Pharmacy Policy Bulletin: J-0465 Strensiq (asfotase alfa) – Commercial and Healthcare Reform	
Number: J-0465	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization:** 1. Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0465-011	**Original Date:** 12/02/2015
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Strensiq (asfotase alfa)
FDA-Approved Indication(s):	• Treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

Background:	• Strensiq is an enzyme replacement therapy which replaces human tissue non-specific alkaline phosphatase (TNSALP). • HPP is caused by mutations in the ALPL gene, which encodes TNSALP enzyme. The mutations lead to a deficiency in TNSALP, which leads to elevations in several TNSALP substrates, including inorganic pyrophosphate (PPi). Elevated extracellular levels of PPi block hydroxyapatite crystal growth, which inhibits bone mineralization and causes an accumulation of unmineralized bone matrix. Insufficient bone mineralization manifests as rickets and bone deformation in infants and children and as osteomalacia (softening of bones) once growth plates close, along with muscle weakness. Replacement of the TNSALP enzyme, upon Strensiq treatment, reduces the enzyme substrate levels. • Onset of HPP and Signs and Symptoms: ○ Perinatal-onset HPP presents at birth or in utero based on prenatal ultrasound. Signs and symptoms of perinatal HPP include skeletal abnormalities including chest wall deformities, as well as long bones that are short or bowed or both. The skeleton is hypomineralized. ○ Infantile-onset HPP is defined as symptoms appearing at < 6 months of age. Signs and symptoms include delays in gross motor milestones and static myopathy. There is a “failure to thrive” due to delayed weight and growth. Sometimes the skull bones fuse (craniosynostosis), which can lead to a deformed head (brachycephaly) and intracranial hypertension. This leads to bulging of the eyes (proptosis). Radiographs reveal changes consistent with rickets (softened, weakened, and deformed

bones). Other bone abnormalities include chest and rib deformities leading to pulmonary insufficiency and breathing difficulties. Vitamin B6-dependent seizures may occur.
    - Juvenile HPP is defined as symptoms that appear between 6 months and 18 years of age. Sometimes craniosynostosis with intracranial hypertension occurs. Skeletal malformations may become apparent at 2 to 3 years of age. Bone and joint pain may occur. Premature loss of deciduous teeth (before 5 years of age) with the roots intact. There is diminished muscle tone (hypotonia). Some are weak with delayed walking, and then with a distinct, waddling gait.
- Laboratory Tests:
    - The diagnosis of HPP can be confirmed by the identification of either pathogenic biallelic variants of the gene encoding ALPL or a pathogenic heterozygous variant in ALPL. The hallmark laboratory finding in HPP is low alkaline phosphatase (ALP) activity.
    - ALP is an enzyme in the body that is needed for the development of strong, healthy bones. When a person has persistently low ALP, this can contribute to many of the symptoms of HPP including frequent bone injuries and premature tooth loss. A normal ALP result is typically 44 to 147 IU/L or 0.73 to 2.45 µkat/L. ALP levels fluctuate throughout the life cycle. Normal levels in adolescence and pregnancy skew higher.
    - Pyridoxal 5'-phosphate (PLP) are substrates for ALP and are elevated in patients with HPP. PLP is a product of vitamin B6. It is a supportive value for the diagnosis of HPP. A normal PLP result is typically 5 to 50 mcg/L and levels > 100 mcg/L may be suggestive of HPP.
- ICD-10 Code Information:
    - ICD-10: E83.31 “Familial hypophosphatemia” may apply to Strensiq; however, the prescriber must confirm that the member has a specific diagnosis of perinatal/infantile- and juvenile-onset HPP.
- Prescribing considerations:
    - Strensiq should be prescribed by or in consultation with an endocrinologist or a provider who specializes in the treatment of perinatal/infantile-onset HPP or juvenile-onset HPP.
    - The 80 mg/0.8 mL vial of Strensiq should not be used in pediatric patients weighing less than 40 kg.
    - Ophthalmology examinations and renal ultrasounds are recommended at baseline and periodically during treatment with Strensiq to monitor for signs and symptoms of ophthalmic and renal ectopic calcifications and for changes in vision or renal function.
    - A black box warning for hypersensitivity reactions, including anaphylaxis, was added in 2024. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. Only initiate therapy under the supervision of a healthcare provider with appropriate medical monitoring and support measures. If a severe hypersensitivity reaction (for example, anaphylaxis) occurs, discontinue Strensiq and immediately initiate appropriate medical treatment, including the use of epinephrine.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Strensiq may be approved when all of the following criteria are met **(A. through C.):**

A. Strensiq is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a provider who specializes in the treatment of perinatal/infantile- or juvenile-onset hypophosphatasia (HPP).

B. The member has a documented diagnosis of perinatal/infantile- or juvenile-onset HPP (no ICD-10 code) supported by all of the following **(1., 2., and 3.)**:

1. Documentation of ALPL gene mutation(s).

2. Serum alkaline phosphatase (ALP) level below the age-adjusted normal range per the laboratory reference range.

3. Plasma pyridoxal-5'-phosphate (PLP) above the upper limit of normal per the laboratory reference range.

C. The member has a documented history of onset of signs and symptoms of HPP prior to 18 years of age.

II. Reauthorization

When a benefit, reauthorization of Strensiq may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced a positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

- None

References:

1. Strensiq [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; July 2024
2. Whyte MP. Physiological role of alkaline phosphatase explored in hypophosphatasia. *Ann N Y Acad Sci*. 2010; 1192:190-200.
3. Saraff V, Narayanan V, Lawson A, et al. A diagnostic algorithm for children with low alkaline phosphatase activities: lessons learned from laboratory screening for hypophosphatasia. *Journal of Pediatrics*, 2015;172:181-86.
4. Asfotase alfa (Strensiq). Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017. Appendix 7, Natural history of hypophosphatasia. Available from: https://www.ncbi.nlm.nih.gov/books/NBK476057/. Accessed July 9, 2025.
5. National Organization for Rare Disorders. Hypophosphatasia. Available at: https://rarediseases.org/rare-diseases/hypophosphatasia/. Accessed July 9, 2025.
6. Hypophosphatasia. What is the significance of low alkaline phosphatase (ALP)? Available at: https://hypophosphatasia.com/faqs/what-is-the-significance-of-low-alp. Accessed July 9, 2025.
7. Soft Bones. Low ALP: Could it be HPP? Available at: https://softbones.org/low-alkaline-phosphatase-alp/. Accessed July 9, 2025.

8. Mayo Clinic Laboratories. Pyridoxal 5-Phosphate, Plasma. Available at: https://pediatric.testcatalog.org/show/PLP. Accessed July 9, 2025.