PreferredOne®ATION POLICY

POLICY: Enzyme Replacement Therapy – Strensiq® (asfotase alfa for subcutaneous use – Alexion Pharmaceuticals, Inc.)

REVIEW DATE: 07/17/2019

OVERVIEW

Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).[1] Strensiq is an enzyme replacement therapy which replaces human tissue non-specific alkaline phosphatase (TNSALP). Strensiq is produced via recombinant DNA technology in Chinese hamster ovary cells. It is a soluble glycoprotein composed of two identical polypeptide chains, each containing TNSALP, bound to the Fc domain of human immunoglobulin G_1 and a deca-aspartate peptide for targeting the bone.

Disease Overview

Hypophosphatasia (HPP) is an inherited metabolic disease caused by a loss-of-function mutation in the gene which codes for TNSALP.[2] TNSALP is tissue bound and expressed in high concentrations in the liver, kidney, neurons, neutrophils, bone and teeth.[2,3] In HPP, inorganic pyrophosphate and pyridoxal 5'-phosphate, substrates for TNSALP, are increased and lead to disease manifestations. Inorganic pyrophosphate is an inhibitor of bone mineralization, and its accumulation leads to rickets and osteomalacia. Pyridoxal 5'-phosphate, a derivative of vitamin B_6, is necessary for the synthesis of gamma aminobutyric acid (GABA). However, for pyridoxal 5'-phosphate to enter the neuron, it must be dephosphorylated to allow pyridoxal to enter the neuron where it is rephosphorylated. The decreased synthesis of GABA in HPP leads to seizures.

HPP is a rare disease, with an estimated live-birth incidence, for the severe forms of HPP, of 1:100,000 in Canada and approximately 1:300,000 in Europe.[2,4] Prevalence in certain populations, such as Canadian Mennonites may be as high as 1:2,500 births. Disease severity can range from neonatal death with almost no skeletal mineralization to dental problems in adults without any bone symptoms.[2-4] In patients most severely affected by HPP, mortality ranges from 50% to nearly 100% during infancy.[2]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Strensiq. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Strensiq as well as the monitoring required for adverse events and long-term efficacy, approval requires Strensiq to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Strensiq is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Hypophosphatasia – Perinatal/Infantile- and Juvenile-Onset.** Approve for 3 years if the patient meets ALL of the following criteria (A, B, C, AND D):
   - **A)** Diagnosis is supported by one of the following (i, ii, or iii):
     - **i.** Molecular genetic testing documenting tissue non-specific alkaline phosphatase (*ALPL*) gene mutation; OR
     - **ii.** Low baseline serum alkaline phosphatase activity; OR
     - **iii.** An elevated level of a tissue non-specific alkaline phosphatase substrate (i.e., serum pyridoxal 5'-phosphate, serum or urinary inorganic pyrophosphate, urinary phosphoethanolamine); AND
   - **B)** Patient meets one of the following (i or ii):
     - **i.** Patient currently has, or has a history of clinical manifestations consistent with hypophosphatasia (e.g., skeletal abnormalities, premature tooth loss, muscle weakness, poor feeding, failure to thrive, respiratory problems, Vitamin B_6-dependent seizures); OR
     - **ii.** Patient has a family history (parent or sibling) of hypophosphatasia without current clinical manifestations of hypophosphatasia; AND
   - **C)** Disease onset ≤ 18 years of age; AND
   - **D)** Strensiq is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of hypophosphatasia or related disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Strensiq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Strensiq® injection [prescribing information]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; January, 2018.
2. White MP. Hypophosphatasia: Enzyme Replacement Therapy Brings New Opportunities and New Challenges. *J Bone Miner Res*. 2017;32:667-675.
3. Orima H. Pathophysiology of Hypophosphatasia and the Potential Role of Asfotase Alfa. *Ther Clin Risk Manag*. 2016;12:777-786.
4. Millan JL, Plotkin H. Hypophosphatasia – Pathophysiology and Treatment. *Actual Osteol*. 2012;8:164-182.

OTHER REFERENCES UTILIZED

- Whyte MP, Greenberg CR, Salman NJ, et al. Enzyme-replacement therapy in life-threatening hypophosphatasia. *N Engl J Med.* 2012;366:904-913.

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Provides free aids and services to people with disabilities to communicate effectively with us, such as:

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If you need these services, contact a Grievance Specialist.

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Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

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