Canadian Expert Drug Advisory Committee
Final Recommendation – Plain Language Version

VELAGLUCERASE ALFA
(VPRIV – Shire Human Genetic Therapies Inc.)
Indication: Gaucher Disease

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that VPRIV, which is also called velaglucerase alfa, be listed for the treatment of type 1 Gaucher Disease (GD1) by Canada's publicly funded drug plans that provide funding for Cerezyme (which is also called imiglucerase), when it is cost saving to do so.

Reasons for the Recommendation:

1. In one small study with 35 patients with GD1, VPRIV was not inferior to imiglucerase in terms of improving the average blood hemoglobin concentration.
2. VPRIV usually costs less than imiglucerase, depending on the patient's weight and the dose required.

Of Note:

1. On a per unit (U) basis, VPRIV ($4.89/U) costs less than imiglucerase ($6.15/U). However, imiglucerase is available in 200 U and 400 U vials (compared with 400 U vials only of VPRIV). Therefore, because the extra drug in the vials has to be thrown away, for some patients, imiglucerase may cost less than VPRIV (e.g., children who weigh less than 10 kg and who need doses of 45 U/kg to 60 U/kg).
2. The Committee noted that VPRIV is not an alternative for patients in whom imiglucerase does not provide enough benefit.

Background:

VPRIV belongs to a class of drugs called enzyme replacement therapies. VPRIV is approved by Health Canada for treatment of children and adults with GD1. It works by replacing the missing enzyme glucocerebrosidase, which breaks down a type of lipid (fat) called glucocerebroside, in adults and children who do not produce enough of the enzyme on their own. The reduced enzyme levels in patients cause this lipid to collect in white blood cells in some organs, including the brain, bone marrow, liver, and spleen. Treatment with VPRIV helps to replace the low enzyme levels, which helps to reduce the lipid deposits. The active ingredient in VPRIV is velaglucerase alfa, which is an enzyme similar to the naturally occurring human enzyme glucocerebrosidase.

VPRIV comes in vials containing 400 U of VPRIV as a powder. After the powder is mixed with liquid, each vial contains 100 U/mL. The dose approved by Health Canada is 60 U/kg, administered every other week as a 60-minute infusion into the vein.

Summary of CEDAC Considerations:

To make its decision, the Committee considered the following information prepared by the Common Drug Review (CDR): a review of the medical studies of VPRIV and a review of economic information prepared by the manufacturer of VPRIV. CEDAC also considered information that patient groups submitted about outcomes and issues important to patients who have the condition for which the drug is indicated, or who might use the drug.

Clinical Trials

CEDAC reviewed one study of patients with GD1. Study HGT-GCB-039 (study 039) was a nine-month study that was conducted in more than one country. It investigated whether infusion of VPRIV 60 U/kg into the vein every two weeks was not inferior to imiglucerase 60 U/kg infusion into the vein every two weeks. Thirty-five patients received either VPRIV or imiglucerase. Most of the patients in the study had not received a previous enzyme replacement therapy for GD1 and had mild anemia (low blood hemoglobin), and also had either thrombocytopenia (low platelet count) or enlarged (swollen) organs. In each treatment group, 6% of patients stopped taking part during the study.

Drawbacks of the study include the small number of patients, the fact that there were different numbers of children under the age of seven years in the two groups, and that the reasoning for the definition of “not inferior” was not clear. In addition, the patients did not have to have symptoms in order to take part in the study, and therefore the results of this study may not be the same for patients with symptoms.

Outcomes

Outcomes were defined in advance in the CDR systematic review protocol. Of these, the Committee discussed the following: blood results, including hemoglobin concentration and platelet count; liver and spleen size changes; quality of life; serious side effects; and side effects. The main purpose of the study was to measure the average change in blood hemoglobin concentration from study start to week 41. If the change in blood hemoglobin concentration with VPRIV was not more than 1 g/dL lower than with imiglucerase, then VPRIV would be found to be not inferior to imiglucerase.

Outcomes of importance identified by patient groups were noticeably missing from the study; these include bone complications, pain, and fatigue.

Results

Efficacy or Effectiveness

- The average blood hemoglobin concentrations improved from the time of study start to week 41 for both treatments (looking at data from all of the patients who started the study): from 11.5 g/dL to 13.1 g/dL in the VPRIV group, and from 10.5 g/dL to 11.9 g/dL in the imiglucerase group. VPRIV was reported to be not inferior to imiglucerase because the difference between the two treatments for the change in blood hemoglobin concentration was 0.136 g/dL. When only data from patients who completed the whole study were used, VPRIV was also found to be not inferior to imiglucerase.

