AGALSIDASE BETA RESUBMISSION  
(Fabrazyme® – Genzyme Canada)

Description:
Agalsidase beta (Fabrazyme®) is indicated for use in patients with confirmed diagnosis of Fabry disease. It reduces globotriaosylceramide (GL-3) levels in the vascular endothelium.

Recommendation:
CEDAC recommends that agalsidase beta not be listed.

Reasons for recommendation:
1. One 20-week randomized controlled trial (RCT) involving 58 people compared agalsidase beta with placebo and showed reduced interstitial capillary endothelial cell GL-3 levels. However, this trial failed to show a clinical benefit of agalsidase beta on a range of tests of neurologic, renal and cardiac function. The RCT reported no significant improvement in quality of life.

A second unpublished RCT involving 82 patients with a mean follow-up of 18 months compared agalsidase beta with placebo. The primary endpoint was the time to the first occurrence of a “clinically significant” renal, cardiac or cerebrovascular event and/or death. The manufacturer has requested that these results remain confidential, pending publication and pursuant to the Confidentiality Guidelines of the Procedures for CDR.

Two unpublished open-label extension trials of the first RCT mentioned above were also reviewed. In these observational trials, all patients received agalsidase beta for 30 and 42 months, respectively. The manufacturer has requested that these results remain confidential pursuant to the Confidentiality Guidelines of the Procedures for CDR.

Having reviewed all of the information mentioned above, it is CEDAC’s opinion that although this medication affects certain surrogate markers, its impact on clinically meaningful outcomes has not been proven in randomized trials or observational studies.

2. Agalsidase beta is given by intravenous infusion once every two weeks. In clinical trials, infusion reactions occurred in 59% of patients. These reactions occurred despite pre-treating some patients with nonsteroidal anti-inflammatory drugs and antihistamines and the concurrent use of systemic corticosteroids to manage these reactions.
3. The per-patient treatment cost of agalsidase beta is high at $290,599 per year (excluding pharmacy mark-up) for a 70 kg person with Fabry disease. The company provided no evaluation of the cost-effectiveness of agalsidase beta. However, given the drug’s annual cost, and the results of clinical trials to date, agalsidase beta is unlikely to be cost-effective, using conventional criteria.

4. It is not known at what stage of Fabry disease agalsidase beta treatment should be initiated. It is not clear whether this agent will be able to reverse existing damage from Fabry disease, or whether its role will be preventive.

Of Note:
1. It is estimated that there are fewer than 300 people in Canada with Fabry disease, so this disease is rare.

2. To date, there is no treatment that alters the natural course of Fabry disease. Treatment is symptomatic or aimed at the disease’s complications (e.g., dialysis for end-stage kidney disease).

3. Using conventional criteria, agalsidase beta has not been shown to be cost-effective, though this by itself, is only one of the factors that may be used in making a decision about funding. Agalsidase beta has demonstrated a biological effect in a debilitating disease for which patients have no other options to treat their underlying disease. 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 agalsidase beta would raise questions about equity, since drugs that have not been shown to be cost-effective for other diseases are not generally reimbursed.

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