Strensiq (asfotase alfa)
Policy Number: C9425-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
6/1/2016	6/19/2019	6/19/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J3490 (NOC)- Unclassified drugs	RxPA	Q3 2019 20190828C9425-A

PRODUCTS AFFECTED:
Strensiq (asfotase alfa)

DRUG CLASS:
Hypophosphatasia (HPP) Agents

ROUTE OF ADMINISTRATION:
Subcutaneous

PLACE OF SERVICE:
Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered.

AVAILABLE DOSAGE FORMS:
Strensiq SOLN 18MG/0.45ML (1 vial or box of 12 vials) , Strensiq SOLN 28MG/0.7ML (1 vial or box of 12 vials), Strensiq SOLN 40MG/ML (1 vial or box of 12 vials), Strensiq SOLN 80MG/0.8ML (1 vial or box of 12 vials)

FDA-APPROVED USES:
Treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

REQUIRED MEDICAL INFORMATION:
A. PERINATAL/INFANTILE HPP – ONSET HPP:
1. Prescriber attests to diagnosis of Perinatal (onset before birth)/Infantile hypophosphatasia (HPP)-onset hypophosphatasia (HPP) or Juvenile-onset hypophosphatasia (HPP)
AND
2. Documentation of Tissue Non-Specific Alkaline Phosphatase (TNSALP) substrate level ELEVATION, indicated by at least ONE (1) of the following: (a) Serum alkaline phosphatase (ALP) activity/level: LOW (below the gender- and age-specific reference range determined by each reference laboratory OR (b) Serum pyridoxal 5'-phosphate (PLP) level: Elevated (above the upper limit of normal at baseline) AND member has not received vitamin B6 (Pyridoxine; Pyridoxal 5'-Phosphate) supplementation in the previous week OR (c) Serum or urine

phosphoethanolamine (PEA) level: ELEVATED OR (d) Urine inorganic pyrophosphate (PPi) level: ELEVATED
AND

3. Radiographic evidence of HPP confirmed by: Osteopenia, osteoporosis, or low bone mineral content for age detected by dual-energy x-ray absorptiometry (DEXA)
AND
4. FOR ADULTS ONLY (>18 YEARS OF AGE): Clinical documentation or documented history of skeletal and/or dental manifestations indicative of hypophosphatasia, such as: [TWO] Rickets, Osteomalacia, Rachitic deformities (rachitic chest, bowed legs, knock-knees), Craniosynostosis (premature closure of skull bones), Delay in skeletal growth resulting in delay of motor development, History of vitamin B6 dependent seizures, Nephrocalcinosis or history of elevated serum calcium, History or presence of non-traumatic postnatal fracture and delayed fracture healing, dental manifestations (i.e. premature loss of primary teeth prior to 5 years of age, defective mineralization of bone and/or teeth)
AND
5. Prescriber attests that history of onset of signs/symptoms of HPP before 18 years of age [NOTE: Adult-onset (onset at 18 years or older) do not meet criteria.]
AND
6. Documentation of Member's weight that has been taken within the last four weeks to ensure accurate weight based dosing
AND
7. Prescriber attests that patient has completed a baseline Ophthalmology exam, renal ultrasound, respiratory status exam and a radiology report that can be used to determine efficacy

DURATION OF APPROVAL: Initial authorization: 6 months Continuation of treatment: 12 months

QUANTITY: Juvenile-onset HPP: 6 mg/kg/week subcutaneously, Perinatal/infantile-onset HPP: 9 mg/kg/week subcutaneously

NOTE: 6 times per week regimen may NOT be authorized; 2 mg/kg 3 times per week dosing only*
*The FDA-approved labeling allows for Strensiq to be injected three times per week or six times per week. Strensiq is covered as a three times per week injection.

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified endocrinologist, geneticist, metabolic specialist, bone and mineral specialist, physician specialist experienced in the treatment of metabolic bone disorders. Submit consultation notes if applicable.

