# STRENSIQ® (asfotase alfa) Prescription (Rx) Form for the Treatment of Pediatric-Onset* Hypophosphatasia (HPP)

**Phone:** 1-844-787-6747 (ext 8008) **Fax:** 1-844-787-2527

**Fax this form to PANTHERx Rare to document medical necessity for initiating treatment.**
**Note: Additional Information may be required based on insurance plan.**

**Patients with perinatal/infantile- and juvenile-onset HPP*

## Patient information

First name:_____ Last name:_____

Address:_____

City:_____ State:_____ ZIP code:_____

Date of birth:_____ Sex: ☐ Male ☐ Female

Email address:_____

Phone:_____

☐ Home ☐ Work ☐ Cell

☐ OK to leave message ☐ OK to text

Parent (guardian)/caregiver name(s) (if applicable):

_____

## Primary diagnosis:

☐ ICD-10: E83.3 - Disorders of phosphorus metabolism and phosphatases

☐ ICD-10: E83.31 - Familial hypophosphatemia (perinatal/infantile- and juvenile-onset HPP)†

☐ ICD-10: E83.39 - Other disorders of phosphorus metabolism (perinatal/infantile- and juvenile-onset HPP)†

†*These ICD-10 diagnosis codes are not intended to be promotional or to encourage or suggest a use of drug that is inconsistent with FDA-approved use. The codes provided are not exhaustive and additional codes may apply. Descriptions in parentheses were added by Alexion for clarification and do not appear in these ICD-10 codes.*

## Required labs and/or documentation:

☐ Alkaline phosphatase (ALP)

☐ Pyridoxal-5'-phosphate (PLP) or phosphoethanolamine (PEA)

☐ Perinatal/infantile-onset HPP signs and symptoms

☐ Juvenile-onset HPP signs and symptoms

☐ Current HPP signs and symptoms

*Please attach copies of lab values if available.*

## Prescription for STRENSIQ

Patient's current weight: _____kg or _____lb

Date of weight: ____/____/____

STRENSIQ is a weight-based medication with two concentrations, 40 mg/1.0 mL and 80 mg/0.8 mL, which can be utilized independently or in combination depending on a patient's weight. **It is recommended to check both dosing concentration boxes below for patients weighing >40 kg to permit specialty pharmacy PANTHERx Rare to determine vial strengths and minimize waste.**

### Dosing concentration

☐ 40 mg/1.0 mL

### Dosing frequency

☐ 1 mg/kg, 6 times per week

☐ 2 mg/kg, 3 times per week

Other:_____

*--- and/or ---*

☐ 80 mg/0.8 mL
*(is not recommended for use in pediatric patients <40 kg)*

☐ 1 mg/kg, 6 times per week

☐ 2 mg/kg, 3 times per week

Other:_____

Dispense 28-day supply

Refill X 11 or

Other:_____

**Pharmacy will dispense needles and syringes required for subcutaneous administration of STRENSIQ.**

## Prescriber information

First name:_____ Last name:_____

Professional designation:_____

Physician specialty:_____ NPI#:_____

Office contact name:_____

Office contact phone:_____

Office contact email:_____

Preferred method of contact: ☐ Phone ☐ Email

Clinic/hospital affiliation:_____

Address:_____

City:_____State:_____ ZIP code:_____

Phone:_____ Fax:_____

## Healthcare and prescription drug insurance information

*Please attach copies of both sides of patient's healthcare and prescription drug insurance card(s).*

Primary insurance:_____

Member ID:_____

Group number:_____

Policy holder first name:_____

Policy holder last name:_____

Pharmacy Benefit Manager (PBM):_____

Rx BIN:_____

Rx PCN:_____

Rx Group:_____

## Prescriber authorization

PLEASE NOTE: In New York, please attach copies of all prescriptions on official New York State prescription forms.
I authorize the Specialty Pharmacy as my designated agent and on behalf of my patient to forward the above statement of medical necessity and furnish any information on this form to the insurer of the above-named patient.

SIGNATURE STAMPS NOT ACCEPTABLE

_____ _____

Prescriber signature (dispense as written) Date

SIGNATURE STAMPS NOT ACCEPTABLE

_____ _____

Prescriber signature (substitution permitted) Date

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

## 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)]*.**

## 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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US/STQ-H/0574 V1 07/2024

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

# Hypophosphatasia Signs and Symptoms Checklist

This simplified guide is intended to aid in documenting observed/reported history of signs and symptoms for patients who are diagnosed with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP). HPP is an inherited, multisystemic, rare metabolic disorder characterized by deficient alkaline phosphatase activity that may progress over time.[1-4]

## INDICATION

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## 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.**

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**Please see additional Important Safety Information throughout and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.**

# Hypophosphatasia Signs and Symptoms Checklist

It is encouraged to accurately capture the following information in the patient's chart notes: 1) current signs and symptoms and 2) signs and symptoms prior to age 18 per the product label. Attaching the checklist is not sufficient documentation of HPP for many payers.

| Signs/Symptoms (This list may not be exhaustive and all patients may not present the same way.[5] Treatment may not have an impact on all the signs and symptoms listed and inclusion below does not imply efficacy.) | | Currently presenting with | History of symptoms prior to age 18 |
|---|---|---|---|
| Neurologic | Vitamin $B_6$-responsive seizures (in infants)[1] | ☐ | ☐ |
| | Increased intracranial pressure (in infants)[1,6-9] | ☐ | ☐ |
| | Headaches[4,8,9] | ☐ | ☐ |
| | Mood (anxiety, depression)[4,8,9] | ☐ | ☐ |
| Dental | Premature tooth loss/nontraumatic tooth loss (with root intact)[1,4] | ☐ | ☐ |
| | Poor/abnormal dentition[1,4] | ☐ | ☐ |
| Skeletal/ Orthopedic | Hypomineralization[7] | ☐ | ☐ |
| | Skeletal deformities (eg, enlarged wrist and ankle joints, abnormal skull shape)[1] | ☐ | ☐ |
| | Fractures/pseudofractures (slow to heal)[1,4,10-12] | ☐ | ☐ |
| | Craniosynostosis (in infants)[1,6,7] | ☐ | ☐ |
| | Rachitic chest (in infants)[1,6,13] | ☐ | ☐ |
| | Rickets[1] | ☐ | ☐ |
| | Bowed legs or knock knees[1] | ☐ | ☐ |
| | Bone pain[1] | ☐ | ☐ |
| | Osteomalacia[1,7] | ☐ | ☐ |

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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

## Signs/Symptoms

(This list may not be exhaustive and all patients may not present the same way.[5] Treatment may not have an impact on all the signs and symptoms listed and inclusion below does not imply efficacy.)

