Strensiq (asfotase alfa) Prior Authorization Program Summary

This program applies to Commercial, GenPlus, NetResults A series, SourceRx, and Health Insurance Marketplace formularies.

OBJECTIVE
The intent of the Strensiq Prior Authorization (PA) Program is to encourage appropriate selection of patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies. Criteria will approve doses that are at or below the maximum FDA labeled dose.

TARGET AGENT
Strensiq (asfotase alfa)

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18 mg/0.45 mL injection	30905610002020	M, N, O, Y
28 mg/0.7 mL injection	30905610002030	M, N, O, Y
40 mg/1 mL injection	30905610002040	M, N, O, Y
80 mg/0.8 mL injection	30905610002050	M, N, O, Y

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Strensiq will be approved when ALL of the following are met:

1. The patient has a diagnosis of either perinatal/infantile- OR juvenile-onset hypophosphatasia (HPP) evidenced by the following:
    A. The patient was ≤ 18 years of age at onset
    AND
    B. The patient has/had clinical manifestations consistent with hypophospatasia at the age of onset prior to age 18 (e.g. vitamin B6-dependent seizures, skeletal abnormalities: such as rachitic chest deformity leading to respiratory problems or bowed arms/legs, "failure to thrive")
    AND
    C. The patient has/had radiographic imaging to support the diagnosis of hypophospatasia at the age of onset prior to age 18 (e.g. infantile rickets, alveolar bone loss, craniosynostosis)
    AND
    D. Molecular genetic test has been completed confirming mutations in the *ALPL* gene that encodes the tissue nonspecific isoenzyme of ALP (TNSALP)
    AND
    E. Reduced activity of unfractionated serum alkaline phosphatase (ALP) in the absence of bisphosphonate therapy (i.e. below the normal lab reference range for age and sex)
    AND
    F. ONE of the following: elevated urine concentration of phosphoethanolamine (PEA), elevated serum concentration of pyridoxal 5'-phosphate (PLP) in the absence of vitamin supplements within one week prior to the test, or elevated urinary inorganic pyrophosphate (PPi)

AND

2. The prescriber is a specialist in the area of the patient's disease (e.g. endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's disease
   AND
3. The patient does not have any FDA labeled contraindication(s) to therapy with Strensiq (asfotase alfa)
   AND
4. The requested quantity is within FDA labeled dosing (prescriber must provide patient's weight)

Length of Approval: 6 months

Renewal Evaluation
Strensiq (asfotase alfa) will be approved when ALL the following are met:

1. The patient has been previously approved for Strensiq (asfotase alfa) through the Prime Therapeutics PA process
   AND
2. The prescriber is a specialist in the area of the patient's disease (e.g. endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's disease
   AND
3. The patient has responded to treatment with Strensiq (asfotase alfa) as evidenced by an improvement and/or stabilization (upon subsequent renewals) respiratory status, growth, or radiographic findings from baseline (documentation from the medical record is required to be submitted)
   AND
4. The patient does not have any FDA labeled contraindication(s) to therapy with Strensiq (asfotase alfa)
   AND
5. The requested quantity is within FDA labeled dosing (prescriber must provide patient's weight)

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[1]

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

Dosing

Perinatal/Infantile-Onset HPP

2 mg/kg subcutaneously three times per week, or 1 mg/kg six times per week. The dose may be increased to 3 mg/kg three times per week for insufficient efficacy.

Juvenile-Onset HPP

2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week.

CLINICAL RATIONALE[1-5]

HPP is the inborn error of metabolism that features low serum alkaline phosphatase (ALP) activity caused by loss-of-function mutation(s) within the gene (*ALPL* gene) that encodes the tissue nonspecific isoenzyme of ALP (TNSALP). TNSALP controls skeletal and dental mineralization by hydrolyzing inorganic pyrophosphate, an inhibitor of hydroxyapatite crystal growth. Insufficient activity can lead to chest wall instability and respiratory complications in perinatal and infantile forms. Natural substrates of TNSALP that accumulate in hypophosphatasia include inorganic pyrophosphate (PPi), phosphoethanolamine (PEA), and pyridoxal 5'-phosphate (PLP), the principal circulating form of vitamin B6.

Perinatal HPP features extreme skeletal disease obvious at birth; survival beyond birth is rare. Infantile HPP develops prior to 6 months of age and has an estimated 50% mortality during infancy typically due to respiratory complications. Patients develop rickets, failure to thrive, hypotonia, myopathy, and is often complicated by hypercalcemia, nephrocalcinosis, craniosynostosis, and vitamin B6-dependent seizures. Although spontaneous improvement sometimes occurs in infantile hypophosphatasia, substantial bone disease and weakness often persist. Skeletal deterioration typically results in death from respiratory insufficiency. In both forms, hypomineralization leads to thoracic instability, fractures, and deformities, and sometimes even pulmonary hypoplasia in perinatal HPP.
Juvenile HPP tends to be less severe than those that appear in infancy. Affected children may have short stature, bowed legs, enlarged wrist and ankle joints (metaphyseal flares that appear as "swollen joints"), muscle weakness, and abnormal skull shape.

Although the disease spectrum is a continuum, six clinical forms are usually recognized based on age at diagnosis and severity of features:

- Perinatal (severe) hypophosphatasia characterized by respiratory insufficiency and hypercalcemia
- Perinatal (benign) hypophosphatasia with prenatal skeletal manifestations that slowly resolve into one of the milder forms
- Infantile hypophosphatasia with onset between birth and age six months of rickets without elevated serum alkaline phosphatase activity
- Childhood (juvenile) hypophosphatasia that ranges from low bone mineral density for age with unexplained fractures to rickets, and premature loss of primary teeth with intact roots

- Adult hypophosphatasia characterized by stress fractures and pseudofractures of the lower extremities in middle age, sometimes associated with early loss of adult dentition
- Odontohypophosphatasia characterized by premature exfoliation of primary teeth and/or severe dental caries without skeletal manifestations

Asfotase alfa is the first approved therapy for perinatal, infantile and juvenile-onset HPP. Improved overall survival and ventilator-free survival was seen with asfotase alfa patients versus historical controls in both perinatal and infantile HPP. Juvenile-onset HPP patients treated with asfotase alfa showed improvements in growth and bone health.

REFERENCES

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2. *J Clin Endocrinol Metab* 2015; Nov 3: jc20153462.
3. *NEJM* 2012; 366: 904-913
4. Mornet, E., et al. Hypophophatasia. Last Update: February 4, 2016. http://www.ncbi.nlm.nih.gov/books/NBK1150/
5. National Organization for Rare Disorders (NORD). Hypophosphatasia. Accessed August 2017.