RXADVANCE
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Clinical Policy Title:	asfotase alfa
Policy Number:	RxA.498
Drug(s) Applied:	Strensiq®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Asfotase alfa (Strensiq®) is a tissue nonspecific alkaline phosphatase. It is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
asfotase alfa (Strensiq®)	Perinatal/infantile-onset HPP	6 mg/kg SC per week as either: • 2 mg/kg three times per week, or • 1 mg/kg six times per week The dose may be increased for lack of efficacy (e.g. no improvement in respiratory status, growth, or radiographic findings) up to 9 mg/kg per week, administered as 3 mg/kg SC three times per week.	9 mg/kg/week
asfotase alfa (Strensiq®)	Juvenile-onset HPP	6 mg/kg SC per week as either: • 2 mg/kg three times per week, or • 1 mg/kg six times per week	6 mg/kg/week

Dosage Forms

- Single-use vials: 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, 80 mg/0.8 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all)**:**

1. Diagnosis of perinatal/infantile- or juvenile-onset HPP as evidenced by all of the following (a, b, and c):
   a. Age of onset is < 18 years;
   b. Presence of one of the following laboratory indices (i or ii):
      i. Mutation in the *ALPL* gene encoding for tissue non-specific alkaline phosphatase (TNSALP)*;
      ii. Serum alkaline phosphatase (ALP) below the age-adjusted normal range and either of the following (a or b):
         a) Plasma pyridoxal 5'-phosphate (PLP; main circulating form of vitamin B6) above the upper limit of normal (ULN);
         b) Urinary phosphoethanolamine (PEA) above the ULN;
   c. History of one of the following HPP clinical manifestations (i, ii, iii, or iv):
      i. Vitamin B6-dependent seizures;
      ii. Failure to thrive or growth failure/short stature;
      iii. Nephrocalcinosis with hypercalcemia/hypercalciuria;
      iv. Skeletal abnormalities and associated impairments (any of the following):
         a) Craniosynostosis (premature fusion of one or more cranial sutures) with increased intracranial pressure;
         b) Rachitic chest deformity (costochondral junction enlargement seen in advanced rickets) with associated respiratory compromise;
         c) Limb deformity with delayed walking or gait abnormality;
         d) Compromised exercise capacity due to rickets and muscle weakness;
         e) Low bone mineral density for age with unexplained fractures;
         f) Alveolar bone loss with premature loss of deciduous (primary) teeth;
2. Prescribed by or in consultation with an endocrinologist;
3. Dose does not exceed the following (a or b):
   a) Perinatal/infantile-onset HPP: 9 mg/kg per week;
   b) Juvenile-onset HPP: 6 mg/kg per week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

**TNSALP is an ALP isoenzyme; a functional mutation in the gene (ALPL) encoding for TNSALP results in low TNSALP activity (as evidenced by a low serum ALP level) and increased levels of TNSALP substrates (PLP and PEA).*

II. Continued Therapy Approval

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy, as evidenced by improvement in any of the following on initial re-authorization request:
   a. Height velocity;
   b. Respiratory function;
   c. Skeletal manifestations (e.g., bone mineralization, bone formation and remodeling, fractures, deformities);
   d. Motor function, mobility, or gait;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Perinatal/infantile-onset HPP: 9 mg/kg per week;
   b. Juvenile-onset HPP: 6 mg/kg per week.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

ALP: Alkaline phosphatase
FDA: Food and Drug Administration
HPP: Hypophosphatasia
PEA: Phosphor ethanol amine
PLP: pyridoxal 5'-phosphate
TNSALP: Tissue non-specific alkaline phosphatase
ULN: Upper limit of normal

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Some STRENSIQ-treated patients with initial therapeutic response to STRENSIQ subsequently developed worsening in disease-associated laboratory and radiographic biomarkers (some in association with neutralizing antibodies) suggesting possible immune-mediated effects on STRENSIQ's pharmacologic action resulting in disease progression. If patients experience progression of HPP symptoms or worsening of disease-associated laboratory and imaging biomarkers after a period of initial therapeutic response to STRENSIQ, consider obtaining anti-asfotase alfa antibody testing by contacting STRENSIQ Medical Information at Alexion at 1-888-765-4747 or by email at medinfo@alexion.com. Close clinical follow up is recommended.
- In pediatric patients <40 kg, do not use the 80 mg/0.8 mL vial; systemic exposure of asfotase alfa achieved with this higher concentration (80 mg/0.8 mL) is lower than that achieved with the other vial strengths which have a lower concentration. A lower exposure may not be adequate for this subgroup of patients.

References

1. Strensiq® Prescribing Information. Boston, MA: Alexion Pharmaceuticals, Inc.; June 2020. Available at https://strensiq.com/. Accessed August 28, 2020.
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3. Scott LJ. Asfotase alfa in perinatal/infantile-onset and juvenile-onset hypophosphatasia: A guide to its use in the USA. Bio Drugs. 2016; 30:41-48. DOI 10.1007/s40259-016-0161-x.
4. Whyte MP, Rockman-Greenberg C, Ozono K, et al. Asfotase alfa treatment improves survival for perinatal and infantile hypophosphatasia. J Clin Endocrinol Metab. January 2016; 101(1):334-42. Doi: 10.1210/jc.2015-3462. Epub 2015 Nov 3.

5. Orimo H. Pathophysiology of hypophosphatasia and the potential role of asfotase alfa. Ther Clin Risk Manag. May 17, 2016; 12:777-86. Doi: 10.2147/TCRM.S87956. eCollection 2016.
6. Mornet E, Nunes ME. Hypophosphatasia. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. 2007 Nov 20 [updated 2016 Feb 4]. Available at https://www.ncbi.nlm.nih.gov/books/NBK1150/. Accessed August 28, 2020.
7. Bishop N. Clinical management of hypophosphatasia. Clin Cases miner Bone Metab. 2015; 12(2): 170-173.
8. Kishnani PS, et al. Monitoring guidance for patients with hypophosphatasia treated with asfotase alfa. Mol Genetics and Metab. 2017;122:4-17.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 4. Added Appendix D: General Information. 5. References were updated.	8/28/2020	12/7/2020