Sample Letter of Medical Necessity for STRENSIQ® (asfotase alfa)
Injection for Subcutaneous Use

Payers may request a letter of medical necessity to support coverage of STRENSIQ. The letter should explain why the drug is medically necessary for the specific patient and may include supporting documentation (eg, medical records, peer-reviewed literature, Prescribing Information, clinical treatment history, etc). The letter may be submitted as part of a prior authorization (PA) request, with the claim form, or in response to a payer's request for additional documentation. The letter should include patient-specific information, be on your letterhead, be signed by the prescriber, and be submitted to a payer to support a PA request or claim for STRENSIQ.

This sample letter of medical necessity is provided for informational purposes only and is not based on legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for STRENSIQ or that any payment received will cover providers' costs.

INDICATION

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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **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, skin erythema, rash, pruritus and oral hypoesthesia.

  Inform patients and/or caregivers of the signs and symptoms of hypersensitivity reactions and have them seek immediate medical care should signs and symptoms occur. If a severe hypersensitivity reaction occurs, discontinue STRENSIQ treatment and initiate appropriate medical treatment. Consider the risks and benefits of re-administering STRENSIQ to individual patients following a severe reaction. If the decision is made to re-administer the product, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.
- **Lipodystrophy:** Localized lipodystrophy, including lipoatrophy (depression in the skin) and lipohypertrophy (enlargement or thickening of tissue), 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.

Please see Important Safety Information on pages 1 and 4 and the full Prescribing Information for STRENSIQ® (asfotase alfa).

US/STQ-H/0196 03/22

[John Doe, MD]
[Address]
[City, State ZIP]
[(888) 555-5555]

SAMPLE ONLY
Please copy onto your letterhead.

[Date]
[Contact Name], [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP Code]

Letter of Medical Necessity for STRENSIQ® (asfotase alfa)
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Dear [Contact Name],

I am writing on behalf of my patient, [First Name] [Last Name], to request that [name of health insurance company] approve coverage and appropriate reimbursement associated with [Mr/Ms/Mrs/other title] [Patient's Last Name]'s treatment with STRENSIQ® (asfotase alfa), an enzyme replacement therapy. STRENSIQ is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

Patient Medical Overview
[First Name] [Last Name] is a[n] [age]-year-old [gender] born [MM/DD/YYYY] who requires treatment with STRENSIQ after being diagnosed with [perinatal/infantile- OR juvenile-onset HPP], ICD-10-CM diagnosis [list ICD-10-CM diagnosis code(s); see Common Prior Authorization Criteria for STRENSIQ Resource for codes]. The patient was diagnosed as of [date of diagnosis MM/DD/YYYY], after first showing onset of HPP symptoms at age [insert age of onset]. [Mr/Ms/Mrs/other title] [Patient's Last Name] has been in my care for HPP since [MM/DD/YYYY].

Medical History (Including Clinical Signs, Symptoms, and Laboratory Results) [see page 3 for further details]
[Provide relevant HPP clinical signs and symptoms and describe the severity of disease of your patient's current presentation and disease progression based on your medical opinion. Also, provide required laboratory results (eg, low age- and sex-adjusted ALP levels, elevated serum pyridoxal 5-phosphate [PLP]/vitamin B6 [B6] level or phosphoethanolamine [PEA] level substrates). Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need, and previous treatments/management strategies for HPP.]

In my medical opinion, STRENSIQ is the most appropriate treatment for [First Name] [Last Name]'s HPP based on the clinical efficacy and safety data.

Treatment Plan
I have prescribed the following, based on the recommended regimen for HPP in the Prescribing Information for STRENSIQ: [Describe the patient's prescribed dosage and frequency based on patient's diagnosis, body weight, etc].

Summary
Based on the above facts, I am confident you will agree that STRENSIQ is indicated and medically necessary for this patient. For your convenience, I am enclosing [list enclosures such as supporting clinical documentation, Prescribing Information, FDA approval letter for STRENSIQ in HPP, copy of patient's insurance card, etc].

If you have any further questions, please feel free to call me at [physician's phone number] to discuss.

Thank you in advance for your immediate attention to this request.

