Clinical Policy: Asfotase Alfa (Strensiq)

Reference Number: PA.CP.PHAR.328
Effective Date: 01/18
Last Review Date: 10/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by f Pennsylvania Health and Wellness® clinical policy for asfotase alfa (Strensiq™).

FDA Approved Indication(s)
Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that Strensiq is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all):

1. Diagnosis of perinatal/infantile- or juvenile-onset hypophosphatasia (HPP) as evidenced by all of the following (a, b and c):
   a. Age of onset is < 18 years;
   b. Presence of one of the following laboratory indices (i or ii):
      i. Mutation in the ALPL gene encoding for tissue non-specific alkaline phosphatase (TNSALP)*;
      ii. Serum alkaline phosphatase (ALP) below the age-adjusted normal range and either of the following (a or b):
         a) Plasma pyridoxal 5'-phosphate (PLP; main circulating form of vitamin B6) above the upper limit of normal (ULN);
         b) Urinary phosphoethanoloamine (PEA) above the ULN;
   c. History of one of the following HPP clinical manifestations:
      i. Vitamin B6-dependent seizures;
      ii. Failure to thrive or growth failure/short stature;
      iii. Nephrocalcinosis with hypercalcemia/hypercalcuria;
      iv. Skeletal abnormalities and associated impairments (any of the following):
         a) Craniosynostosis (premature fusion of one or more cranial sutures) with increased intracranial pressure;
         b) Rachitic chest deformity (costochondral junction enlargement seen in advanced rickets) with associated respiratory compromise;
         c) Limb deformity with delayed walking or gait abnormality;
         d) Compromised exercise capacity due to rickets and muscle weakness;
         e) Low bone mineral density for age with unexplained fractures;
         f) Alveolar bone loss with premature loss of deciduous (primary) teeth;
2. Prescribed by or in consultation with an endocrinologist;
3. Prescribed dose does not exceed the following (a or b):
   a. Perinatal/infantile-onset HPP: 9 mg/kg in split doses per week;
   b. Juvenile-onset HPP: 6 mg/kg in split doses per week.

**TNSALP is an ALP isoenzyme; a functional mutation in the gene (ALPL) encoding for TNSALP results in low TNSALP activity (as evidenced by a low serum ALP level) and increased levels of TNSALP substrates (PLP and PEA).*

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PMN.53

II. Continued Approval

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;;
2. Member is responding positively to therapy, as evidenced by improvement in any of the following on initial re-authorization request:
   a. Height velocity;
   b. Respiratory function;
   c. Skeletal manifestations (e.g., bone mineralization, bone formation and remodeling, fractures, deformities);
   d. Motor function, mobility, or gait;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Perinatal/infantile-onset HPP: 9 mg/kg per week;
   b. Juvenile-onset HPP: 6 mg/kg per week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;; or
2. Refer to CP.PMN.53

Background

Description/Mechanism of Action:

Strensiq (asfotase alfa) is a soluble glycoprotein composed of two identical polypeptide chains. Each chain consists of the catalytic domain of human tissue non-specific alkaline phosphatase (TNSALP), the human immunoglobulin G1 Fc domain and a deca-aspartate peptide used as a bone targeting domain. Strensiq is a TNSALP produced by recombinant DNA technology in a Chinese hamster ovary cell line. TNSALP is a metallo-enzyme that catalyzes the hydrolysis of phosphomonoesters with release of inorganic phosphate and alcohol. Asfotase alfa has a specific activity of 620 to 1250 units/mg. One activity unit is defined as the amount of asfotase alfa required to form 1 µmol of p-nitrophenol from pNPP per minute at 37°C.

Hypophosphatasia (HPP) is caused by a deficiency in TNSALP enzyme activity, 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 which 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.

Formulations:
Strensiq (asfotase alfa) is a sterile, preservative-free, aqueous solution for subcutaneous administration. Strensiq is supplied in glass single-use vials containing asfotase alfa in the following strengths:

- 18 mg/0.45 mL (0.45 mL)
- 28 mg/0.7 mL (0.7 mL)
- 40 mg/mL (1 mL)
- 80 mg/0.8 mL (0.8 mL)

Appendices

Appendix A: Abbreviation/Acronym Key

ALP: alkaline phosphatase
FDA: Food and Drug Administration
HPP: hypophosphatasia
PEA: phosphoethanolamine
PLP: pyridoxal 5'-phosphate
TNSALP: tissue non-specific alkaline phosphatase
ULN: upper limit of normal

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications
Not applicable

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; added diagnosis confirmation and specialist requirements along with specific criteria for confirmation of positive response to therapy for renewals; references reviewed and updated.	07/18	

References

1. Strensiq Prescribing Information. New Haven, CT: Alexion Pharmaceuticals, Inc.; January 2018. Available at http://strensiq.com/images/Strensiq_PRESCRIBING_INFORMATION.pdf. Accessed July 13, 2018.
2. Beck C, Morback H, Stenzel M. Hypophosphatasia: Recent advances in diagnosis and treatment. Open Bone J. 2009; 1:8-15.
3. Scott LJ. Asfotase alfa in perinatal/infantile-onset and juvenile-onset hypophosphatasia: A guide to its use in the USA. Bio Drugs. 2016; 30:41-48. DOI 10.1007/s40259-016-0161-x.
4. Whyte MP, Rockman-Greenberg C, Ozono K, et al. Asfotase alfa treatment improves survival for perinatal and infantile hypophosphatasia. J Clin Endocrinol Metab. January 2016; 101(1):334-42. doi: 10.1210/jc.2015-3462. Epub 2015 Nov 3.
5. Orimo H. Pathophysiology of hypophosphatasia and the potential role of asfotase alfa. Ther Clin Risk Manag. May 17, 2016; 12:777-86. doi: 10.2147/TCRM.S87956. eCollection 2016.
6. Mornet E, Nunes ME. Hypophosphatasia. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. 2007 Nov 20 [updated 2016 Feb 4]. Available at https://www.ncbi.nlm.nih.gov/books/NBK1150/. Accessed August 30, 2017.
7. Bishop N. Clinical management of hypophosphatasia. Clin Cases miner Bone Metab. 2015; 12(2): 170-173.
8. Kishnani PS, et al. Monitoring guidance for patients with hypophophatasia treated with asfotase alfa. Mol Genetics and Metab. 2017;122:4-17.