## ASFOTASE ALFA

| Generic | Brand | HICL | GCN | Exception/Other |
|---|---|---|---|---|
| ASFOTASE ALFA | STRENSIQ | 42649 | | |

### GUIDELINES FOR USE

### INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is this a request for treatment of perinatal/infantile-onset hypophosphatasia (HPP)?

   If yes, continue to #2.
   If no, continue to #3.

2. Does the patient have a documented diagnosis of perinatal/infantile-onset hypophosphatasia (HPP) and have **ALL** of the following criteria been met?
   - Prescribed by or in consultation with an endocrinologist
   - Patient was 6 months of age or younger at hypophosphatasia (HPP) onset
   - Positive for a tissue non-specific alkaline phosphatase (TNSALP) (ALPL) gene mutation as confirmed by genetic testing **OR** meets at least **TWO** of the following criteria:
     - Serum alkaline phosphatase (ALP) level below that of normal range for patient age
     - Serum pyridoxal-5'-phosphate (PLP) levels elevated **AND** patient has not received vitamin $B_6$ supplementation in the previous week
     - Urine phosphoethanolamine (PEA) level above that of normal range for patient age
     - Radiographic evidence of hypophosphatasia (HPP) (e.g., flared and frayed metaphyses, osteopenia, widened growth plates, areas of radiolucency or sclerosis)
     - Presence of **two or more** of the following:
       - Rachitic chest deformity
       - Craniosynostosis (premature closure of skull bones)
       - Delay in skeletal growth resulting in delay of motor development
       - History of vitamin $B_6$ dependent seizures
       - Nephrocalcinosis or history of elevated serum calcium
       - History or presence of non-traumatic postnatal fracture and delayed fracture healing

   If yes, continue to #5.
   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

3. Is this a request for treatment of juvenile-onset hypophosphatasia (HPP)?

   If yes, continue to #4.
   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

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## ASFOTASE ALFA

**INITIAL CRITERIA (CONTINUED)**

4. Does the patient have a documented diagnosis of juvenile-onset hypophosphatasia (HPP) and have **ALL** of the following criteria been met?
   - Prescribed by or in consultation with an endocrinologist
   - Patient was 18 years of age or younger at hypophosphatasia (HPP) onset
   - Positive for a tissue non-specific alkaline phosphatase (TNSALP) (ALPL) gene mutation as confirmed by genetic testing **OR** meets at least **TWO** of the following criteria:
     - Serum alkaline phosphatase (ALP) level below that of normal range for patient age
     - Serum pyridoxal-5'-phosphate (PLP) levels elevated **AND** patient has not received vitamin $B_6$ supplementation in the previous week
     - Urine phosphoethanolamine (PEA) level above that of normal range for patient age
     - Radiographic evidence of hypophosphatasia (HPP) (e.g., flared and frayed metaphyses, osteopenia, osteomalacia, widened growth plates, areas of radiolucency or sclerosis)
     - Presence of **two or more** of the following:
       - Rachitic deformities (rachitic chest, bowed legs, knock-knees)
       - Premature loss of primary teeth prior to 5 years of age
       - Delay in skeletal growth resulting in delay of motor development
       - History or presence of non-traumatic fractures or delayed fracture healing

   If yes, continue to #5.
   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

5. Does the patient meet **ALL** of the following criteria?
   - Patient is not currently receiving treatment with a bisphosphonate [e.g., Boniva (ibandronate), Fosamax (alendronate), Actonel (risedronate)].
   - Patient does not have serum calcium or phosphate levels below the normal range.
   - Patient does not have a treatable form of rickets.

   If yes, **approve for 6 months by HICL.**
   **APPROVAL TEXT:** Renewal requires that, while on therapy with Strensiq, the patient experiences a documented improvement in skeletal characteristics of hypophosphatasia (HPP) (e.g., improvement of irregularity of the provisional zone of calcification, physeal widening, metaphyseal flaring, radiolucencies, patchy osteosclerosis, ratio of mid-diaphyseal cortex to bone thickness, gracile bones, bone formation and fractures).

