Strensiq (asfotase alfa)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Strensiq (asfotase alfa) drug policy is to ensure the safe, clinically appropriate and cost-effective use of Strensiq while maintaining optimal therapeutic outcomes.

Strensiq is a tissue nonspecific alkaline phosphatase approved by the Food and Drug Administration (FDA) for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

POLICY

Required Documentation

The following information is necessary to initiate the prior authorization review:

- *ALPL* molecular genetic testing results
- Serum alkaline phosphatase (ALP) level
- Tissue-nonspecific alkaline phosphatase (TNSALP) substrate level (ie, serum pyridoxal 5'-phosphate [PLP] level, serum or urine phosphoethanolamine [PEA] level, urinary inorganic pyrophosphate [PPi] level)

Initial Criteria for Approval

I. Strensiq (asfotase alfa) may be considered **medical necessary** for the treatment of HPP when ALL of the following criteria are met:
   - Diagnosis must be made by or in consultation with a geneticist, metabolic specialist, endocrinologist or bone and mineral specialist
   - The patient has clinical signs and/or symptoms of hypophosphatasia (See Appendix A)
   - The onset of the disease was perinatal/infantile or juvenile

- The diagnosis was confirmed by the presence of mutation(s) in the ALPL gene as detected by ALPL molecular genetic testing OR the diagnosis is supported by ALL of the following:
  - Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
  - A serum alkaline phosphatase level below the gender- and age-specific reference range of the laboratory performing the test
  - Elevated TNSALP substrate level (ie, serum PLP level, serum or urine PEA level, urinary PPi level)
  - The member does not have a known negative genetic test result for mutation of the ALPL gene

Approval will be for **6 months**

Continuation of Therapy

II. Strensiq (asfotase alfa) may be considered **medically necessary** for the **continuation of** treatment of HPP when ALL of the following criteria are met:
- Patient must meet initial criteria for approval above; **AND**
- The patient has responded to therapy with Strensiq with an improvement and/or stabilization (upon subsequent renewals) in clinical signs and/or symptoms of hypophosphatasia (i.e. respiratory status, radiographic findings, growth)

Approval will be for **12 months**

III. Strensiq (asfotase alfa) is considered **not medically necessary** for patients who do not meet the criteria set forth above.

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 (eg, short limbs, abnormally shaped chest, soft skull bone)
- Respiratory problems (eg, 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 (eg, 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])

CLINICAL RATIONALE

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. The disease is progressive and can be potentially life-threatening, leading to progressive and debilitating damage to multiple vital organs, as well as bone deformity, pain and muscle weakness, respiratory failure, and seizures. Based on the age at diagnosis, 4 types have been identified: perinatal, infantile, childhood, and adult types of HPP. The presenting signs and symptoms of hypophosphatasia depend upon the age of presentation and vary from death *in utero* to relatively simple problems with dentition in adult life. Disease severity is inversely related to the age at onset. 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. The prevalence of later-onset HPP is unknown because symptoms may not be recognized.

Strensiq (asfotase alfa) was granted breakthrough therapy designation, orphan drug designation, and a rare pediatric disease priority review voucher by the FDA on October 23, 2015. Strensiq is the first recombinant fusion protein, and TNSALP approved for the treatment of patients with perinatal/infantile- and juvenile-onset HPP. Results from four prospective, open-label studies in 99 patients with perinatal-, infantile-, or juvenile-onset HPP demonstrated the safety of Strensiq (asfotase alfa), improved overall survival, improved ventilator-free survival, and improved radiographic changes compared with a historical cohort of untreated patients. Strensiq (asfotase alfa) is not associated with any significant adverse events, although injection site reactions are common. Strensiq (asfotase alfa) provides the first available treatment for perinatal/infantile- and juvenile-onset HPP.

Additionally, since Strensiq's FDA approval in 2015, multiple clinical trials conducted globally have demonstrated the short and long-term safety and efficacy of Strensiq in adult and pediatric patients with perinatal/infantile- and juvenile-onset HPP.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD Diagnostic Codes.

- N/A

REFERENCES

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POLICY HISTORY

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