Asfotase Alfa (Strensiq™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO006

Description

Asfotase alfa is a tissue nonspecific alkaline phosphatase fusion protein considered a form of enzyme replacement therapy.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
asfotase alfa (Strensiq)	18mg/0.45mL vial	infantile, pediatric, or juvenile onset hypophosphatasia	24 vials/28 days	190484
	28mg/ 0.7mL		24 vials/ 28 days	190485
	40mg/ 1 mL vial		24 vials/ 28 days	190486
	80mg/ 0.8 mL vial		24 vials/ 28 days	190488

*See appendix A for dose recommendations

Initial Evaluation

I. Asfotase alfa (Strensiq) may be considered medically necessary when the following criteria below are met:
   A. Diagnosis is made by or in consultation with a geneticist, metabolic specialist, endocrinologist, or bone and mineral specialist; **AND**
   B. A diagnosis of **perinatal/infantile-onset and juvenile-onset hypophosphatasia (HPP)** when the following are met:
      1. Documented tissue-non-specified alkaline phosphatase (TNSALP) gene mutation status; **OR**
      2. Documented serum alkaline phosphatase (ALP) level below the age and gender-adjusted normal range; **AND**
         i. Elevated TNSALP substrate levels as determined by age and gender specific reference range:
            a. Plasma pyridoxal-5'-phosphate (PLP); **OR**
            b. Urine concentration of phosphoethanolamine (PEA); **OR**
            c. Urinary inorganic pyrophosphate level (PPi); **AND**
      3. Onset of perinatal/infantile or juvenile-onset HPP occurring prior to the age of 12, as may be documented by the signs and/or symptoms, which may include, but are not limited to the following:

i. Respiratory insufficiency, vitamin B6 responsive seizures, hypotonia, failure to thrive, delayed walking, waddling gate, dental abnormalities, low-trauma fracture; **OR**
ii. Radiographic evidence supporting the diagnosis of HPP prior to the age of 12 (e.g. craniosynostosis, infantile rickets, non-traumatic fracture); **AND**

4. One of the following
   i. Baseline ophthalmologic examination and renal ultrasound; **OR**
   ii. Provider attestation member will be monitored for ectopic calcification

II. Asfotase alfa (Strensiq) is considered <u>not medically necessary</u> when criteria above are not met and/or when used for:
   A. Adult-onset HPP
   B. Odontohypophosphatasia
   C. Pseudophypophosphatasia
   D. Other forms or causes of osteomalacia: X-linked hypophosphatemia, low bone mass, inappropriate treatment with bisphosphonates, osteoporosis

Renewal Evaluation

II. Renewal of asfotase alfa (Strensiq) may be considered medically necessary when the following criteria below are met:
   A. Diagnosis is made by or in consultation with a geneticist, metabolic specialist, endocrinologist, or bone and mineral specialist; **AND**
   B. A diagnosis of **perinatal/infantile-onset and juvenile-onset hypophosphatasia (HPP)** when the following are met:
      1. Documented tissue-non-specified alkaline phosphatase (TNSALP) gene mutation status; **OR**
      2. Documented serum alkaline phosphatase (ALP) level below the age and gender-adjusted normal range; **AND**
         i. Elevated TNSALP substrate levels as determined by age and gender specific reference range:
            a. Plasma pyridoxal-5'-phosphate (PLP); **OR**
            b. Urine concentration of phosphoethanolamine (PEA); **OR**
            c. Urinary inorganic pyrophosphate level (PPi); **AND**
      3. Onset of perinatal/infantile or juvenile-onset HPP occurring prior to the age of 12, as may be documented by the signs and/or symptoms, which may include, but are not limited to the following**:**
         i. Respiratory insufficiency, vitamin B6 responsive seizures, hypotonia, failure to thrive, delayed walking, waddling gate, dental abnormalities, low-trauma fracture; **OR**

ii. Radiographic evidence supporting the diagnosis of HPP prior to the age of 12 (e.g. craniosynostosis, infantile rickets, non-traumatic fracture); **AND**

4. One of the following:
   i. Documentation of recent ophthalmologic examination and renal ultrasound, in addition to baseline; **OR**
   ii. Provider attests to the continuance of monitoring for ectopic calcifications.