| | | Currently presenting with | History of symptoms prior to age 18 |
|---|---|---|---|
| **Growth/ Development (children)** | Failure to thrive[1,4] | ☐ | ☐ |
| | Delayed/missed motor milestones[1,4] | ☐ | ☐ |
| | Short stature[1] | ☐ | ☐ |
| **Respiratory (in infants)** | Respiratory failure[1,4,7,14] | ☐ | ☐ |
| | Respiratory complications (eg, respiratory support)[15] | ☐ | ☐ |
| | Respiratory problems (eg, pneumonia)[14] | ☐ | ☐ |
| **Muscular/ Rheumatologic** | Muscle weakness[1] | ☐ | ☐ |
| | Fatigue[8] | ☐ | ☐ |
| | Hypotonia[1] | ☐ | ☐ |
| | Muscle/joint pain[1] | ☐ | ☐ |
| | Delayed walking[1,10] | ☐ | ☐ |
| | Waddling gait[1,10] | ☐ | ☐ |
| | Pseudogout[4,15] | ☐ | ☐ |
| **Renal** | Hypercalcemia[4,15-17] | ☐ | ☐ |
| | Hypercalciuria[4,15-17] | ☐ | ☐ |
| | Nephrocalcinosis[4,15-17] | ☐ | ☐ |

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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# The Alexion support service team is here to help you and your patients navigate this journey.

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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.

**Name:** [ ]

**Phone:** [ ]

**Email:** [ ]

ALEXION ACCESS NAVIGATOR

Alexion Access Navigator is a dedicated resource website for US HCPs and their offices that contains downloadable access and reimbursement materials for STRENSIQ.

www.AlexionAccessNavigator.com/Strensiq

## IMPORTANT SAFETY INFORMATION (cont'd)

### 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

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### 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.

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**References: 1.** Rockman-Greenberg C. *Pediatr Endocrinol* Rev. 2013;10(suppl 2):380-388. **2.** McKiernan FE, et al. *J Bone Miner Res.* 2014;29(7):1651-1660. **3.** Rush ET, et al. *Orphanet J Rare Dis.* 2019;14(1):201. **4.** Kishnani PS, et al. *Mol Genet Metab.* 2017;122(1-2):4-17. **5.** Mornet E. *Metabolism.* 2018;82:142-155. **6.** Whyte MP. *Nat Rev Endocrinol.* 2016;12(4):233-246. **7.** Bishop N, et al. *Arch Dis Child.* 2016;101(6):514-515. **8.** Bianchi ML, et al. *Osteoporos Int.* 2020;31(8):1445-1460. **9.** Colazo JM, et al. *Osteoporos Int.* 2019;30(2):469-480. **10.** 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. **11.** NORD. Hypophosphatasia. Accessed March 30, 2023. https://rarediseases.org/rare-diseases/hypophosphatasia/ **12.** Mornet E, Nunes ME. Hypophosphatasia. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews®.* University of Washington; 2007. Accessed March 30, 2023. https://www.ncbi.nlm.nih.gov/books/NBK1150/ **13.** Whyte M. In: Thakker RV, et al, eds. *Genetics of Bone Biology and Skeletal Disease.* Academic Press; 2013:337-360. **14.** Whyte MP, et al. *J Pediatr.* 2019;209:116-124.e4. **15.** Högler W, et al. *BMC Musculoskelet Disord.* 2019;20(1):80. **16.** Weber TJ, et al. *Metabolism.* 2016;65(10):1522-1530. **17.** Fallon MD, et al. *Medicine (Baltimore).*1984;63(1):12-24.

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# An Overview of Access and Support Resources

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

Alexion is committed to providing access and educational support to physicians and their offices for patients who have been prescribed STRENSIQ. This overview includes the important steps in the STRENSIQ access process and the resources available. It is intended for educational purposes only and does not guarantee coverage or access to treatment.

## 1 STRENSIQ is Prescribed

You have diagnosed a patient with perinatal/infantile- or juvenile-onset hypophosphatasia (HPP) and have prescribed STRENSIQ. Now what?

## 2 Benefit Investigation

After you have prescribed STRENSIQ, Alexion's contracted specialty pharmacy, PANTHERx, will conduct a benefit investigation with the patient's health plan.

## 3 Prior Authorization

Once the benefit investigation is complete, PANTHERx will share the health plan's prior authorization (PA) requirements with you. Each patient will have different requirements based on their unique health plan.

## 4 Prior Authorization Approval

Once all PA requirements have been completed and submitted to the patient's health plan, the PA will either be approved or denied. If approved, PANTHERx will ship STRENSIQ to the patient. If denied, you will need to determine the reason and the best course of action specific to your patient's health plan.

## 5 Reauthorization

After your patient has begun therapy on STRENSIQ, health plans will require a reauthorization. Reauthorization timelines and requirements will vary based on each patient's unique health plan.

### INDICATION

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### WARNINGS AND PRECAUTIONS

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The Alexion support service team is here to help you and your patients navigate this journey. Your Regional Account Manager is your main point of contact and will connect you directly with your assigned representatives from each of the groups below.

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**Field Reimbursement Managers (FRMs):**

The FRM team is available to help you navigate the landscape when it comes to getting STRENSIQ approved for your patients based on their individual insurance situation.

www.alexionaccessnavigator.com/strensiq

ONESOURCE® Personalized Patient Support from Alexion

**OneSource™** is a free, personalized patient support program offered by Alexion. After enrolling in OneSource™, your patient will be matched with a dedicated OneSource™ Case Manager who can provide personalized support, including access to:

- Education on their disease and treatment
- Connections to other people impacted by HPP
- Information on copay support and financial assistance programs
- Treatment support

**P: 888-765-4747**
**OneSource@Alexion.com**
**www.AlexionOneSource.com**

PANTHERRARE

**This specialty pharmacy dispenses STRENSIQ and provides:**

- Help coordinating your patient's prescription
- Shipments and ongoing refills
- Instructions for self-administration
- 24/7 support

**P: 844-787-6747 (ext 8008)**
**F: 844-787-2527**
**strensiqrph@pantherxrare.com**
**www.pantherxrare.com**

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

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# PATIENT SERVICES ENROLLMENT FORM

**EMAIL:** OneSource@Alexion.com
**PHONE:** 1.888.765.4747 8:30 AM to 8 PM ET Monday–Friday
**FAX:** 1.800.420.5150
**MAIL:** 100 College St., New Haven, CT 06510

ONESOURCE®
Personalized Patient Support from Alexion

FOR PATIENT

## WE'RE HERE TO HELP EVERY STEP OF THE WAY

OneSource™ is a free, personalized patient support program offered by Alexion and is designed to support patients' specific needs. Whether just starting or continuing an Alexion treatment, we can help you understand your or your loved one's condition, navigate insurance coverage, provide information about options for financial support, connect you with others who can relate, and more.

For more information, visit **www.AlexionOneSource.com**.

