PRIOR AUTHORIZATION POLICY

POLICY: Enzyme Replacement Therapy – Strensiq Prior Authorization Policy
- Strensiq® (asfotase alfa subcutaneous injection – Alexion)

REVIEW DATE: 07/31/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Strensiq, a tissue non-specific alkaline phosphatase (TNSALP), 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 TNSALP.

Disease Overview

HPP is an inherited metabolic disease caused by a loss-of-function pathogenic variant 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.

- **Strensiq® (asfotase alfa subcutaneous injection – Alexion)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Hypophosphatasia – Perinatal/Infantile- and Juvenile-Onset.** Approve for 1 year if the patient meets ALL the following (A, B, C, and D):
   - **A)** Diagnosis is supported by ONE of the following (i, ii, or iii):
     - **i.** Molecular genetic testing documenting pathogenic tissue non-specific alkaline phosphatase (*ALPL*) gene variants; 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; OR
       Note: Examples of clinical manifestations include skeletal abnormalities, premature tooth loss, muscle weakness, poor feeding, failure to thrive, respiratory problems, vitamin B_6-dependent seizures.
     - **ii.** Patient has a family history (parent or sibling) of hypophosphatasia without current clinical manifestations of hypophosphatasia; AND
   - **C)** Disease onset $\leq$ 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 COVERED

- **Strensiq® (asfotase alfa subcutaneous injection – Alexion)**

is(are) considered experimental, investigational, or unproven for ANY other use(s).

REFERENCES

1. Strensiq® subcutaneous injection [prescribing information]. Cheshire, CT: Alexion; July 2024.

2. Whyte 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/26/2023
Annual Revision	**Hypophosphatasia – Perinatal/Infantile- and Juvenile-Onset:** For diagnosis by genetic testing, rephrased the term "mutation" to "pathogenic variant"	07/31/2024