Sincerely,
[Physician's Name], MD
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures
[Supporting clinical documentation, Prescribing Information, FDA approval letter for STRENSIQ in HPP, copy of patient's insurance card, etc]

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Medical History (Including Clinical Signs, Symptoms, and Laboratory Results)

Below are some clinical signs and symptoms for HPP – please include any relevant documentation that is applicable to your patient's clinical presentation or medical history as well as applicable laboratory or test results.

Perinatal/Infantile-Onset

- ☐ Skeletal manifestations and/or generalized hypomineralization (eg, short limbs, rachitic features, abnormally shaped chest, craniosynostosis, soft skull bone, rib fractures, etc)[1]
- ☐ Vitamin B6–dependent seizures[1]
- ☐ Muscular hypotonia and/or weakness[1]
- ☐ Measure of HPP-related rickets (the 7-point Radiographic Global Impression of Change [RGI-C] scale and Rickets Severity Scale [RSS])[1]
- ☐ Respiratory problems (eg, pneumonia)[1,2]
- ☐ Hypercalcemia[1,2]

Juvenile-Onset

- ☐ Premature loss of deciduous teeth with root in tact[1]
- ☐ Frequent fractures (nontraumatic and nonhealing)[1]
- ☐ Skeletal manifestations (eg, enlarged wrist and ankle joints, abnormal skull shape)[1]
- ☐ Bone and joint pain[1]
- ☐ Short stature[1]
- ☐ Bowed legs or knock knees[1]
- ☐ Fatigue[3]
- ☐ Rickets[1]
- ☐ Delayed walking and/or waddling gait[1,2]
- ☐ Missed motor milestones[1]

Laboratory and Other Test Results

- ☐ A serum **tissue-nonspecific alkaline phosphatase (TNSALP)** level below the sex- and age-specific reference range of the laboratory performing the test[1]
- ☐ Elevated TNSALP substrate level **(eg, serum pyridoxal 5-phosphate (PLP)/vitamin B6 level or phosphoethanolamine [PEA] level)**[1]
- ☐ **Radiographic imaging** demonstrating skeletal abnormalities[1]
- ☐ Gait assessment **(ie, using Modified Performance Oriented Mobility Assessment-Gait [mPOMA-G] scale)**[4]
- ☐ Mobility assessment **(ie, 6-Minute Walk Test [6MWT])**[4]

***ALPL* Genetic Test Results**

- ☐ If the payer requires a genetic test, include the results and refer to the articles in the "Genetic Testing and Diagnostic Criteria," "Genetic Testing: Negative Test Result/Undetectable Mutations," and/or "Genetic Testing: Variant of Unknown Significance" sections of the *Compendium of Hypophosphatasia (HPP) References for STRENSIQ* for additional information
  - o Note to physician: **If you choose not to conduct genetic testing when required by the payer**, refer to the articles in the "Genetic Testing and Diagnostic Criteria" section of the *Compendium of Hypophosphatasia (HPP) References for STRENSIQ* for additional information
  - o **If you have an inconclusive test**, refer to the articles in the "Genetic Testing: Variant of Unknown Significance" and/or "Genetic Testing: Negative Test Result/Undetectable Mutations" sections of the *Compendium of Hypophosphatasia (HPP) References for STRENSIQ* for additional information

Please see Important Safety Information on pages 1 and 4 and the full Prescribing Information for STRENSIQ® (asfotase alfa).

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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont.)

- **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 or not 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

Overall, the most common adverse reactions (≥ 10%) reported were injection site reactions (63%). Other common adverse reactions included 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 and may be unreliable for clinical decision making.

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.

Please see Important Safety Information on pages 1 and 4 and the full Prescribing Information for STRENSIQ® (asfotase alfa).

References: 1. Rockman-Greenberg C. Hypophosphatasia. *Pediatr Endocrinol Rev*. 2013;10(suppl 2):380-388. **2.** Whyte MP. Hypophosphatasia: nature's window on alkaline phosphatase function in humans. In: Bilezikian J, Raisz L, Martin TJ, eds. *Principles of Bone Biology*. 3rd ed. Academic Press; 2008:1573-1598. **3.** Bianchi ML, Bishop NJ, Guañabens N, et al. Hypophosphatasia in adolescents and adults: overview of diagnosis and treatment. *Osteoporos Int*. 2020;31(8):1445-1460. **4.** STRENSIQ. Prescribing information. Alexion Pharmaceuticals, Inc.

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