**Complete this form to get started with support!**

### INSTRUCTIONS FOR PATIENTS:

To enroll in OneSource, please follow these steps:

1. **Read** the Authorization to Share Health Information Terms on **this page**
2. **Complete** all required information on **Page 2**
3. **Email or fax Page 2** and copies of the front and back of your medical insurance and pharmacy coverage cards **to OneSource**
   **Email:** OneSource@Alexion.com | **Fax:** 1.800.420.5150

### PREFER TO COMPLETE THE FORM DIGITALLY?

**Scan the QR Code**

**or visit**
**www.AlexionOneSource.com**

## AUTHORIZATION TO SHARE HEALTH INFORMATION TERMS

Alexion Pharmaceuticals, Inc. ("Alexion") offers patient services including educational resources, case management support, and financial assistance for eligible patients.

By signing the next page, I give permission for my healthcare providers, health plans, other insurance programs, pharmacies, and other healthcare service providers ("My Healthcare Entities") to share information, including protected health information relating to my medical condition, treatment, and health insurance coverage (collectively "My Information") with Alexion and companies working at its direction so that Alexion may use and disclose My Information to:

- review my insurance coverage and eligibility for benefits for treatment with an Alexion product;
- coordinate treatment with an Alexion product, as well as related services, such as arranging home infusion services or vaccination services;
- provide me with educational and promotional materials, contact me about market research or clinical studies, or otherwise contact me about Alexion products, services, programs, or other topics that Alexion thinks may interest me
- remove identifiers from My Information and combine such resulting information with other information for research, regulatory submissions, business improvement projects, and publication purposes; and
- (as applicable to my Alexion product) review my vaccination and prophylaxis history and provide corresponding patient support, such as sending reminders about potential upcoming vaccinations.

I understand that My Healthcare Entities may receive payment from Alexion in exchange for sharing My Information.

I understand that My Information is also subject to the Alexion Privacy Notice available at https://alexion.com/Legal#privacy, and that the Alexion Privacy Notice provides additional information about Alexion's privacy practices and the rights that may be available to me. Although Alexion has implemented privacy and security controls designed to help protect My Information, I understand that once My Information has been disclosed to Alexion, the Health Insurance Portability and Affordability Act ("HIPAA") may not apply and may be subject to redisclosure.

I understand that I may refuse to sign this Authorization and that My Healthcare Entities may not condition treatment, payment, enrollment, or eligibility for benefits on whether I sign this Authorization. I also understand that if I do not sign this Authorization, I will not be able to receive support through the Alexion OneSource™ Patient Support Program.

This Authorization expires ten (10) years from the date next to my signature, unless I cancel/revoke it sooner, or unless a shorter time frame is required by applicable law.

I understand that I may revoke my authorization, or unsubscribe or modify the services I receive, at any time by mailing a letter to Alexion OneSource Patient Support Program, 100 College Street, New Haven, CT 06510 or by emailing OneSource@Alexion.com. I also understand that modifying my authorization will not affect any use or disclosure of My Information that occurred before Alexion received notice of my cancellation. I also understand I have a right to receive a copy of this Authorization after it is signed and can request a copy at any time by contacting OneSource at 1.888.765.4747.

**OneSource Services**
Alexion services and support are subject to change. Participation is voluntary, and person(s) may be removed from Alexion services for code of conduct violations.

# PATIENT SERVICES ENROLLMENT FORM

**EMAIL:** OneSource@Alexion.com
**PHONE:** 1.888.765.4747 8:30 AM to 8 PM ET Monday-Friday
**FAX:** 1.800.420.5150
**MAIL:** 100 College St., New Haven, CT 06510

ONESOURCE®
Personalized Patient Support from Alexion

FOR PATIENT

## BE SURE TO COMPLETE ALL REQUIRED FIELDS AND SIGN AND DATE THE FORM

If information is incomplete, it could delay our ability to enroll you in OneSource. OneSource can start offering you personalized support once you have fully completed and submitted this form.

**Contact OneSource if you have any questions while completing the form.**

**NOTE TO PRESCRIBERS:** If you are sending this form to a specialty pharmacy, please include **BOTH pages 1 and 2**

Fields in red with asterisks are required.*

## PATIENT INFORMATION

| PATIENT NAME (FIRST, MIDDLE INITIAL, LAST)* | DATE OF BIRTH (MM/DD/YYYY)* | GENDER: ☐ MALE ☐ FEMALE ☐ NON-BINARY<br>PREFER TO SELF-DESCRIBE: |
|---|---|---|
| ADDRESS* | | |
| CITY* | STATE* | ZIP* |
| PRIMARY PHONE NUMBER*<br>☐ MOBILE ☐ HOME | OK TO SEND TEXT MESSAGES FOR PATIENT SUPPORT? ☐ YES ☐ NO<br>OK TO LEAVE A PHONE MESSAGE? ☐ YES ☐ NO | |
| PATIENT DIAGNOSIS | | |
| PREFERRED LANGUAGE<br>☐ ENGLISH ☐ SPANISH ☐ OTHER _____ | PATIENT EMAIL<br>☐ NONE | |
| LEGAL PATIENT REPRESENTATIVE* (REQUIRED IF A PATIENT IS A MINOR)<br>NAME: PHONE: | RELATIONSHIP TO PATIENT | EMAIL |
| DESIGNATED CARE PARTNER<br>NAME: PHONE: | RELATIONSHIP TO PATIENT | EMAIL |

## PRESCRIBING PHYSICIAN'S INFORMATION

| PROVIDER NAME | PROVIDER PHONE NUMBER | PROVIDER EMAIL |
|---|---|---|
| | | |

## AUTHORIZATION TO SHARE HEALTH INFORMATION

By signing below, I acknowledge that I have read and agree to the Authorization to Share Health Information terms on the previous page.

SIGN HERE*

SIGNATURE OF PATIENT OR LEGALLY AUTHORIZED REPRESENTATIVE DATE (MM/DD/YYYY)

## CONSENT FOR COPAY PROGRAM (OPTIONAL)

By signing below, I acknowledge that I have read and agree to the Alexion OneSource CoPay Program eligibility terms and conditions available at https://alexiononesource.com/CoPay or on request by contacting OneSource at 1.888.765.4747.

SIGNATURE OF PATIENT OR LEGALLY AUTHORIZED REPRESENTATIVE DATE (MM/DD/YYYY)

## CONSENT FOR AUTOMATED TEXT COMMUNICATIONS (OPTIONAL)

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SIGNATURE OF PATIENT OR LEGALLY AUTHORIZED REPRESENTATIVE DATE (MM/DD/YYYY)

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US/ALL/0473 V4 03/2025

ALEXION
AstraZeneca Rare Disease

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

# STARTING STRENSIQ®

**Have you just been prescribed STRENSIQ and you're not sure where to start?**
The STRENSIQ Starter Kit is a great resource for the information you will need to start taking STRENSIQ.

