Clinical Policy: Asfotase Alfa (Strensiq)

Reference Number: CP.PHAR.328
Effective Date: 03/17
Last Review Date: 03/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® 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 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: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If member has received at least 6 months of treatment, 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.
4. 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.

Approval duration: 6 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

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)

FDA Approved Indications:
Strensiq (asfotase alfa) is a a bone-targeted human recombinant tissue nonspecific alkaline phosphatase (TNSALP) fusion protein (enzyme replacement therapy), available in a subcutaneous injectable formulation, and indicated for:

- Treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

Appendices
Appendix A: Abbreviation Key
HPP: hypophosphatasia
PLP: pyridoxal 5'-phosphate
PEA: phosphoethanoloamine
pNPP: para-nitrophenyl phosphate
PPi: inorganic pyrophosphate
TNSALP: tissue non-specific alkaline phosphatase
ULN: upper limit of normal
ALP: alkaline phosphatase

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
New policy developed, specialist reviewed	1/17	03/17

References
1. Strensiq Prescribing Information. Cheshire, CT: Alexion Pharmaceuticals, Inc.; October 2015. Available

at http://strensiq.com/images/Strensiq_PRESCRIBING_INFORMATION.pdf. Accessed October 10, 2016.
2. Beck C, Morback H, Stenzel M. Hypophosphatasia: Recent advanced 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 October 10, 2016.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.