Canadian HPP Prescribing Guidelines Overview

Asfotase alfa Prescribing Criteria

For enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of perinatal, infantile, and childhood/juvenile-onset hypophosphatasia (HPP). Patients must have documented onset of signs/symptoms of HPP prior to 12 years of age. All requests for ERT with asfotase alfa (Strensiq®) should be first approved by the Canadian HPP Clinical Expert Committee. The province will send the HPP ERT Application Forms with their own complementary forms.

General Preamble

Confirmed diagnosis of perinatal/infantile or juvenile -onset hypophosphatasia (HPP) means:

- Confirmed diagnosis via genetic testing (documented tissue-nonspecific alkaline phosphatase (TNSALP) gene mutations(s) OR
- Serum alkaline phosphatase (ALP) level below the age and sex-adjusted normal range and plasma pyridoxal-5-phosphate (PLP) above the upper limit of normal AND
- Documented HPP- related skeletal abnormalities AND
- Patient is not an adult (18 years) at the time treatment is initiated AND
- Patient does not have odonto- or pseudo- HPP (i.e. craniosynostosis alone, premature loss of deciduous teeth alone and vitamin D deficiency to be ruled out) AND
- Management team/criteria in place that will follow recommendations re initiation, continuation and withdrawal of treatment in all patients approved for treatment including those with severe perinatal HPP

Patients should be initiated on treatment and followed in a specialized clinic with expertise in the diagnosis and management of HPP. Goals of therapy should be developed on a case-by-case basis prior to the initiation of therapy. For all patients with HPP, regardless of age at diagnosis, the pre-specified goals met at initiation of therapy should be reassessed following a trial of 24 weeks of therapy (24-48 weeks, in perinatal HPP); if Continuation Criteria are not met, the treatment should not be continued. 'Withdrawal of treatment criteria' yet to be developed.

Initiation Criteria – Perinatal/Infantile HPP:

- Assessed by a multidisciplinary management team who determines that the criteria noted above have been met as well as documented signs/symptoms that may include failure to thrive, poor growth, vomiting, hypercalcemia, B6-responsive seizures and/or respiratory failure with or without lung hypoplasia, and severe skeletal manifestations of HPP **(Neonatal HPP Management Guidelines)**
- Management team agrees to follow the Guidelines for Management of Severe Perinatal HPP **(Neonatal HPP Management Guidelines)**
- 24-48 week trial to be followed by reassessment by a metabolic specialist and multidisciplinary team, if applicable

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Initiation Criteria – Childhood HPP (after 6 months of age):

- Assessed by a metabolic specialist who determines that the criteria noted above have been met as well as documented signs/symptoms that include gait disturbance, rickets and RGIC score +/-Thacher score, bowing of legs, short stature unexplained by other reasons and, where applicable, pain scale score
- If treatment approved by HPP National Clinical Expert Committee recommends **beginning 24 week trial** , to be followed by reassessment by the referring metabolic specialist who issues report to HPP Clinical Expert committee providing the following information:
    - **24 week assessment** to determine response to treatment
        - Full clinical reassessment with weight, height, head circumference
            - Assess functional status with fait, muscle strength, mobility, pain, with repeat 6MWT and validated questionnaires ideally administered by physiotherapist
            - Quality of Life reassessment using validated questionnaire
            - Review medication history
        - BMI and nutritional health
        - Dental Health – teeth lost or gained
        - Radiographs to assess any healing of HPP skeletal abnormalities
        - Safety Monitoring- monitor, record and report any adverse effects including adverse skin reactions

Continuation Criteria after initial 24 week treatment trial completed:

- Additional 24 week trial (if recommended by Committee) is to be followed by reassessment by a metabolic specialist and further report to the Committee **as above** but in addition
    - Renal Ultrasound yearly
    - Ophthalmologic assessment yearly.
    - DEXA every 2 years
- Thereafter yearly follow-up reports with information as requested above are submitted to Canadian HPP Clinical Expert Committee for continued renewal of drug or reasons for withdrawal.