**Requesting your STRENSIQ Starter Kit is as easy as calling 1-888-765-4747 or emailing OneSource@alexion.com.**

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

### INDICATION

**What is STRENSIQ?**
STRENSIQ is a prescription medicine used to treat people with perinatal, infantile, and juvenile onset hypophosphatasia (HPP).

**Please see full Prescribing Information and Patient Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding severe allergic (hypersensitivity) reactions.**

## IMPORTANT SAFETY INFORMATION

**What is the most important information I should know about STRENSIQ?**
**STRENSIQ may cause serious side effects, including severe allergic (hypersensitivity) reactions.** Allergic reactions are common with STRENSIQ treatment and can be severe and life-threatening. Severe allergic reactions have happened in some people within minutes after receiving STRENSIQ and more than 1 year after starting treatment with STRENSIQ. Stop using STRENSIQ and go to the nearest hospital emergency room right away if you or your loved one get any of the following signs and symptoms of a serious allergic reaction:

- difficulty breathing
- choking sensation
- swelling of your eyes, lips, or tongue
- dizziness
- nausea or vomiting
- fever
- headache
- sweating
- feeling irritable
- chills
- skin redness
- skin rash or hives
- itching or numbness of the tongue, lips, cheeks, or gums

**What are the other possible side effects of STRENSIQ?**
**STRENSIQ may cause other serious side effects, including:**

- **skin thickening or pits at the injection site (lipodystrophy).** Lipodystrophy is common and has happened after several months in people treated with STRENSIQ.
- **calcium build-up in the eyes and kidneys.** People with HPP are at increased risk for developing calcium build-up in the body. Calcium build-up in the eyes and kidneys has happened and is a common side effect of STRENSIQ. Calcium build-up in the eyes and kidneys may also happen in people with HPP who are not treated with STRENSIQ. Your healthcare provider should check your eyes and kidneys before and during treatment with STRENSIQ.
- **immune-related effects.** You may develop antibodies during treatment that may decrease how well STRENSIQ works. Tell your healthcare provider right away if you get worsening symptoms of HPP including: difficulty breathing, difficulty walking, feeling tired, bone pain, stiff joints, or loss of appetite.

**The most common side effects of STRENSIQ include** local skin injection site reactions such as skin redness, bruising, color change, pain, itching, hardening of the skin (induration), swelling, and bumps. These are not all the possible side effects of STRENSIQ. For more information, ask your healthcare provider or pharmacist. Call your healthcare provider for medical advice about side effects.

**You will begin receiving STRENSIQ under the supervision of a healthcare provider. Tell your healthcare provider about all your medical conditions, including if you:**

- have had an allergic reaction to STRENSIQ.
- are pregnant or plan to become pregnant. It is not known if STRENSIQ will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if STRENSIQ passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you use STRENSIQ.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

There is a registry for people who use STRENSIQ. The purpose of this registry is to collect information about HPP and about what happens when you use STRENSIQ for a long time. For more information about this registry, talk with your healthcare provider or go to www.hppregistry.com

**To report SUSPECTED SIDE EFFECTS, 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 and Patient Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding severe allergic (hypersensitivity) reactions.**

# WHAT'S IN YOUR STRENSIQ STARTER KIT

## Your STRENSIQ Starter Kit will include:

- OneSource™ Brochure
- STRENSIQ Patient Brochure
- STRENSIQ Patient Journal and Symptom Tracker
- Medical Alert Card
- Patient Education Event Card
- STRENSIQ Prescribing Information

**If you have any questions, you can call OneSource™ at 1-888-765-4747**

ALEXION
AstraZeneca Rare Disease

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US/STQ-H/0580 V1 05/2024

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

## HIGHLIGHTS OF PRESCRIBING INFORMATION

**These highlights do not include all the information needed to use STRENSIQ safely and effectively. See full prescribing information for STRENSIQ.**

**STRENSIQ® (asfotase alfa) injection, for subcutaneous use**
**Initial U.S. Approval: 2015**

**WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS**

***See full prescribing information for complete boxed warning.***

- **Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. (5.1)**
- **Initiate STRENSIQ under the supervision of a healthcare provider with appropriate medical monitoring and support measures. (5.1)**
- **If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue STRENSIQ and immediately initiate appropriate medical treatment, including use of epinephrine. (5.1)**

### RECENT MAJOR CHANGES

| | |
|---|---|
| Boxed Warning | 7/2024 |
| Dosage and Administration (2.1) | 7/2024 |
| Warnings and Precautions (5.1) | 7/2024 |

### INDICATIONS AND USAGE

STRENSIQ is a tissue nonspecific alkaline phosphatase indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP). (1)

### DOSAGE AND ADMINISTRATION

Perinatal/Infantile-Onset HPP (2.2)

- Recommended dosage regimen is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.
- The dose may be increased to 3 mg/kg three times per week for insufficient efficacy.

Juvenile-Onset HPP (2.3)

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

Preparation and Weight-Based Dosing (2.4):

- *Caution:* Do not use the 80 mg/0.8 mL vial in pediatric patients weighing less than 40 kg because the systemic asfotase alfa exposure achieved with the 80 mg/0.8 mL vial (higher concentration) is lower than that achieved with the other strength vials (lower concentration). A lower exposure may not be adequate for this subgroup of patients.
- See full prescribing information for tables of weight-based dosing by treatment regimen.

Administration (2.5):

- For subcutaneous injection only.
- Rotate injection sites. Do not administer to areas that are reddened, inflamed or swollen.

### DOSAGE FORMS AND STRENGTHS

Injection: 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, or 80 mg/0.8 mL solution in single-dose vials. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

- Lipodystrophy: Localized reactions were reported after several months of treatment; follow proper injection technique and rotate injection sites. (5.2)
- Ectopic Calcifications (eye and kidneys): Monitor using ophthalmologic examinations and renal ultrasounds at baseline and periodically during treatment. (5.3)
- Possible Immune-Mediated Clinical Effects: Evaluate patients for antibody formation if clinically indicated. (5.4)

### ADVERSE REACTIONS

Most common adverse reactions (≥ 10%) are injection site reactions, lipodystrophy, ectopic calcifications and hypersensitivity reactions. (6.1)

**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.**

### DRUG INTERACTIONS

- Drug Interference with Laboratory Tests: Alkaline Phosphatase (ALP) is used as a detection reagent in many laboratory tests and the presence of asfotase alfa in clinical laboratory samples could result in erroneous test results. Inform laboratory personnel and discuss use of an alternative testing platform for patients on treatment. (7.1)
- Serum Alkaline Phosphatase: Serum ALP measurements are expected to be elevated during treatment and may be unreliable for clinical decision making. (7.1)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

**Revised: 7/2024**

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**FULL PRESCRIBING INFORMATION: CONTENTS***


**WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS**

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## FULL PRESCRIBING INFORMATION

**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)]*.**

### 1 INDICATIONS AND USAGE

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

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Recommendations Prior to STRENSIQ Treatment

Initiate STRENSIQ under the supervision of a healthcare provider with appropriate medical monitoring and support measures *[see Warnings and Precautions (5.1)]*.