   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

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## ASFOTASE ALFA

**INITIAL CRITERIA (CONTINUED)**

**DENIAL TEXT:** Our guideline for **ASFOTASE ALFA (Strensiq)** requires a documented diagnosis of perinatal/infantile-onset hypophosphatasia (HPP) or juvenile-onset hypophosphatasia (HPP). Additional guideline requirements apply.

**For patients with perinatal/infantile-onset hypophosphatasia (HPP), all of the following criteria must be met:**

- Prescribed by or in consultation with an endocrinologist
- Patient was 6 months of age or younger at hypophosphatasia (HPP) onset
- Positive for a tissue non-specific alkaline phosphatase (TNSALP) (ALPL) gene mutation as confirmed by genetic testing **OR** meets at least **TWO** of the following criteria:
  - Serum alkaline phosphatase (ALP) level below that of normal range for patient age
  - Serum pyridoxal-5'-phosphate (PLP) levels elevated **AND** patient has not received vitamin $B_6$ supplementation in the previous week
  - Urine phosphoethanolamine (PEA) level above that of normal range for patient age
  - Radiographic evidence of hypophosphatasia (HPP) (e.g., flared and frayed metaphyses, osteopenia, widened growth plates, areas of radiolucency or sclerosis)
  - Presence of **two or more** of the following:
    - Rachitic chest deformity
    - Craniosynostosis (premature closure of skull bones)
    - Delay in skeletal growth resulting in delay of motor development
    - History of vitamin $B_6$ dependent seizures
    - Nephrocalcinosis or history of elevated serum calcium
    - History or presence of non-traumatic postnatal fracture and delayed fracture healing

**For patients with juvenile-onset hypophosphatasia (HPP), all of the following criteria must be met:**

- Prescribed by or in consultation with an endocrinologist
- Patient was 18 years of age or younger at hypophosphatasia (HPP) onset
- Positive for a tissue non-specific alkaline phosphatase (TNSALP) (ALPL) gene mutation as confirmed by genetic testing **OR** meets at least **TWO** of the following criteria:
  - Serum alkaline phosphatase (ALP) level below that of normal range for patient age
  - Serum pyridoxal-5'-phosphate (PLP) levels elevated **AND** patient has not received vitamin $B_6$ supplementation in the previous week
  - Urine phosphoethanolamine (PEA) level above that of normal range for patient age
  - Radiographic evidence of hypophosphatasia (HPP) (e.g., flared and frayed metaphyses, osteopenia, osteomalacia, widened growth plates, areas of radiolucency or sclerosis)

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## ASFOTASE ALFA

**INITIAL CRITERIA (CONTINUED)**

- Presence of **two or more** of the following:
  - Rachitic deformities (rachitic chest, bowed legs, knock-knees)
  - Premature loss of primary teeth prior to 5 years of age
  - Delay in skeletal growth resulting in delay of motor development
  - History or presence of non-traumatic fractures or delayed fracture healing

**Strensiq will not be approved for the following patients:**

- Patients currently receiving treatment with a bisphosphonate [e.g., Boniva (ibandronate), Fosamax (alendronate), Actonel (risedronate)]
- Patients with serum calcium or phosphate levels below the normal range
- Patients with a treatable form of rickets

**RENEWAL CRITERIA**

1. During the last 6 months of treatment, has the patient experienced improvement in the skeletal characteristics of hypophosphatasia (HPP) (e.g., improvement of the irregularity of the provisional zone of calcification, physeal widening, metaphyseal flaring, radiolucencies, patchy osteosclerosis, ratio of mid-diaphyseal cortex to bone thickness, gracile bones, bone formation and fractures)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   **DENIAL TEXT:** Our guideline for **ASFOTASE ALFA (Strensiq)** renewal requires that the patient has experienced an improvement in the skeletal characteristics of hypophosphatasia (HPP) (e.g., improvement of the irregularity of the provisional zone of calcification, physeal widening, metaphyseal flaring, radiolucencies, patchy osteosclerosis, ratio of mid-diaphyseal cortex to bone thickness, gracile bones, bone formation and fractures).