AND

C. The documentation of a positive response to therapy with asfotase alfa, which may include the improvement and/or stabilization (upon subsequent renewals) in the clinical signs and symptoms of hypophosphatasia.

Supporting Evidence

I. Perinatal/infantile and juvenile-onset HPP are the pediatric variants of hypophosphatasia, which is a rare, genetic disorder that impairs bone metabolism. Associated with a high mortality rate, survival rate has been estimated at less than 50% by one year of age in infancy due to rachitic deformities developed by six months of age; the diagnosis is lethal in the perinatal setting. Juvenile HPP is associated with premature loss of deciduous teeth, delayed walking and waddling gait. Due to the risk of fractures, bone deformities and failure to thrive, there is risk for abnormal growth and development in pediatric patients diagnosed with perinatal/infantile or juvenile-onset HPP.

- Approval by the FDA was based on three pivotal trials (ENB-002-08/ENB-003-08, ENB-010-10, and ENB-006-09/ENB-008-10) conducted in 13 pediatric patients (five subjects with perinatal/infantile-onset HPP; eight subjects with juvenile-onset HPP).
  i. A Kaplan-Meier analysis of pooled overall survival data (n=68) was compared with a natural history group (n=48). This analysis showed an overall survival rate of 91% (n=68) of treated subjects when compared with 27% (n=48) of the historical control group.
  ii. In the juvenile-onset population, efficacy was assessed based on the Tinetti Modified Performance Oriented Mobility Assessment – Gait (mPOMA-G) scale. It was agreed by the FDA that change-in-gate is considered a surrogate marker and is not interpreted as an improvement in clinical outcome. Radiographic analysis showed improvement in all subjects with treatment however, using change in rickets severity and assess by the Radiographic Global Impression of Change (RGI-C) scale, when compared to control group.
- HPP is a broadly expressed disorder ranging from death to arthropathy without bone disease. Prognosis is largely based on skeletal complications, with the most severe disease affecting patients with perinatal/infantile or juvenile-onset of HPP.

- Adult-onset hypophosphatasia is characterized by poor healing, bone pain, recurrent fracture and increased incidence of pyrophosphate arthropathy and chondrocalcinosis. As onset presents during middle-age, the benefit of enzyme replacement is unknown in the adult population.
- The presence of a defective TNSALP allele without sign or symptoms of dental or arthritic complications determines helps determine the patient is a carrier only.
- Ectopic calcification has been reported. Per label, monitoring for ectopic calcification by means of ophthalmic examination and renal ultrasound is recommended at baseline and periodically during treatment.

Investigational or Not Medically Necessary Uses

I. Adult-onset HPP
   A. Asfotase alfa (Strensiq) is FDA-indicated for the treatment of members with perinatal/infantile- and juvenile-onset HPP; these populations are known to have the most severe disease and the benefit of enzyme replacement therapy is supported by data.
   B. There are limited to no research studies to support the efficacy of asfotase alfa (Strensiq) in the setting of adult-onset HPP without history of infantile and/or juvenile onset HPP. Evidence is currently limited to case-reports only.
   C. Adult-onset HPP treatment is currently limited to supportive therapy.

II. Odontohypophosphatasia
   A. Odontohypophosphatasia, expressed in dental complications alone, is the mildest and most prevalent form of hypophosphatasia. This diagnosis is typically associated with otherwise normal and/or good health condition.