#### 2.2 Dosage for Perinatal/Infantile-Onset HPP

The recommended dosage regimen of STRENSIQ for the treatment of perinatal/infantile-onset HPP is 6 mg/kg per week administered subcutaneously as either:

- 2 mg/kg three times per week, or
- 1 mg/kg six times per week. Injection site reactions may limit the tolerability of the six times per week regimen *[see Adverse Reactions (6.1)]*.

The dose of STRENSIQ may be increased for lack of efficacy (e.g., no improvement in respiratory status, growth, or radiographic findings) up to 9 mg/kg per week administered subcutaneously as 3 mg/kg three times per week.

#### 2.3 Dosage for Juvenile-Onset HPP

The recommended dosage regimen of STRENSIQ for the treatment of juvenile-onset HPP is 6 mg/kg per week administered subcutaneously as either:

- 2 mg/kg three times per week, or
- 1 mg/kg six times per week. Injection site reactions may limit the tolerability of the six times per week regimen *[see Adverse Reactions (6.1)]*.

#### 2.4 Preparation and Weight-Based Dosing Tables

*Caution:* Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg because the systemic exposure of asfotase alfa achieved with the 80 mg/0.8 mL vial (higher concentration) is lower than that achieved with the other strength vials (lower concentration). A lower exposure may not be adequate for this subgroup of patients *[see Dosage Forms and Strengths (3), Clinical Pharmacology (12.3)]*.

1. Determine the total weekly volume needed for the prescribed dosage based on the patient's weight and recommended dosage. Follow these steps to determine the patient dose.

   Total weekly dose (mg) = patient's weight (kg) x prescribed dose (mg/kg/week)

   Total injection volume (mL) per week = Total dose (mg/week) divided by the STRENSIQ concentration (40 mg/mL or 100 mg/mL). Note product concentrations are: 40 mg/mL (vial strengths 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL) or 100 mg/mL (vial strength 80 mg/0.8 mL).

   Round total injection volume to the nearest hundredth of a mL

   Total number of vials per week = Total injection volume divided by vial volume (mL)
2. Determine the number of injection days per week (three or six per week).
3. Determine dose per injection day. Patient weights should be rounded to the nearest kilogram when determining dose. Use the following tables for guidance, for patients administering 2 mg/kg three times per week (Table 1), 1 mg/kg six times per week (Table 2) and for dose escalations to 3 mg/kg three times per week, recommended only for patients with perinatal/infantile-onset HPP *[see Dosage and Administration (2.2)]* (Table 3).

**Table 1: Weight-Based Dosing for Administration of 2 mg/kg Three Times per Week**

| Body Weight (kg)* | Dose to Inject | Volume to Inject | Vial Configuration |
|---|---|---|---|
| 3 | 6 mg | 0.15 mL | 18 mg/0.45 mL |
| 4 | 8 mg | 0.2 mL | 18 mg/0.45 mL |
| 5 | 10 mg | 0.25 mL | 18 mg/0.45 mL |
| 6 | 12 mg | 0.3 mL | 18 mg/0.45 mL |
| 7 | 14 mg | 0.35 mL | 18 mg/0.45 mL |
| 8 | 16 mg | 0.4 mL | 18 mg/0.45 mL |
| 9 | 18 mg | 0.45 mL | 18 mg/0.45 mL |
| 10 | 20 mg | 0.5 mL | 28 mg/0.7 mL |
| 15 | 30 mg | 0.75 mL | 40 mg/1 mL |
| 20 | 40 mg | 1 mL | 40 mg/1 mL |
| 25 | 50 mg | 1.25 mL | Two 28 mg/0.7 mL vials |
| 30 | 60 mg | 1.5 mL | Two 40 mg/1 mL vials |
| 35 | 70 mg | 1.75 mL | Two 40 mg/1 mL vials |
| 40 | 80 mg | 0.8 mL | 80 mg/0.8 mL |
| 50 | 100 mg | 1 mL | Two 80 mg/0.8 mL vials |
| 60 | 120 mg | 1.2 mL** | Two 80 mg/0.8 mL vials |
| 70 | 140 mg | 1.4 mL** | Two 80 mg/0.8 mL vials |
| 80 | 160 mg | 1.6 mL** | Two 80 mg/0.8 mL vials |

* Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

** 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.

**Table 2: Weight-Based Dosing for Administration of 1 mg/kg Six Times per Week**

| Body Weight (kg)* | Dose to Inject | Volume to Inject | Vial Configuration |
|---|---|---|---|
| 3 | 3 mg | 0.08 mL | 18 mg/0.45 mL |
| 4 | 4 mg | 0.1 mL | 18 mg/0.45 mL |
| 5 | 5 mg | 0.13 mL | 18 mg/0.45 mL |
| 6 | 6 mg | 0.15 mL | 18 mg/0.45 mL |
| 7 | 7 mg | 0.18 mL | 18 mg/0.45 mL |
| 8 | 8 mg | 0.2 mL | 18 mg/0.45 mL |
| 9 | 9 mg | 0.23 mL | 18 mg/0.45 mL |
| 10 | 10 mg | 0.25 mL | 18 mg/0.45 mL |
| 15 | 15 mg | 0.38 mL | 18 mg/0.45 mL |
| 20 | 20 mg | 0.5 mL | 28 mg/0.7 mL |
| 25 | 25 mg | 0.63 mL | 28 mg/0.7 mL |
| 30 | 30 mg | 0.75 mL | 40 mg/1 mL |
| 35 | 35 mg | 0.88 mL | 40 mg/1 mL |
| 40 | 40 mg | 1 mL | 40 mg/1 mL |
| 50 | 50 mg | 0.5 mL | 80 mg/0.8 mL |
| 60 | 60 mg | 0.6 mL | 80 mg/0.8 mL |
| 70 | 70 mg | 0.7 mL | 80 mg/0.8 mL |
| 80 | 80 mg | 0.8 mL | 80 mg/0.8 mL |
| 90 | 90 mg | 0.9 mL | Two 80 mg/0.8 mL vials |
| 100 | 100 mg | 1 mL | Two 80 mg/0.8 mL vials |

* Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

**Table 3: Weight-Based Dosing for Administration of 3 mg/kg Three Times per Week – Only for Perinatal/Infantile-Onset HPP***

| Body Weight (kg)** | Dose to Inject | Volume to Inject | Vial Configuration |
|---|---|---|---|
| 3 | 9 mg | 0.23 mL | 18 mg/0.45 mL |
| 4 | 12 mg | 0.3 mL | 18 mg/0.45 mL |
| 5 | 15 mg | 0.38 mL | 18 mg/0.45 mL |
| 6 | 18 mg | 0.45 mL | 18 mg/0.45 mL |
| 7 | 21 mg | 0.53 mL | 28 mg/0.7 mL |
| 8 | 24 mg | 0.6 mL | 28 mg/0.7 mL |
| 9 | 27 mg | 0.68 mL | 28 mg/0.7 mL |
| 10 | 30 mg | 0.75 mL | 40 mg/1 mL |
| 15 | 45 mg | 1.13 mL*** | Two 28 mg/0.7 mL vials |
| 20 | 60 mg | 1.5 mL*** | Two 40 mg/1 mL vials |
| 25 | 75 mg | 1.88 mL*** | Two 40 mg/1 mL vials |

* A regimen of 3 mg/kg three times per week is recommended only for patients with perinatal/infantile-onset HPP *[see Dosage and Administration (2.2)]*

** Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

*** 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.

4. Take the unopened STRENSIQ vial(s) out of the refrigerator 15 to 30 minutes before injecting to allow the liquid to reach room temperature.

