Strensiq®
(asfotase alfa) for injection | 40 mg/mL

Adult Radiographic Evidence for STRENSIQ Prior Authorizations and Reauthorizations

INDICATION

STRENSIQ® (asfotase alfa) is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Initiate STRENSIQ under the supervision of a healthcare provider with appropriate medical monitoring and support measures. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue STRENSIQ and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur *[see Warnings and Precautions (5.1)]*.

Please see Important Safety Information on pages 1 and 4, and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

Introduction

The **Adult Radiographic Evidence for STRENSIQ Prior Authorizations and Reauthorizations** is an interactive resource that provides information regarding possible prior authorization and reauthorization criteria for STRENSIQ in adults. Radiographic evidence may be required by payers to detect any skeletal manifestations of hypophosphatasia (HPP). Please refer to each patient's chart and individual coverage policy to assess if radiographic evidence may be needed for STRENSIQ prior authorization or reauthorization.

This guide is intended for educational purposes only. Obtaining and submitting the evidence detailed within this educational tool does not guarantee coverage of STRENSIQ. Specific coverage criteria will differ for each patient based on their health plans.

As health plans may have different requirements, it is important to understand the benefit investigation for the key clinical and coverage criteria that applies to each patient given their unique plan. Additionally, it is recommended to contact your patient's health plan to confirm the specific requirements for your patient's coverage policy.

Rationale for Radiographic Evidence in HPP

- **HPP is a rare, heterogenous, genetic disease characterized by a decrease in the activity of tissue non-specific alkaline phosphatase (TNSALP).**[1]
  - TNSALP is encoded within the ALPL gene, which is abundantly expressed in the skeleton, liver, kidney, and developing teeth.[1]
  - TNSALP activity is essential for bone and teeth mineralization, and loss-of-function mutations are associated with skeletal hypomineralization, which is the predominant clinical manifestation of HPP.[1]
    - It is important to note that adult patients with HPP may experience disability, mobility issues, and burden of disease regardless of skeletal involvement.[2]
  - The clinical presentation of HPP in adults is highly variable including pain due to stress fractures or pseudofractures, osteomalacia, osteoarthropathy, and/or chondrocalcinosis.[1]
- **As such, some payers may require radiographic evidence to support prior authorization or reauthorization of therapy with STRENSIQ.**
- **Common examples of radiographic evidence accepted by payers are osteopenia, osteoporosis, or low bone mineral content for age as detected by x-rays as well as bone fractures or pseudofractures as detected by bone scans.**[3,4]

Radiographic Assessments Used to Measure HPP Progression and/or Response to Therapy

The table below shows commonly accepted radiographic evidence of HPP in adult patients. This may not be a comprehensive list:

Radiographic Evidence	
	Metatarsal stress fractures[1,4,5]
	Osteomalacia with lateral pseudofractures[1,4-6]
	Premature tooth loss/nontraumatic tooth loss (with root intact)[5,6]
	Osteopenia, osteoporosis, or low bone mineral content for age[1,4,5]

Your Alexion Field Reimbursement Manager (FRM) is available to help assist you in this process and answer any questions you may have about your patient's insurance policy requirements.

Additionally, please contact your patient's health plan to confirm the radiographic evidence required for STRENSIQ prior authorization or reauthorization.

STRENSIQ® (asfotase alfa) INDICATION & IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

