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

# Renal and Ophthalmologic Assessments 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 5 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.**

# Introduction

The Renal and Ophthalmologic Assessments for STRENSIQ Prior Authorizations and Reauthorizations is an interactive resource which provides information regarding possible prior authorization and reauthorization criteria for STRENSIQ. Please refer to each patient's chart and individual coverage policy to assess which of the following assessments may be needed for STRENSIQ prior authorization or reauthorization.

This guide is intended for educational purposes only. Performance of one or all of the assessments in this resource does not guarantee coverage of STRENSIQ.

# Table of Contents

## Assessments



**These assessments are appropriate for perinatal/infantile, juvenile, and adult patients with hypophosphatasia (HPP).[1]**

# Renal Ultrasound

## What is a Renal Ultrasound?

- A renal ultrasound is a noninvasive diagnostic exam that produces images, which are used to assess the size, shape, and location of the kidneys and related structures.[2,3]
- Ultrasounds can detect cysts, tumors, abscesses, obstructions, fluid collection, and infection within or around the kidneys.[2,3]

## Why is a Renal Ultrasound used in HPP?

- Patients with HPP are at increased risk for developing ectopic calcifications of the kidneys (nephrocalcinosis) or renal stones. As such, an advisory panel of physicians experienced in the management of HPP recommends renal ultrasounds at baseline and periodically during treatment to monitor for signs and symptoms of ectopic calcifications and changes in renal function.[1,4]

## How often should a Renal Ultrasound be conducted in HPP?

- In perinatal/infantile patients, it is recommended that nephrocalcinosis be assessed at baseline and every 3 months. In children and adult patients, nephrocalcinosis should be assessed at baseline, 6 months, and then annually.[1] Because nephrocalcinosis and renal stones are possible at any age with HPP, it is recommended to conduct renal ultrasounds at baseline and every 6 to 12 months as clinically indicated for continuous monitoring.[1,4] Nephrocalcinosis should be monitored during the acute phase until stable.[1]

## How is a Renal Ultrasound performed?

- **Site of care:** Renal ultrasounds are performed at medical facilities by doctors or other healthcare providers including radiologists or sonographers.[3,5] Patients may be referred to radiology in a hospital, specialty imaging or outpatient facility, or a separate radiology clinic to undergo a renal ultrasound. Review your patient's healthcare policy to identify if there is a preferred site of care or location for your patient to receive a renal ultrasound.

## Coding and billing information[6]:

| CPT | Description |
|---|---|
| **76770** | Ultrasound, retroperitoneal (eg, renal, aorta, nodes), real time with image documentation; complete |
| **76775** | Ultrasound, retroperitoneal (eg, renal, aorta, nodes), real time with image documentation; limited |
| **76776** | Ultrasound, transplanted kidney, real time and duplex Doppler with image documentation |

# Ophthalmology Exam

## What is an Ophthalmology Exam?

- An ophthalmology exam typically includes checking a patient's medical history, visual acuity, prescription for corrective lens, pupils, peripheral vision, eye movement, eye pressure, front part of the eyes, and retina and optic nerve. The provider may suggest other assessments to further examine a patient's eyes as needed.[7]

## Why is an Ophthalmology Exam used in HPP?

- Patients with HPP are at increased risk for developing ectopic calcifications of the eye (cornea and conjunctiva). As such, an advisory panel of physicians experienced in the management of HPP, recommends ophthalmologic examinations at baseline and periodically during treatment to monitor for signs and symptoms of ectopic calcifications and changes in vision function.[1,4]

## How often should an Ophthalmology Exam be conducted in HPP?

- For perinatal and infantile patients, it is recommended that an ophthalmologist follow up every 3 months for the first year and every 6 months thereafter to monitor for increased intracranial pressure as well as ectopic eye calcifications in addition to clinical monitoring.[1] Because ectopic calcifications are possible at any age with HPP, it is recommended to conduct ophthalmic examination at baseline and then every 1 year or as clinically indicated.[1,4]

## How is an Ophthalmology Exam performed?

- **Site of care:** Ophthalmology exams are performed by ophthalmologists or optometrists in their office.[7] Patients may be referred to an appropriate eye care provider in a hospital or outpatient clinic. Review your patient's healthcare policy to identify if there is a preferred site of care or location for your patient to receive an ophthalmology exam.

## Coding and billing information[6]:

| CPT | Description |
|---|---|
| 92004 | Ophthalmological services: medical examination and evaluation with initiation of diagnostic and treatment program; comprehensive, new patient, 1 or more visits |
| 92014 | Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; comprehensive, established patient, 1 or more visits |

*Note: These CPT codes represent those most commonly used for comprehensive ophthalmological exams. For non-comprehensive examinations as well as specialized examinations, please refer to the 2023 CPT codes and descriptions as published by the American Medical Association.*

**You can find more information regarding the ophthalmology exam on the American Academy of Ophthalmology website.**

**References: 1.** Kishnani PS, Rush ET, Arundel P, et al. Monitoring guidance for patients with hypophosphatasia treated with asfotase alfa. *Mol Genet Metab*. 2017;122:4-17. **2.** Johns Hopkins Medicine. Kidney ultrasound. Baltimore, Maryland. Accessed June 5, 2023. https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/kidney-ultrasound **3.** Cleveland Clinic. Ultrasound. April 12, 2022. Accessed June 5, 2023. https://my.clevelandclinic.org/health/diagnostics/4995-ultrasound **4.** Shapiro JR, Lewiecki EM. Hypophosphatasia in adults: clinical assessment and treatment considerations. *J Bone Miner Res.* 2017;32(10):1977-1980. **5.** American College of Radiology. Renal ultrasound. Published July 11, 2022. Accessed August 31, 2023. https://www.radiologyinfo.org/en/info/ultrasound-renal **6.** American Medical Association. 2023 CPT Professional. 2022. CPT © 2022 American Medical Association. All rights reserved. CPT® is a registered trademark of the American Medical Association. **7.** Churchill J, Gudgel DT. What is an ophthalmologist? December 8, 2022. Accessed June 6, 2023. https://www.aao.org/eye-health/tips-prevention/what-is-ophthalmologist

# 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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