   Do not warm STRENSIQ in any other way (for example, do not warm it in a microwave or in hot water).
5. Inspect the solution in the vial(s) for particulate matter and discoloration. STRENSIQ is supplied as a clear, slightly opalescent or opalescent, colorless to slightly yellow aqueous solution; a few small translucent or white particles may be present. Discard any vial(s) not consistent with this appearance.
6. Assemble injection supplies. Administer STRENSIQ using sterile disposable 1 mL syringes and ½ inch injection needles, between 25 to 29 gauge are recommended. The use of two different gauge needles is recommended, a larger bore needle (e.g. 25 gauge) for withdrawal of the medication, and a smaller bore needle (e.g. 29 gauge) for the injection. For doses greater than 1 mL, the injection volume should be split equally between two 1 mL syringes. Always use a new syringe and needle for each injection.
7. Remove vial cap, aseptically prepare the vial and insert the syringe into the vial to withdraw the prescribed dose for administration. Do not shake.
8. Remove any air bubbles in the syringe and verify the correct dose.
9. STRENSIQ vials are for one time use only. Discard any unused product.

### 2.5 Administration

STRENSIQ is for subcutaneous injection only.

- When administering two injections, use two separate injection sites.
- Administer STRENSIQ within 3 hours upon removal of the vial(s) from refrigeration.
- Rotate the injection from among the following sites to reduce the risk of lipodystrophy: abdominal area, thigh, deltoid, or buttocks *[see Warnings and Precautions (5.2), Adverse Reactions (6.1)]*.
- Do NOT administer injections in areas that are reddened, inflamed, or swollen.
- Inject STRENSIQ subcutaneously into the determined site and properly dispose of the syringe and the needle.

## 3 DOSAGE FORMS AND STRENGTHS

STRENSIQ is a clear, slightly opalescent or opalescent, colorless to slightly yellow aqueous solution; few small translucent or white particles may be present. The product is available as:

- Injection: 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, or 80 mg/0.8 mL solution in single-dose vials

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Hypersensitivity Reactions Including Anaphylaxis

Life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with enzyme replacement therapies, including STRENSIQ. 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 *[see Adverse Reactions (6.1)]*.

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.

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. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur.

### 5.2 Lipodystrophy

Localized lipodystrophy, including lipoatrophy and lipohypertrophy, has been reported at injection sites after several months in patients treated with STRENSIQ in clinical trials *[see Adverse Reactions (6.1)]*. Advise patients to follow proper injection technique and to rotate injection sites *[see Dosage and Administration (2.5)]*.

### 5.3 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.

### 5.4 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 *[see Immunogenicity (6.2)]*. 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 *[see Adverse Reactions (6.3)]*. 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.

## 6 ADVERSE REACTIONS

The following adverse reactions are described below and elsewhere in the labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*
- Lipodystrophy *[see Warnings and Precautions (5.2)]*
- Ectopic Calcifications *[see Warnings and Precautions (5.3)]*
- Possible Immune-Mediated Clinical Effects *[see Warnings and Precautions (5.4)]*

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to STRENSIQ in 99 patients with perinatal/infantile- or juvenile onset HPP (age 1 day to 58 years) treated with STRENSIQ, most for more than 2 years (range 1 day to 312 weeks [78 months]): 51 patients received at least 96 weeks (24 months) of treatment and 39 patients received 168 weeks (42 months) or more of treatment *[see Clinical Studies (14)]*.

Common Adverse Reactions

Overall, the most common adverse reactions reported were injection site reactions (63%). Other common adverse reactions included lipodystrophy (28%), ectopic calcifications (14%), and hypersensitivity reactions (12%).

Table 4 summarizes the adverse reactions that occurred at a rate of at least 10% in clinical trials following subcutaneous injection of STRENSIQ by patient population and STRENSIQ dosage regimen.

The frequency of injection site reactions, lipodystrophy and ectopic calcification were higher in patients with juvenile-onset HPP as compared to perinatal/infantile-onset HPP patients.

The majority of injection site reactions resolved within a week. Two patients experienced injection site reactions that led to reductions of their STRENSIQ dose. One patient switched from six times per week dosing to 3 times per week dosing as a result of injection site reactions. One other patient experienced a severe injection site reaction of injection site discoloration and withdrew from the trial.

**Table 4: Adverse Reactions Reported in at Least 10% of Patients with Perinatal/Infantile- or Juvenile-onset HPP Enrolled in STRENSIQ Clinical Trials**

| | Perinatal/ Infantile-onset HPP | | | Juvenile-onset HPP |
|---|---|---|---|---|
| **Adverse Reaction Category or Term** | **STRENSIQ less than or equal to 6 mg/kg per week (N=66) n (%)** | **STRENSIQ more than 6 mg/kg/ week[a] (N=13) n (%)** | **Total (N=79) n (%)** | **STRENSIQ (N=20) n (%)** |
| **Injection site reactions** | 38 (58) | 6 (46) | 44 (56) | 18 (90) |
| Erythema | 29 (44) | 3 (23) | 32 (41) | 15 (75) |
| Discoloration/ Hypopigmentation | 11 (17) | 1 (8) | 12 (15) | 8 (40) |
| Pain/Tenderness | 10 (15) | 1 (8) | 11 (14) | 8 (40) |
| Pruritus/Itching | 10 (15) | 0 (0) | 10 (13) | 7 (35) |
| Swelling | 8 (12) | 0 (0) | 8 (10) | 6 (30) |
| Induration | 9 (14) | 1 (8) | 10 (13) | 3 (15) |
| Macule | 4 (6) | 0 (0) | 4 (5) | 7 (35) |
| Reaction, not otherwise specified | 6 (9) | 1 (8) | 7 (9) | 4 (20) |
| Bruising | 6 (9) | 0 (0) | 6 (8) | 4 (20) |
| Nodule | 2 (3) | 0 (0) | 2 (3) | 2 (10) |
| Other injection site reactions[b] | 10 (15) | 3 (23) | 13 (17) | 4 (20) |
| **Ectopic calcifications** | 3 (5) | 0 (0) | 3 (4) | 11 (55) |
| **Lipodystrophy** | 12 (18) | 2 (15) | 14 (18) | 14 (70) |
| Injection site atrophy | 4 (6) | 2 (15) | 6 (8) | 8 (40) |
| Injection site hypertrophy | 5 (8) | 0 (0) | 5 (6) | 6 (30) |
| Other lipodystrophy[c] | 4 (6) | 0 (0) | 4 (5) | 1 (5) |
| **Hypersensitivity reactions** | 7 (11) | 3 (23) | 10 (13) | 2 (10) |
| Vomiting/emesis | 2 (3) | 2 (15) | 4 (5) | 2 (10) |
| Other hypersensitivity reactions[d] | 6 (9) | 2 (15) | 8 (10) | 2 (10) |

