Ontario Ministry of Health and Long-Term Care

Ontario Public Drug Programs
Aldurazyme® (laronidase) – Mucopolysaccharidosis Type I (MPS I)
Reimbursement Guidelines

Version 1 – October 2011

The Ministry will consider requests for reimbursement of Aldurazyme® (laronidase) for the treatment of mucopolysaccharidosis type I (MPS I) through the Inherited Metabolic Diseases (IMD) program.

To be eligible for funding, patients are required to meet the specified reimbursement criteria. Patients must also be registered in the IMD program. Copies of the registration form may be downloaded from the IMD program website at http://www.health.gov.on.ca/english/providers/program/drugs/funded_drug/fund_inherited_drug.html

Physicians may use the attached 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 Ontario Public Drug Programs (OPDP) 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 and Long-Term Care has developed a funding framework for Drugs for Rare Diseases (DRDs).

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.

This innovative approach reviews drugs based on "best available evidence" and helps to predict the potential benefit or lack of benefit of a drug treatment in specific groups of patients. The evaluation framework helps to identify individuals who may potentially benefit from a particular drug and where funding may be considered.

For details regarding the Ontario DRD Evaluation Framework, please visit: http://www.health.gov.on.ca/english/providers/program/drugs/how_drugs_approv/review_rare_diseases.html

Reimbursement Criteria:

Initial funding for Aldurazyme® (laronidase) may be considered where the patient meets the following criteria:

Hurler-Scheie Patients:

Diagnosis of Hurler-Scheie based on the following confirmatory results:

- Enzymology testing (α-L-iduronidase deficiency/absence) measured in an appropriate tissue such as leukocytes or cultured skin fibroblasts

AND

- Mutational analysis

AND

- **At least one** of the following clinical features of MPS I:
  - Sleep disordered breathing: patients with an apnea/hypopnea incidence of > 5 events/hour of total sleep time or more than 2 severe episodes of desaturation (oxygen saturation < 80%) in an overnight sleep study
  - Respiratory function tests: patients with **persistent** FVC < 80% of predicted value for height (r*equire 2 measures of FVC < 80% measured within 6 months, at least 1 month apart*)
  - Cardiac: myocardial dysfunction as indicated by a reduction in ejection fraction to less than 56% (normal range 56% - 78%) OR a reduction in fraction shortening to < 25% (normal range 25%-46%)
  - Joint contractures: patients developing restricted range of movement of joints of greater than 15 degrees from normal in shoulders, neck, hips, knees, elbows, or hands

(ALL of the following tests must be provided: overnight sleep study, respiratory function tests, cardiac tests, and joint contracture tests. If there is joint contracture involvement, please indicate the number of joints affected.)

Hurler Patients:

Diagnosis of Hurler based on the following confirmatory results:

- Enzymology testing (α-L-iduronidase deficiency/absence) measured in an appropriate tissue such as leukocytes or cultured skin fibroblasts

AND

- Mutational analysis
  If less than 2 severe mutations are identified, require **at least one** of the following clinical features of MPS I:
  - Sleep disordered breathing: patients with an apnea/hypopnea incidence of > 5 events/hour of total sleep time or more than 2 severe episodes

of desaturation (oxygen saturation < 80%) in an overnight sleep study
- Respiratory function tests: patients with **persistent** FVC < 80% of predicted value for height (r*equire 2 measures of FVC < 80% measured within 6 months, at least 1 month apart*)
- Cardiac: myocardial dysfunction as indicated by a reduction in ejection fraction to less than 56% (normal range 56% - 78%) OR a reduction in fraction shortening to < 25% (normal range 25%-46%)
- Joint contractures: patients developing restricted range of movement of joints of greater than 15 degrees from normal in shoulders, neck, hips, knees, elbows, or hands

AND

- Patient will be undergoing hematopoietic stem cell transplantation (HSCT) **and** shows evidence of significant airway or other cardiopulmonary complications or these complications are anticipated to arise prior to HSCT (r*equire estimated date of HSCT)*

AND

- Patient less than 2 years of age

- Patient has no other life-threatening disease where prognosis is unlikely to be influenced by Enzyme Replacement Therapy [ERT] (e.g. neuroblastoma, leukemia, etc.)

- Treatment should be supervised by medical specialists with expertise in the management of MPS I

- Dosage:
  - 0.58 mg/kg body weight, administered IV weekly
  - Higher doses will not be funded

Duration of approval for Hurler-Scheie patients: 1 year

Duration of approval for Hurler patients: Funding approved until 3 months post HSCT.

Exclusion Criteria:
The following patients are not eligible for funding:
- Scheie patients
- Hurler patients who are not proceeding to HSCT
- Pregnant or lactating Hurler-Scheie patients

If a patient falls under the following categories, the Ministry will NOT consider funding of Aldurazyme® (laronidase) since it is unlikely that ERT therapy will benefit the patient in terms of disease stabilization.
- Patient's life expectancy less than 6 months irrespective of cause
- Patient on chronic invasive mechanical ventilation

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

Hurler-Scheie Patients:

- Patient demonstrates an improvement or stabilization/ no progression of disease activity as indicated by **ALL** of the following clinical features:
  - Sleep disordered breathing
  - Respiratory function tests:
    - Patients < 7 years old: FVC or 6MWT (if available)
    - Patients ≥ 7 years old: FVC or 6MWT (required)
  - Cardiac: ejection fraction OR fraction shortening
  - Joint contractures (require stability or reduction in the number of joints affected as well as signs of stability/improvement in joint contractures based on traditional measures)

Note: Case-by-case consideration will be provided for each individual request.

- 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

- Patient has no other life-threatening disease where prognosis is unlikely to be influenced by Enzyme Replacement Therapy [ERT] (e.g. neuroblastoma, leukemia, etc.)

- Patient has not developed a life-threatening complication to ERT (including severe infusion-related adverse reactions) not treatable by other therapeutic measures and is unlikely to benefit from further ERT

- Patient has adhered with prescribed infusion protocol for optimal management of the disease

- Patient has adhered to all safety and effectiveness monitoring of the treatment

- Treatment should be supervised by medical specialists with expertise in the management of MPS 1

- Dosage:
  - 0.58 mg/kg body weight, administered IV weekly
  - Higher doses will not be funded

Hurler Patients:

No renewals for Hurler patients will be accepted as HSCT transplantation should be completed.

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

Stop Rules for Hurler-Scheie Patients:
Evidence of **persisten**t* disease progression despite regular ERT therapy as indicated by:
- Respiratory function worsens while on ERT therapy, represented by a 15% reduction in % predicted FVC or 6 MWT

OR

- Cardiac dysfunction worsens while on ERT therapy, represented by a 15% reduction in ejection fraction where the cardiac dysfunction is attributable to myocardial weakening not caused by valvular disease.

**If a 15% drop in respiratory function (measured by FVC) or ejection fraction is sustained over 2 consecutive 3 month intervals, patient may not be eligible for continued reimbursement of ERT therapy.*