Reference number(s)
1974-A

SPECIALTY GUIDELINE MANAGEMENT

STRENSIQ (asfotase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

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

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initiation of therapy:
   1. Documentation of presence of condition before the age of 18, if applicable
   2. Documentation confirming diagnosis which includes one of the following:
      a. Genetic testing results confirming a mutation in the *ALPL* gene, or
      b. Submission of ALL of the following:
         i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
         ii. A serum alkaline phosphatase (ALP) level below the gender and age-specific reference range of the laboratory performing the test
         iii. Elevated tissue non-specific alkaline phosphatase (TNSALP) substrate level (i.e., serum pyridoxal 5-phosphate (PLP) level, serum or urine proximity extension immunoassay (PEA) level, urinary inorganic pyrophosphate (PPi) level)

B. Continuation of therapy:
   Medical records of at least one of the following:
   1. Radiographic Global Impression of Change (RGI-C) rating
   2. Height and weight measurements as measured by z-scores
   3. Modified Performance Oriented Mobility Assessment-Gait (MPOMA-G) score
   4. Distance walked in the 6 Minute Walk Test (6MWT)

III. CRITERIA FOR INITIAL APPROVAL

Perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)
Authorization of 12 months may be granted for treatment of HPP when all of the following criteria are met:

A. The member has clinical signs and/or symptoms of hypophosphatasia (See Appendix A).
B. The onset of the disease was perinatal/infantile or juvenile. If the member is 18 years of age or older at the time of the request, documentation of the presence of the condition before the age of 18 must be provided (e.g., member began experiencing symptoms at age 10).

C. The diagnosis was confirmed by one of the following (1 or 2):
   1. The presence of a known pathological mutation in the *ALPL* gene as detected by *ALPL* molecular genetic testing
   2. The diagnosis is supported by ALL of the following:
      a. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
      b. A serum alkaline phosphatase (ALP) level below the gender- and age-specific reference range of the laboratory performing the test
      c. Elevated tissue-nonspecific alkaline phosphatase (TNSALP) substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPi level)

D. Member's weekly dose will not exceed the following:
   1. 9 mg/kg weekly in a member with perinatal/infantile-onset HPP
   2. 6 mg/kg weekly in a member with juvenile-onset HPP

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit when both of the following are met:

A. Member is experiencing benefit from therapy as demonstrated by one of the following:
   1. Member has experienced improvement in skeletal manifestations from baseline as assessed by the Radiographic Global Impression of Change (RGI-C) scale
   2. Member is less than 18 years of age and has experienced an improvement in height and weight compared to baseline, as measured by z-scores
   3. Member has experienced an improvement in step length by at least 1 point in either foot compared to baseline based on the Modified Performance Oriented Mobility Assessment-Gait (MPOMA-G) scale
   4. Member has experienced an improvement in 6 Minute Walk Test compared to baseline

B. Member's weekly dose will not exceed the following:
   1. 9 mg/kg weekly in a member with perinatal/infantile-onset HPP
   2. 6 mg/kg weekly in a member with juvenile-onset HPP

V. APPENDIX

Appendix A. Examples of Signs and Symptoms of HPP

A. Perinatal/infantile-onset HPP:
   - Generalized hypomineralization with rachitic features, chest deformities and rib fractures
   - Skeletal abnormalities (e.g., short limbs, abnormally shaped chest, soft skull bone)
   - Respiratory problems (e.g., pneumonia)
   - Hypercalcemia
   - Failure to thrive
   - Severe muscular hypotonia and weakness
   - Nephrocalcinosis secondary to hypercalciuria
   - Swallowing problems
   - Seizures

B. Juvenile-onset HPP:
   - Premature loss of deciduous teeth
   - Failure to thrive with anorexia, nausea, and gastrointestinal problems
   - Short stature with bowed legs or knock knees
   - Skeletal deformities (e.g., enlarged wrist and ankle joints, abnormal skull shape)

- Bone and joint pain
- Rickets
- Fractures
- Delayed walking
- Waddling gait

Appendix B. Examples of Radiographic Findings that Support HPP Diagnosis

- Infantile rickets
- Alveolar bone loss
- Focal bony defects of the metaphyses
- Metatarsal stress fractures
- Osteomalacia with lateral pseudofractures
- Osteopenia, osteoporosis, or low bone mineral content for age (as detected by dual-energy x-ray absorptiometry [DEXA])

VI. REFERENCES

1. Strensiq [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; June 2020.
2. Bianchi ML. Hypophosphatasia: an overview of the disease and its treatment. *Osteoporos Int.* 2015; 26(12):2743-57.
3. Mornet E, Nunes ME. Hypophosphatasia. GeneReviews [Internet]. Available at http://www.ncbi.nlm.nih.gov/books/NBK1150 Updated February 4, 2016. Accessed August 5, 2021.
4. Whyte, MP. Hypophosphatasia: An overview for 2017. Bone. 2017;102:15-25.