[a] Adverse reactions are from the combined period of 6 mg/kg and above (i.e. total drug exposure regardless of starting dose and intermediary doses as long as the patient reached doses > 6 mg/kg)

[b] Other injection site reactions include injection site rash, inflammation, papule, hemorrhage, hematoma, urticaria, warmth, calcification, mass, scar and cellulitis.

[c] Other lipodystrophy includes lipohypertrophy.

[d] Other hypersensitivity reactions include erythema/redness, pyrexia/fever, irritability, nausea, pain, rigor/chills, hypoesthesia oral, headache, flushing, and anaphylaxis.

Less Common Adverse Reactions

Adverse reactions that occurred at rates less than 1% included:

- Hypocalcemia
- Renal Stones
- Chronic hepatitis
- Decreased vitamin B6

Long-Term Safety

In long-term extension trials reflecting a median exposure to STRENSIQ of 142 weeks (range 0.1 weeks to 392 weeks) in 112 patients with perinatal/infantile- (n = 89), juvenile- (n = 22), and adult-onset (n = 1) HPP (age at enrollment = 1 day to 66.5 years), the most common adverse reactions were similar to those reported in Table 4.

### 6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of the antibodies in the studies described below with the incidence of antibodies in other studies or to other asfotase alfa products may be misleading.

During clinical trials, anti-asfotase alfa antibodies have been detected in patients receiving treatment with STRENSIQ using an electrochemiluminescent (ECL) immunoassay. Antibody positive samples were tested to determine the presence of neutralizing antibodies based on in vitro inhibition of the catalytic activity of STRENSIQ.

Among STRENSIQ-treated patients with hypophosphatasia (HPP) in clinical studies who had post-baseline antibody data available, 97/109 (89%) tested positive for anti-asfotase alfa antibodies at some time point during STRENSIQ treatment. Among those 97 patients, 55 (57%) also tested positive for neutralizing antibodies at some time point during STRENSIQ treatment. No correlation was observed between the anti-asfotase alfa antibody titers and the neutralizing antibody (% inhibition) values. Formation of anti-asfotase alfa antibody resulted in a reduced systemic exposure of asfotase alfa *[see Clinical Pharmacology (12.3)]*.

### 6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of STRENSIQ. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Some STRENSIQ-treated patients with initial therapeutic response to STRENSIQ subsequently developed 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 *[see Warnings and Precautions (5.4)]*.

## 7 DRUG INTERACTIONS

### 7.1 Drug Interference with Laboratory Tests

Laboratory Tests Utilizing Alkaline Phosphatase as a Detection Reagent

Studies have shown that there is analytical interference between asfotase alfa and laboratory tests that utilize an alkaline phosphatase (ALP)-conjugated test system, rendering erroneous test results in patients treated with STRENSIQ. ALP-conjugated test systems are utilized to measure substances such as hormones, bacterial antigens and antibodies. Therefore, it is recommended that laboratory assays which do not have ALP-conjugate technology be used when testing samples from patients who are receiving STRENSIQ.

To avoid erroneous test results for patients treated with STRENSIQ, inform laboratory personnel that the patient is being treated with STRENSIQ and discuss the use of a testing platform which does not utilize an ALP-conjugated test system.

Serum Alkaline Phosphatase

High serum ALP measurements detected through clinical laboratory testing are expected in patients receiving STRENSIQ and reflect circulating concentrations of asfotase alfa.

Do not rely on serum ALP measurements for clinical decision making in patients treated with STRENSIQ.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Risk Summary

There are no available data on STRENSIQ use in pregnant women to inform a drug associated risk. In animal reproduction studies, asfotase alfa administered intravenously to pregnant rats and rabbits during the period of organogenesis showed no evidence of fetotoxicity, embryolethality or teratogenicity at doses causing plasma exposures up to 21 and 24 times, respectively, the exposure at the recommended human dose *(see Data)*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

*Animal Data*

Asfotase alfa administered during the period of organogenesis to rats (from gestation Day 6 to Day 19 post-partum) and rabbits (on gestation days 7 to 19) at intravenous doses up to 50 mg/kg/day, approximately 21 and 24 times the human AUC of 65486 ng.h/mL at 2 mg/kg dose administered three times weekly for a 50 kg individual, respectively did not cause any adverse effects on embryofetal development. A pre- and post-natal development study in pregnant rats showed no evidence of adverse effects on pre- and post-natal development at intravenous doses (from Day 6 of gestation to Day 19 postpartum) of asfotase alfa up to 50 mg/kg/day approximately 21 times the human AUC of 65486 ng.h/mL at 2 mg/kg dose administered three times weekly for a 50 kg individual.

### 8.2 Lactation

Risk Summary

There are no data on the presence of asfotase alfa in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for STRENSIQ and any potential adverse effects on the breastfed infant from asfotase alfa or from the underlying maternal condition.

### 8.4 Pediatric Use

The safety and effectiveness of STRENSIQ for the treatment of perinatal/infantile- and juvenile-onset HPP have been established in pediatric patients. Use of STRENSIQ for this indication is based on 4 prospective, open-label clinical trials conducted in 89 pediatric patients with perinatal/infantile-onset or juvenile-onset HPP *[see Clinical Studies (14)]*.

### 8.5 Geriatric Use

No patients with perinatal/infantile- or juvenile-onset HPP aged 65 years were enrolled in clinical trials of STRENSIQ. Therefore, there is no information available to determine whether patients aged 65 years and over respond differently from younger patients.

## 11 DESCRIPTION

Asfotase alfa is a tissue nonspecific alkaline phosphatase (TNSALP) produced by recombinant DNA technology in a Chinese hamster ovary cell line. Asfotase alfa is a soluble glycoprotein composed of two identical polypeptide chains. Each chain contains 726 amino acids with a theoretical mass of 161 kDa. Each chain consists of the catalytic domain of human TNSALP, the human immunoglobulin $G_1$ Fc domain and a deca-aspartate peptide used as a bone targeting domain. The two polypeptide chains are covalently linked by two disulfide bonds.