III. Pseudohypophosphatasia
   A. Resembles infantile hypophosphatasia, however, without low serum alkaline phosphatase. Use of age-dependent reference range is important to differentiate between infantile-onset and pseudohypophosphatasia, or simply a transient elevation in TNSALP substrate.
   B. Causes of pseudohypophosphatasia can include, but are not limited to: cardiac bypass surgery, Celiac disease, Cushing syndrome, hypothyroidism, multiple myeloma, starvation, certain vitamin or mineral deficiencies or intoxications, or improperly collected blood sampling.

IV. Other forms or causes of osteomalacia: X-linked hypophosphatemia, low bone mass, inappropriate treatment with bisphosphonates, osteoporosis.

Appendix A:

Weight-Based Dosing for Administration of **2 mg/kg** three times per week

Body Weight (kg)	Dose to Inject	Volume to Inject	Vial Configuration	Number of Vials per 28 days

3	6 mg	0.15 mL	18mg/0.45mL	12
4	8 mg	0.2 mL	18mg/0.45mL	12
5	10 mg	0.25 mL	18mg/0.45mL	12
6	12 mg	0.3 mL	18mg/0.45mL	12
7	14 mg	0.35 mL	18mg/0.45mL	12
8	16 mg	0.4 mL	18mg/0.45mL	12
9	18 mg	0.45 mL	18mg/0.45mL	12
10	20 mg	0.5 mL	28mg/0.7kmL	12
15	30 mg	0.75 mL	40mg/mL	12
20	40 mg	1 mL	40mg/mL	12
25	50 mg	1.25 mL	Two 28mg/0.7mL	24
30	60 mg	1.5 mL	Two 40mg/mL	24
35	70 mg	1.75 mL	Two 40mg/mL	24
40	80 mg	0.8 mL	80mg/0.8mL	12
50	100 mg	1 mL	Two 80mg/0.8mL	24
60	120 mg	1.2 mL	Two 80mg/0.8mL	24
70	140 mg	1.4 mL	Two 80mg/0.8mL	24
80	160 mg	1.6 mL	Two 80mg/0.8mL	24

Weight-Based Dosing for Administration of **1 mg/kg** six times per week

BodyWeight (kg)	Dose to Inject	Volume to Inject	VialConfiguration	Number of Vials per 28 days
3	3 mg	0.08 mL	18mg/0.45mL	24
4	4 mg	0.1 mL	18mg/0.45mL	24
5	5 mg	0.13 mL	18mg/0.45mL	24
6	6 mg	0.15 mL	18mg/0.45mL	24
7	7 mg	0.18 mL	18mg/0.45mL	24
8	8 mg	0.2 mL	18mg/0.45mL	24
9	9 mg	0.23 mL	18mg/0.45mL	24
10	10 mg	0.25 mL	18mg/0.45mL	24
15	15 mg	0.38 mL	18mg/0.45mL	24
20	20 mg	5 mL	28mg/0.7mL	24
25	25 mg	1.63 mL	28mg/0.7mL	24
30	30 mg	0.75 mL	40mg/mL	24
35	35 mg	0.88 mL	40mg/mL	24
40	40 mg	1 mL	40mg/mL	24
50	50 mg	0.5 mL	80mg/0.8mL	24
60	60 mg	1.6 mL	80mg/0.8mL	24
70	70 mg	0.7 mL	80mg/0.8mL	24
80	80 mg	0.8 mL	80mg/0.8mL	24

References

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Policy Implementation/Update:

Date Created	November 2015
Date Effective	August 2017
Last Updated	September 2019
Last Reviewed	September 2019

Action and Summary of Changes	Date
Transfer to policy format. Added NMC and Supportive Evidence sections. Addition of criterion for appropriate diagnosis, as is recommended by compendia and medical literature. Addition of requirement of diagnosis by a specialist: diagnosis requires assessment of multiple laboratory levels, and combined/compared with clinical presentation. Potential for differential diagnosis is high. Change to initial approval of six months and renewal at 12 months from 3 month initial approval and 6 month renewal. As the overall benefit of Strensiq is seen over the course of pediatric development, a longer renewal period was implemented.	09/2019