- Platelet counts increased by 77.2% and 110.7% from the time of study start to week 41 in the VPRIV and imiglucerase treatment groups, respectively; statistically, these numbers were about the same.
- Both treatments produced important decreases in liver and spleen volumes from the time of study start to week 41 (–1.1% and –1.3% for imiglucerase and VPRIV, respectively, for the liver, and –2.5% and –1.3% for imiglucerase and VPRIV, respectively, for the spleen); statistically, these numbers were about the same.
- There was no significant improvement in quality of life in either the VPRIV or imiglucerase groups, as measured by the SF-36 health survey (a type of questionnaire used to measure health scores) domain scores, or the physical or mental component summary scores of the SF-36.
- The study was too short to give any useful information about bone complications, which, according to patient groups, can be very bad for patients' quality of life.

Harms (Safety and Tolerability)

- More patients in the VPRIV group had a serious side effect compared with patients in the imiglucerase group (three patients compared with none, respectively). Serious side effects in patients on VPRIV included skin allergic reaction, life-threatening seizures, and very low platelet count.
- No patients stopped taking part in the study because of side effects.
- The most commonly seen side effects, in both VPRIV and imiglucerase groups, included joint pains, fevers, flu, colds, and headaches.

Cost and Cost-Effectiveness

The manufacturer submitted economic information comparing the cost of VPRIV with imiglucerase in individuals with GD1. The data used to support the cost comparison were based on study 039, which showed that VPRIV was not inferior to imiglucerase in terms of change in blood hemoglobin concentration.

The average annual cost of VPRIV ranges from $50,830 to $609,960, depending on the weight of the patient (range: 20 kg to 80 kg) and dose of treatment (range: 30 U/kg to 60 U/kg). Compared with imiglucerase (the only other enzyme replacement treatment available for GD1 in Canada), VPRIV could cost $5,720 more or up to $157,560 less per patient per year, depending on the dose of GD1 treatments and the amount of medication that has to be thrown out.

Patient Input Information:

The following is a summary of information provided by one patient group that responded to the CDR Call for Patient Input:

- Bone complications of GD1 were noted to be very bad for quality of life. In addition, physical symptoms such as pain and fatigue cause significant problems for patients and affect their ability to work and participate in leisure activities.
- A recent shortage of imiglucerase due to shutdown of a manufacturing plant in 2009 resulted in interruptions in treatment and caused significant problems for patients. Patients expect that VPRIV could be used instead of imiglucerase, which would provide some peace of mind in case there were problems with the supply of imiglucerase in the future.

Other Discussion Points:

- While VPRIV appears to improve blood counts and organ enlargement (spleen and liver), these effects in themselves do not usually cause many problems unless the blood counts are very low or the organs are much enlarged. The effect of VPRIV on the duration of life is not known.

CEDAC Members Participating:

Dr. Robert Peterson (Chair), Dr. Michael Allan, Dr. Ken Bassett, Dr. Bruce Carleton, Dr. Doug Coyle, Mr. John Deven, Dr. Alan Forster, Dr. Laurie Mallery, Mr. Brad Neubauer, Dr. Lindsay Nicolle, and Dr. Yvonne Shevchuk.

Regrets:

Dr. Anne Holbrook (Vice-Chair)

Conflicts of Interest:

None

About this Document:

The information contained within this plain language version of the Canadian Expert Drug Advisory Committee (CEDAC) Recommendation about this drug is based on the information found within the corresponding technical version of the CEDAC Recommendation.

In making its recommendation, CEDAC considered the best clinical and pharmacoeconomic evidence available, up to that time. Health care professionals and those requiring more detailed information are advised to refer to the technical version available in the CDR Drug Database on the CADTH website (www.cadth.ca).

Background on CEDAC

CEDAC is a committee of the Canadian Agency for Drugs and Technologies in Health (CADTH). The committee is made up of drug evaluation experts and public members. CEDAC provides recommendations about whether or not drugs should be listed for coverage through the participating publicly funded drug plans; however, the individual drug plans make their own decision about whether or not to cover a drug.

In making its recommendations, CEDAC decides if the drug under review ought to be covered by the participating public drug plans based on an evidence-informed review of the medication's effectiveness and safety, and based on an assessment of its cost-effectiveness in comparison with other available treatments. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CEDAC deliberations.

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The manufacturer has reviewed this document and has not requested the deletion of any confidential information.