis. Miglustat is indicated for the treatment of adults with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to constraints such as allergy, hypersensitivity or poor venous access).

Recommendation:
The Canadian Expert Drug Advisory Committee recommends that miglustat not be listed.

Reasons for the Recommendation:
1. The available clinical trials lack adequate control groups and they focus on biochemical, not clinical outcomes. Therefore, there is insufficient evidence that miglustat has a clinically meaningful impact on the key hematologic and bone complications. Moreover, there is insufficient evidence to show whether treatment reduces fatigue, pain, bone complications, or blood product transfusion requirements.

2. In clinical trials, over 90% of patients receiving miglustat experienced diarrhea, and about 50% had weight loss over several weeks of therapy. The extent that diarrhea and weight loss actually diminished over time is not clear because of inadequate patient follow-up.

3. The current standard of care when enzyme replacement therapy is not a therapeutic option includes analgesics, transfusions/bone marrow transplants and measures to prevent or treat fractures and infections. The clinical benefits of miglustat over best supportive therapy to improve quality of life and prevent serious complications must be better supported by valid scientific evidence to justify the estimated $118,700 cost per patient per year.

Of Note:
1. Additional controlled studies are needed to determine the incidence and relationship between cases of neuropathy detected during the extension phase of clinical trials and the dose and duration of therapy.

2. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.