AGE RESTRICTIONS:
Documented history of onset of signs/symptoms of HPP before 18 years of age:
(a) Perinatal/infantile-onset hypophosphatasia: Onset of signs/symptoms of HPP <6 months of age
OR
(b)Juvenile-onset hypophosphatasia: Onset of signs/symptoms of HPP between

GENDER:
Male and female

CONTINUATION OF THERAPY:

A. PERINATAL/INFANTILE HPP – ONSET HPP:

1. Member currently meets ALL initial coverage criteria
AND

2. Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.
   AND
3. Prescriber attests that Member has responded to treatment with Strensiq (asfotase alfa) as evidenced by objective stability and/or continued disease improvement in clinical signs and/or symptoms of hypophosphatasia as compared to BASELINE parameters

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of Strensiq (asfotase alfa) that are not an FDA-approved indication or not included in this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS: None

BACKGROUND:

Hypophosphatasia (HPP) is a rare autosomally inherited metabolic bone disorder, with a range of bone development–related symptoms whose severities depend on the patient's age at disorder onset. HPP is caused by various mutations to the alkaline phosphatase, liver/bone/kidney (ALPL) gene; these mutations result in abnormally low systemic levels of alkaline phosphatase, a key bone mineralization enzyme. HPP affects the development of bones and teeth and the condition disrupts the mineralization process, in which minerals such as calcium and phosphorus are in developing bones and teeth.

HPP symptoms vary depending on severity and age at initial presentation. The signs and symptoms of hypophosphatasia vary widely and can appear anytime from before birth to adulthood. Generally, the earlier the presentation, the more severe the disease.

Signs and symptoms include rickets, softening and weakening of the bones (osteomalacia), bone deformity and a greater incidence of fractures. Hypophosphatasia can also lead to chronic debilitating pain, muscle weakness, generalized seizures due to vitamin B6 deficiency, as well as renal and respiratory complications.

Although adult-onset HPP has relatively mild symptoms such as premature tooth loss, infant- and juvenile-onset HPP are marked by more severe symptoms including cranial hypomineralization, pneumonia, and abnormal bone development. Early-onset HPP forms have mortality rates as high as 50%.

There are no guidelines for the treatment of hypophosphatasia. Management recommendations have focused on supportive care and trying to limit sign/symptom sequelae. Recommendations include vitamin B6 supplementation in patients with seizures, NSAIDs for pain, surgery for individuals with intracranial pressure and/or to repair bone fractures, and regular dental visits to preserve primary dentition.

Clinical trials have tested teriparatide, bone marrow transplantation, and other procedures such as transplantation therapy using bone fragments and cultured osteoblasts, as well as enzyme replacement therapies (ie, asfotase alfa).[4,6]

Enzyme replacement therapy (ERT). Autosomal recessive hypophosphatasia remains an extremely rare and severe condition.

Strensiq (asfotase alfa) is the first therapy approved in the United States for the treatment of patients with perinatal, infantile and juvenile-onset hypophosphatasia (HPP). Strensiq is a recombinant TNSALP fusion protein intended as an enzyme replacement therapy. It is administered via subcutaneous injection 3 or 6 times per week with weight-based dosing. Strensiq was studied in 4 prospective open-label trials conducted in 99 patients with perinatal/infantile- and juvenile-onset hypophosphatasia.[a] The treatment duration and long-term effects of ERT with asfotase alfa remain

unknown for perinatal and infantile HPP. Clinical trials are in Phase IV, with patients treated up to 78 months at the time of FDA approval

APPENDIX:

Appendix 1: Clinical Features of Hypophosphatasia by Type

Several clinical forms of hypophosphatasia (HPP) are currently recognized:[G]

Perinatal HPP (onset before or at birth) is the most pernicious form, resulting in a high percent of stillborn births. Newborns that survive birth have an estimated mortality of about 50% in the first year of life with many complications including respiratory failure due to rachitic chest disease and hypoplastic lungs.

