09-J2000-58

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Reviewed: 12/08/21

Revised: 01/15/22

Subject: Asfotase alfa (Strensiq®)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Hypophosphatasia (HPP) is a rare inherited metabolic disorder caused by a number of loss-of-function mutations in the *ALP* gene, which encodes the tissue nonspecific isozyme of alkaline phosphatase (TNSALP). These mutations affect bone and mineral metabolism. Clinical presentation of an HPP patient may be highly variable by age. The disease is progressive and potentially life-threatening, leading to progressive and debilitating damage to multiple vital organs, as well as bone deformity, pain and muscle weakness, respiratory failure, seizures. Based on the age at diagnosis of skeletal disease, four types have been identified: perinatal, infantile, juvenile, and adult types of HPP. Another form of HPP has also been reported in the literature in which only dental features without skeletal findings have been described; this type is referred to “odonto-HPP.” Estimated prevalence of perinatal and infantile HPP is 1 in 100,000 newborns. Infants exhibiting symptoms within the first 6 months of life have an overall mortality of 73% at 5 years. There are currently no FDA-approved medications for HPP other than supportive treatments.

Asfotase alfa (Strensiq), a human recombinant alkaline phosphatase (ALP) fusion protein, was approved by the U.S. Food and Drug Administration (FDA) in October 2015 for the treatment of patients with perinatal/infantile- and juvenile-onset HPP.

In two prospective studies of perinatal- or infantile-onset hypophosphatasia, asfotase alfa significantly improved overall survival compared with a historical control of untreated patients at age 1 year (97% (n=68) vs 42% (n=48)), and the percentage of patients alive at point of last contact was higher with asfotase alfa use (91% vs 27%); additionally, asfotase alfa significantly improved survival without the need for a ventilator (96% (n=54) vs 31% (n=48)) at age 1 year, and the percentage of patients not on ventilation at point of last contact was also higher with asfotase alfa use (85% vs 25%). In patients requiring any form of respiratory support, 21 of 26 (81%) were alive at the last assessment (median age at assessment, 3.2 years) compared with 1 of 20 (5%) of historical controls. Combined data from 64

perinatal- or infantile-onset and 4 juvenile-onset hypophosphatasia patients showed by month 24, 74% of patients who received asfotase alfa were considered Radiographic Global Impression of Change responders (n=68, minimum increase of 2 on scale), and height and weight improved (as measured by z-score) (n=72).

Asfotase alfa increased height and weight (as measured by z-scores) in juvenile-onset hypophosphatasia patients (n=8; aged 6 to 12 years) compared with a historical cohort of untreated patients (n=32) in a 24-week prospective trial followed by an extension trial for at least 48 months. All patients who received asfotase alfa were considered Radiographic Global Impression of Change responders (minimum increase of 2 on scale) by month 54 compared with 6% of control patients after 56 months. An increase in step length by at least 1 point in either foot was also noted in 6 of 8 patients who received asfotase alfa compared with 1 of 6 control patients. The percent predicted normal values of the 6-minute walk test improved from 0% at baseline (0 of 8 patients) to 100% (6 of 6 patients) by month 48.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of asfotase alfa (Strensiq) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with any of the following:
    a. Perinatal/infantile-onset hypophosphatasia (HPP)
    b. Juvenile-onset hypophosphatasia (HPP)
2. Member's diagnosis of HPP is confirmed by or in consultation with an endocrinologist or a bone and mineral specialist
3. Member has skeletal abnormalities indicative of HPP – documentation from the medical record must be provided
    a. Note: Examples of skeletal abnormalities include chest wall deformities, hypomineralized skeleton, rickets, nonhealing fractures.
4. Member has an alkaline phosphatase (ALP) level below age-adjusted lower limit of normal (table 1) – laboratory documentation must be provided
5. Member has a pyridoxal-5'-phosphate (PLP) level greater than two times laboratory's upper limit of normal – laboratory documentation must be provided
6. Member has an ALPL genetic mutation – laboratory documentation must be provided
7. Member has an onset of clinical signs and symptoms of HPP prior to 12 years of age – documentation from the medical record must be provided
8. Strensiq is prescribed by or in consultation with an endocrinologist or a bone and mineral specialist
9. Dose does not exceed 6 mg/kg/week

Approval duration: 6 months

Continuation of asfotase alfa (Strensiq) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue for treatment of perinatal/infantile- or juvenile-onset HPP **OR** the member has previously met all indication-specific initiation criteria
2. Member's diagnosis of HPP is confirmed by or in consultation with an endocrinologist or a bone and mineral specialist
3. Member has an ALPL genetic mutation – laboratory documentation must be provided
4. Member has demonstrated a clinical improvement in symptoms following initiation of asfotase alfa – documentation from the medical record must be provided
5. Strensiq is prescribed by or in consultation with an endocrinologist or a bone and mineral specialist
6. Dose does not exceed:
    a. Perinatal/infantile-onset HPP: 9 mg/kg/week
    b. Juvenile-onset HPP: 6 mg/kg/week

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Perinatal/Infantile-Onset HPP
    - Recommended dosage regimen is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.
    - The dose may be increased to 3 mg/kg three times per week for insufficient efficacy.
- Juvenile-Onset HPP
    - Recommended dosage regimen is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.

Dose Adjustments

- None

Drug Availability

- Injection: 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, or 80 mg/0.8 mL solution in single-use vials

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Hypersensitivity Reactions
- Lipodystrophy
- Ectopic Calcifications (eye and kidneys)
- Possible Immune-Mediated Clinical Effects

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)
J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

E83.31	Familial hypophosphatemia [perinatal/infantile-hyphen and juvenile-onset hypophosphatasia (HPP)]
E83.39	Other disorders of phosphorus metabolism

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

Table 1. Reference Intervals for Total ALP Activity in Serum or Plasma

Age	Male/Female Reference Intervals (U/L)*
<1 month	60-320
1-11 months	70-350
1-3 years	125-320
4-6 years	150-370
7-9 years	150-440
10-11 years	150-470/150-530
12-13 years	160-500/110-525
14-15 years	130-530/55-305
16-19 years	60-270/40-120
20 years and older	40-120
* Adapted from ARUP Laboratories	

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/08/21.

GUIDELINE UPDATE INFORMATION:

03/15/16	New Medical Coverage Guideline.
03/15/17	Review and revision to guideline; position statement, references.
01/15/18	Review and revision to guideline; position statement, references.
01/15/19	Review and revision to guideline; references.
01/15/20	Review and revision to guideline; references
01/15/21	Review and revision to guideline; references, coding, and position statement
01/15/22	Review and revision to guideline; position statement, references