CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

LARONIDASE
(Aldurazyme® - Genzyme Canada Inc.)

Description:
Laronidase is indicated for long-term enzyme replacement therapy in patients with Mucopolysaccharidosis I (MPS I) to treat the non-central nervous system manifestations of the disease. MPS I results from deficiency of L-iduronidase, an enzyme required for degradation of glycosaminoglycans. MPS I is subdivided into three syndromes, distinguished by a heterogeneous collection of clinical signs and symptoms: Hurler (most severe), Hurler-Scheie, and Scheie (mildest).

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that laronidase not be listed.

Reasons for the recommendation:
1. One six-month, double-blind, placebo controlled randomized controlled trial (RCT) in 45 patients reported a 5.6% mean improvement in forced vital capacity (95% CI 1.15-10.05), and a non-statistically significant median change in the six-minute walk test distance of 38.5 m (95% CI -2.0 to 79.0) in the laronidase group. The study also noted a mean reduction in liver size of 20.2% (p=0.001). The clinical significance of these physiological and anatomical measurements is unknown. No differences were noted in quality of life, as measured by the Childhood Health Assessment Questionnaire (in children) or the Health Assessment Questionnaire (in adults).

2. The majority of patients develop antibodies against laronidase. Their significance for benefit, harm, and dose requirements are unknown. In the above noted RCT, mild infusion reactions were common in patients treated with either active medication or placebo. Of the 45 patients from the RCT who enrolled in the open label observational study and received laronidase, one developed a life-threatening infusion reaction requiring emergency tracheotomy.

3. The medication costs between $100,000 and 900,000 per year, depending on patient weight. Given the average weight of patients enrolled in the clinical trial (40kg), the average annual cost for laronidase would be $434,720 per patient.

Of Note:

1. The medication is not effective for the CNS manifestations of MPS I because it does not cross the blood brain barrier.

2. Approximately 50 - 100 patients with MPS I live in Canada.

3. Laronidase has demonstrated a biological effect in a debilitating disease for which management to date has only included symptomatic therapy. However, it has not been demonstrated to result in improvement in clinical endpoints and its administration can result in life threatening adverse events. Using conventional criteria, laronidase is not cost-effective, though this, by itself, is only one of the factors that is used in making a decision about funding. It has been argued that the costs of drugs to treat rare diseases are often high because of the relatively small number of patients for whom the drug is indicated. On the other hand, reimbursement of laronidase would raise questions about equity, since drugs that have not been shown to be cost-effective for other diseases are not generally reimbursed.