Childhood HPP (also referred as childhood onset; onset between 6 months and 18 years) has variable symptoms; however, premature loss of primary teeth before the age of five is classical feature of HPP. Children may present with delayed mobility, waddling gait, delayed growth, frequent fractures, and osteopenia.

Adult HPP (onset at 18 years or older) can be associated with rickets or early loss of adult teeth. Adults may also suffer from pain due to osteomalacia, fracture, pseudogout, and calcific periarthritis.

Odontohypophosphatasia (only dental clinical symptoms): The mildest form of the condition, called odontohypophosphatasia, only affects the teeth.[1] The milder forms, especially adult forms and odontohypophosphatasia, may be inherited in an autosomal recessive or autosomal dominant manner.

Type	Inheritance	Cardinal Features	Dental Features	Clinical Diagnosis
Perinatal (severe)	AR	Hypomineralization, osteochondral spurs	± [1]	Radiographs, prenatal ultrasound examination
Perinatal (benign)	AR or AD	Long-bone bowing, benign postnatal course	±	Prenatal ultrasound examination, clinical course
Infantile [2]	Mostly AR	Craniosynostosis, Hypomineralization, rachitic ribs, hypercalciuria	Premature loss, deciduous teeth	Clinical course, radiographs, laboratory findings
Childhood (juvenile)	AR or AD	Short stature, skeletal deformity, bone pain/fractures	Premature loss, deciduous teeth (incisors)	Clinical course, radiographs, laboratory findings

Adult [3]	AR or AD	Stress fractures: metatarsal, tibia; chondrocalcinosis	±	Clinical course, radiographs, laboratory findings

Type	Inheritance	Cardinal Features	Dental Features	Clinical Diagnosis
Odontohypophosphatasia	AR or AD	Alveolar bone loss	Exfoliation (incisors), dental caries	Clinical course, dental panorex, laboratory findings

Key:AR = autosomalrecessive; AD = autosomaldominant

1. *In the past individuals with severe phenotypes have typically died before teeth erupted and could be lost. In the new "treated perinatal (severe) and infantile" category, the dental features are not precisely known but emerging data suggests the possibility of such features.*
2. *Rare reported cases of infantile hypophosphatasia that have normal serum alkaline phosphatase activity (in vitro) have been designated "pseudohypophosphatasia." The biochemical and molecular basis of pseudohypophosphasia remains unclear.*
3. *Persons with adult hypophosphatasia may give a history of features typically reported in childhood (juvenile), infantile, and even prenatal hypophosphatasia.*

Appendix 2: Weight-Based Dosing for Administration of 2 mg/kg Three Times per Week

Guidance for 2 mg/kg subQ 3 Times Weekly Dosage Option			
Weight (kg)	Weight-based dose (mg)	Injection volume (mL)	Vial size(s) to use
3	6	0.15	18 mg/0.45 mL
4	8	0.2	18 mg/0.45 mL
5	10	0.25	18 mg/0.45 mL
6	12	0.3	18 mg/0.45 mL
7	14	0.35	18 mg/0.45 mL
8	16	0.4	18 mg/0.45 mL
9	18	0.45	18 mg/0.45 mL
10	20	0.5	28 mg/0.7 mL
15	30	0.75	40 mg/mL
20	40	1	40 mg/mL
25	50	1.25	2 x 28 mg/0.7 mL

30	60	1.5	2 x 40 mg/mL
35	70	1.75	2 x 40 mg/mL
40	80	0.8	80 mg/0.8 mL
50	100	1	2 x 80 mg/0.8 mL
60	120	1.2	2 x 80 mg/0.8 mL
70	140	1.4	2 x 80 mg/0.8 mL
80	160	1.6	2 x 80 mg/0.8 mL

Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg. When preparing a volume for injection greater than 1 mL, split the volume equally between two syringes, and administer two injections. When administering the two injections, use two separate injection sites.

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