Medical Drug Clinical Criteria

Subject:	Strensiq (asfotase alfa)		
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Overview

This document addresses the use of Strensiq (asfotase alfa), a tissue nonspecific alkaline phosphatase (TNSAP) recombinant isozyme developed to target underlying genetic causes of hypophosphatasia (HPP). Strensiq is indicated for the treatment of perinatal/infantile- and juvenile-onset HPP. HPP is a rare inherited error of metabolism caused by mutations of the alkaline phosphatase (ALPL) gene that results in deficient activity of alkaline phosphatase and low levels of the enzyme in serum and bone. This condition disrupts mineralization, in which minerals such as calcium and phosphorus are deposited in developing bones and teeth.

Examples of signs and symptoms of HPP in perinatal/infantile-onset HPP include:

- 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

Examples of signs and symptoms in juvenile-onset HPP include:

- 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

Prior to the development of Strensiq, there was no specific treatment for HPP. The mortality rate for infants and children is 50-100%. FDA approval was based on four ongoing prospective, open-label studies of treatment with Strensiq using historical controls. The ongoing studies are focused on disease development in two areas: perinatal in utero/infantile (less than 6 months of age) and childhood (greater than or equal to 6 months of age).

From the package label, a prospective open-label 24-week trial included 8 juvenile-onset HPP patients and 5 perinatal/ infantile-onset HPP patients, 6 to 12 years of age. All 8 juvenile-onset patients entered the extension study and were treated for at least 48 months. Patients who achieved a Radiolographic Global Impression of Change (RGI-C) score of 2 or higher (corresponding to substantial healing of rickets) were classified as being responders to treatment. All 8 treated patients were rated as responders by Month 54 of treatment. At last assessment, 2/32 (6%) of control patients were rated as responders. Eight of 20 (40%) control patients with juvenile-onset HPP experienced new fractures during the course of treatment. There were insufficient data to assess the effect of Strensiq on fractures. In gait/mobility by month 48, 6 of the 8 treated patients were able to walk longer distances at this time point compared to baseline gait/mobility,

Strensiq has been reported to cause localized lipodystrophy at injection sites after several months of treatment. Patients are advised to rotate injection sites and follow proper injection technique. In clinical trials, Strensiq patients reported signs of ectopic calcification of the

eye including the cornea and conjunctiva, and the kidneys. Ophthalmology examinations and renal ultrasounds are recommended at baseline and periodically during treatment.

Strensiq has a boxed warning for anaphylaxis, which anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. It is advised to initiate Strensiq under the supervision of a healthcare provider with appropriate monitoring and support measures. If a severe hypersensitivity reaction (e.g. anaphylaxis) occurs, discontinue Strensiq and immediately initiate appropriate medical treatment, including the use of epinephrine.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Strensiq (asfotase alfa)

Initial requests for Strensiq (asfotase alfa) may be approved when the following criteria are met:

I. Individual has a diagnosis of one of the following:
   A. Individual has a diagnosis of perinatal/infantile hypophosphatasia (HPP), and had onset of symptoms prior to 6 months of age (Whyte 2012); **OR**
   B. Individual has a diagnosis of juvenile-onset HPP, and had onset of disease ≤ 18 years of age;

AND

II. Documentation is provided that individual's total serum alkaline phosphatase level is below the lower limit of normal for the individual's age and gender at diagnosis (Whyte 2012); **AND**

III. Documentation is provided that individual has plasma pyridoxal 5'-phosphate levels greater than the upper limit of normal at the time of diagnosis (Whyte 2012); **AND**

IV. One of the following:
   A. Radiographic evidence of poor bone mineralization including flared and frayed metaphyses, severe/generalized osteopenia or widened growth plates (Whyte 2012); **OR**
   B. Genetic test results that confirm infantile HPP; **OR**
   C. One of the following:
      1. History or presence of nontraumatic postnatal fracture healing; **OR**
      2. History of elevated serum calcium; **OR**
      3. Functional craniosynostosis with decreased head circumference growth; **OR**
      4. Nephrocalcinosis; **OR**
      5. Rachitic chest deformity; **OR**
      6. Respiratory compromise; **OR**
      7. Vitamin B6-responsive seizures; **OR**
      8. Failure to thrive.

Continuation requests for Strensiq (asfotase alfa) may be approved if the following criteria are met:

I. Individual met the criteria above at the time of initiation; **AND**

II. There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limit to respiratory status, radiographic findings, growth) following asfotase alfa therapy.

Strensiq may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs [when specified as Strensiq (asfotase alfa)]

ICD-10 Diagnosis

E83.31	Familial hypophosphatemia
E83.39	Other disorders of phosphorus metabolism

Document History

Revised: 12/09/2024
Document History:

- 12/09/2024 – Annual Review: Added reference. Wording and formatting changes. Coding Reviewed: No changes.
- 12/11/2023 – Annual Review: Minor wording and formatting changes. Coding Reviewed: No changes.
- 12/12/2022 – Annual Review: Minor wording and formatting changes. Coding Reviewed: No changes.
- 12/13/2021 – Annual Review: Update criteria language to reflect Strensiq's use in juvenile-onset disease. Update criteria language for consistency. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 12/14/2020 – Annual Review: Clarify initial request criteria vs. continuation criteria. Coding Review: No changes.
- 11/15/2019 – Annual Review: Minor wording and formatting changes. Coding Reviewed: No changes
- 11/16/2018 – Annual Review: Initial P&T review of Strensiq clinical guideline. Update criteria with references. HCPCS and ICD-10 coding review: no changes.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
4. Whyte MP, Greenberg CR, Salman NJ, et al. Enzyme-replacement therapy in life-threatening hypophosphatasia. N Engl J Med. 2012; 366(10):904-913.
5. Whyte MP, Madson KL, Phillips D, et al. Asfotase alfa therapy for children with hypophosphatasia. *JCI Insight* 2016; 1(9):e85971. Available at: https://df6sxcketz7bb.cloudfront.net/manuscripts/85000/85971/cache/85971.2-20160727111116-covered-253bed37ca4c1ab43d105aefdf7b5536.pdf
6. Whyte MP, Rockman-Greenberg C, Ozono K, et al. Asfotase alfa treatment improves survival for perinatal and infantile hypophosphatasia. J Clin Endocrinol Metab. 2016; 101(1):334-342.
7. Whyte MP, Zhang F, Wenkert D, et al. Hypophosphatasia: validation and expansion of the clinical nosology for children from 25 years experience with 173 pediatric patients. Bone. 2015; 75:229-239.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.