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**RATIONALE**
To ensure appropriate use of Strensiq consistent with FDA approved indication.

Strensiq (asfotase alfa) is the first therapy approved for the treatment of hypophosphatasia (HPP), a genetic, ultra-rare metabolic disorder. HPP is caused by a mutation in the tissue non-specific alkaline phosphatase (TNSALP) gene, which results in defective bone mineralization. Its prevalence is estimated to be less than 20 patients per one million in the general population and it is estimated to affect approximately one in 100,000 live births. HPP can affect people of all ages and the forms of HPP are classified primarily by the age of onset of symptoms and diagnosis. The clinical manifestations vary widely, ranging from stillbirth without mineralized bone to skeletal abnormalities due to softened bones. In perinatal HPP (onset *in-utero*), signs of HPP manifest *in utero* and may cause stillbirth or neonatal death shortly after birth.

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## ASFOTASE ALFA

**RATIONALE (CONTINUED)**
Patients with infantile HPP (onset prior to 6 months of age) often appear normal at birth but typically present with skeletal abnormalities and failure to thrive within the first 6 months of life. Mortality, usually due to pulmonary complications, has been reported to be as high as 50% within the first year of life. Juvenile or childhood HPP (onset ≥6 months to <18 years), is often first recognized when there is premature loss of the deciduous teeth, and radiographs reveal skeletal defects. First signs of HPP may also present later in life (onset ≥18 years of age); however, some adult patients report a history of early tooth loss or rickets during childhood. In adult HPP, hypomineralization manifests as osteomalacia. Manifestations of the disease can be severe and debilitating, often requiring multiple surgeries, multiple pain medications, and the use of supportive devices to perform activities of daily living.

Current treatment of HPP has been directed toward the management of specific symptoms and complications. The approval of Strensiq is the turning point for patients with HPP for which there is no cure. This biological agent targets the bone and replaces the deficient TNSALP enzyme, thereby preventing or reversing the complications of a defective mineralization process.

**FDA APPROVED INDICATION**
Strensiq is approved for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

**DOSAGE**
Perinatal/Infantile-Onset hypophosphatasia (HPP)
Recommended dosage regimen is 2mg/kg administered subcutaneously three times per week, or 1mg/kg six times per week. Injection site reactions may limit the tolerability of the six times per week regimen. The dosage may be increased to 3mg/kg three times per week for insufficient efficacy.

Juvenile-Onset hypophosphatasia (HPP)
Recommended dosage regimen is 2mg/kg administered subcutaneously three times per week, or 1mg/kg six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.

Please refer to prescribing information for tables of weight-based dosing by treatment regimen.

Strensiq is available as single-use vials in the following strengths: 18mg/0.45ml, 28mg/0.7ml, 40mg/ml, 80mg/0.8ml. The vials must be stored in the original carton until time of use under refrigerated conditions and protected from light. Once removed from refrigeration, Strensiq should be administered within 1 hour.

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# ASFOTASE ALFA

## AVAILABLE STRENGTHS:

- 18mg/0.45ml single-use vial
- 28mg/0.7ml single-use vial
- 40mg/ml single-use vial
- 80mg/0.8ml single-use vial

## REFERENCES


- Strensiq [Prescribing Information]. Cheshire, CT: Alexion Pharmaceuticals, Inc. October 2015.
- FDA [Online Press Release]. FDA approves new treatment for rare metabolic disorder. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468836.htm [Accessed November 2, 2015]
- National Organization for Rare Disorders. Hypophosphatasia. Available at: https://rarediseases.org/rare-diseases/hypophosphatasia/ [Accessed November 2, 2015]
- Beck C., Morbach H., Stenzel M., Colmann H., Schneider P., and Girschick HJ. Hypophosphatasia- Recent Advances in Diagnosis and Treatment. The Open bone Journal, 2009; I:8-15. Available at: http://benthamopen.com/contents/pdf/TOBONEJ/TOBONEJ-1-8.pdf [Accessed November 2, 2015]


| Library | Commercial | NSA |
|---|---|---|
| Yes | Yes | No |

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