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WARNINGS AND PRECAUTIONS

- **Life-threatening hypersensitivity reactions, including anaphylaxis**, have been reported in STRENSIQ-treated patients. Signs and symptoms consistent with anaphylaxis included difficulty breathing, choking sensation, nausea, periorbital edema, and dizziness. These reactions have occurred within minutes after subcutaneous administration of STRENSIQ and have been observed more than 1 year after treatment initiation. Other hypersensitivity reactions have also been reported in STRENSIQ-treated patients, including vomiting, fever, headache, flushing, irritability, chills, erythema, rash, pruritus, and oral hypoesthesia. Consider the risks and benefits of re-administering STRENSIQ following a severe reaction. If the decision is made to re-administer, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.
- **Lipodystrophy:** Localized lipodystrophy, including lipoatrophy and lipohypertrophy has been reported at injection sites after several months in patients treated with STRENSIQ in clinical trials. Advise patients to follow proper injection technique and to rotate injection sites.
- **Ectopic Calcifications:** Patients with HPP are at increased risk for developing ectopic calcifications. Events of ectopic calcification, including ophthalmic (conjunctival and corneal) and renal (nephrocalcinosis, nephrolithiasis), have been reported in the clinical trial experience with STRENSIQ. There was insufficient information to determine whether the reported events were consistent with the disease or due to STRENSIQ. No visual changes or changes in renal function were reported resulting from the occurrence of ectopic calcifications.

  Ophthalmology examinations and renal ultrasounds are recommended at baseline and periodically during treatment with STRENSIQ to monitor for signs and symptoms of ophthalmic and renal ectopic calcifications and for changes in vision or renal function.
- **Possible Immune-Mediated Clinical Effects:** In clinical trials, most STRENSIQ-treated patients developed anti-asfotase alfa antibodies and neutralizing antibodies which resulted in reduced systemic exposure of asfotase alfa. In postmarketing reports, some STRENSIQ-treated patients with initial therapeutic response subsequently developed recurrence and 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. The effect of anti-asfotase alfa antibody formation on the long-term efficacy of STRENSIQ is unknown. There are no marketed anti-asfotase alfa antibody tests. 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.

ADVERSE REACTIONS

In clinical trials, the most common adverse reactions (≥ 10%) reported were injection site reactions (63%), lipodystrophy (28%), ectopic calcifications (14%), and hypersensitivity reactions (12%). Possible immune-mediated clinical effects have been identified during post-approval use of STRENSIQ.

DRUG INTERACTIONS

Drug Interference with Laboratory Tests:

- Laboratory tests utilizing alkaline phosphatase (ALP) as a detection reagent could result in erroneous test results for patients receiving treatment due to the presence of asfotase alfa in clinical laboratory samples. Inform laboratory personnel that the patient is being treated with STRENSIQ and discuss use of an alternative testing platform which does not utilize an ALP-conjugated test system.
- Elevated serum ALP measurements detected through clinical laboratory testing are expected in patients receiving STRENSIQ due to circulating concentrations of asfotase alfa. Do not rely on serum ALP measurements for clinical decision making in patients treated with STRENSIQ.

SPECIAL POPULATIONS

- **Pregnancy & Lactation:** There are no available data on STRENSIQ use in pregnant women, the presence of STRENSIQ in human milk, or the effects on the breastfed infant or on milk production, to inform a drug associated risk.

To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Please see full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

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References: 1. Bianchi ML. Hypophosphatasia: an overview of the disease and its treatment. *Osteoporos Int*. 2015;26:2743-2757. **2.** Dahir KM, Kishnani PS, Martos-Moreno GA, et al. Impact of muscular symptoms and/or pain on disease characteristics, disability, and quality of life in adult patients with hypophosphatasia: a cross-sectional analysis from the Global HPP Registry. *Front Endocrinol (Lausanne)*. 2023;14:1138599. **3.** Aetna. Medical clinical policy bulletin. Asfotase alfa (Strensiq). February 12, 2016. Updated January 6, 2023. Accessed April 12, 2024. https://www.aetna.com/cpb/medical/data/900_999/0901.html **4.** Whyte MP. Hypophosphatasia: an overview for 2017. *Bone*. 2017;102:15-25. **5.** Nunes ME. Hypophosphatasia. In: Adam MP, Everman DB, Mirzaa GM, et al, eds. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2024. Accessed April 12, 2024. https://www.ncbi.nlm.nih.gov/books/NBK1150/ **6.** Kishnani PS, Rush ET, Arundel P, et al. Monitoring guidance for patients with hypophosphatasia treated with asfotase alfa. *Mol Genet Metab*. 2017;122(1-2):4-17.

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