STRENSIQ (asfotase alfa) injection is a sterile, preservative-free, nonpyrogenic, clear, slightly opalescent or opalescent, colorless to slightly yellow, with few small translucent or white particles, aqueous solution for subcutaneous administration. STRENSIQ is supplied in glass single-dose vials containing asfotase alfa; dibasic sodium phosphate, heptahydrate; monobasic sodium phosphate, monohydrate; and sodium chloride at a pH between 7.2 and 7.6. Table 5 describes the content of STRENSIQ vial presentations.

**Table 5: Content of STRENSIQ Vial Presentations**

| Ingredient | Quantity per Vial | | | |
|---|---|---|---|---|
| Asfotase Alfa | 18 mg/ 0.45 mL | 28 mg/ 0.7 mL | 40 mg/ mL | 80 mg/ 0.8 mL |
| Dibasic sodium phosphate, heptahydrate | 2.48 mg | 3.85 mg | 5.5 mg | 4.4 mg |
| Monobasic sodium phosphate, monohydrate | 0.28 mg | 0.43 mg | 0.62 mg | 0.5 mg |
| Sodium chloride | 3.94 mg | 6.13 mg | 8.76 mg | 7.01 mg |

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

HPP is caused by a deficiency in TNSALP enzyme activity, which leads to elevations in several TNSALP substrates, including inorganic pyrophosphate (PPi). TNSALP is a metallo-enzyme that catalyzes the hydrolysis of phosphomonoesters with release of inorganic phosphate and alcohol. Elevated extracellular levels of PPi block hydroxyapatite crystal growth which inhibits bone mineralization and causes an accumulation of unmineralized bone matrix which manifests as rickets and bone deformation in infants and children and as osteomalacia (softening of bones) once growth plates close, along with muscle weakness. Replacement of the TNSALP enzyme upon STRENSIQ treatment reduces the enzyme substrate levels.

### 12.2 Pharmacodynamics

Perinatal/infantile- and juvenile-onset HPP patients treated with STRENSIQ had reductions in plasma TNSALP substrates, PPi and pyridoxal 5'-phosphate (PLP) within 6 to 12 weeks of treatment. Reductions in plasma PPi and PLP levels did not correlate with clinical outcomes.

Bone biopsy data from perinatal/infantile-onset and juvenile-onset HPP patients treated with STRENSIQ demonstrated decreases in osteoid volume and thickness indicating improved bone mineralization.

### 12.3 Pharmacokinetics

Based on data in 38 HPP patients, the pharmacokinetics of asfotase alfa exhibit dose proportionality across the dose range of 0.3 mg/kg to 3 mg/kg once every other day (three times a week) and appear to be time-independent. Steady state exposure was achieved as early as three weeks after the administration of the first dose. The elimination half-life following subcutaneous administration was approximately 5 days.

Table 6 summarizes the pharmacokinetic parameters following multiple doses in 20 HPP patients after subcutaneous administration of STRENSIQ at 2 mg/kg three times per week in Study 2 (age of less than or equal to 5 years) and Study 3 (age of greater than 5 to 12 years), indicating the pharmacokinetics were similar between patients in the two age groups.

**Table 6: Summary of Pharmacokinetic Parameters Following Multiple Subcutaneous Administration of STRENSIQ 2 mg/kg Three Times per Week**

| | Study 2 | Study 3 |
|---|---|---|
| **N** | 14 | 6 |
| Age (year) | 3.4 ± 2.1 (0.2, 6.2) | 8.6 ± 2.2 (6.1, 12.6) |
| Weight at baseline (kg) | 11.2 ± 5.0 (2.9, 17.1) | 21.2 ± 7.9 (11.4, 35.4) |
| $t_{last}$ (h) | 48.1 ± 0.1 (47.9, 48.3) | 48.0 ± 0.1 (48.0, 48.1) |
| $t_{max}$ (h) | 14.9 ± 10.4 (0, 32.2) | 20.8 ± 10.0 (11.9, 32.2) |
| $C_{max}$ (ng/mL) | 1794 ± 690 (856, 3510) | 2108 ± 788 (905, 3390) |
| $AUC_t$ (h*ng/mL) | 66042 ± 25758 (27770, 119122) | 89877 ± 33248 (37364, 142265) |
| Accumulation Ratio[a] | 1.5 | 3.9 |

[a] Ratio values reflect the fold increase of $AUC_t$ from Week 1 based on mean $AUC_t$ values. Data are presented as mean ± standard deviation (range). Study 3 includes patients with perinatal/infantile- or juvenile-onset of disease. $t_{last}$, time of last concentration; $t_{max}$, time of maximal concentration; $C_{max}$, maximal concentration; $AUC_t$, area under the concentration-time curves over a dosing interval of 48 hours

Population PK analysis of asfotase alfa concentrations supports weight-based dosing because body weight is a major covariate of asfotase alfa clearance. The formulation concentration had an impact on the systemic exposure of asfotase alfa in HPP patients. The higher concentration formulation (80 mg/0.8 mL vial) achieved an approximately 25% lower systemic asfotase alfa exposure (i.e., concentrations and AUC) compared to the lower concentration formulations (18 mg/0.45 mL, 28 mg/0.7 mL or 40 mg/mL vials) at the same dose of STRENSIQ *[see Dosage and Administration (2.2)]*.

Anti-Drug Antibody Effects on Pharmacokinetics

Formation of anti-drug antibodies resulted in reduced systemic exposure of asfotase alfa.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with asfotase alfa. Asfotase alfa at intravenous doses up to 50 mg/kg/day administered daily in pregnant rats (approximately 21 times the human AUC of 65486 ng.h/mL at 2 mg/kg dose administered three times weekly for a 50 kg individual) was found to have no adverse effect on fertility and reproductive performance of male and female rats.

## 14 CLINICAL STUDIES

### 14.1 Perinatal/Infantile-Onset HPP

Study 1 was a 24-week prospective single-arm trial in 11 patients with severe perinatal/infantile-onset HPP. In this study, 7/11 (64%) were female and 10/11 (91%) patients were white, and age ranged from 3 weeks to 39.5 months. Severe perinatal/infantile-onset HPP was defined as biochemical, medical history and radiographic evidence of HPP as well as the presence of any of the following: rachitic chest deformity, vitamin B6-dependent seizures, or failure to thrive. Ten of 11 patients completed the 24-week trial and continued treatment in the extension phase. Nine patients have been treated for at least 216 weeks (54 months) and 4 patients have been treated for over 240 weeks (60 months). Patients received subcutaneous STRENSIQ 3 mg/kg per week for the first month; subsequently, dose increases up to 9 mg/kg per week were allowed for changes in weight and/or for lack of efficacy. All 10 patients required dose increases up to 6 mg/kg per week or higher; 9 patients increased between 4 and 24 weeks after starting treatment and 1 patient increased after 70 weeks due to suboptimal clinical response. One patient's dose was decreased from 9 mg/kg per week to 6 mg/kg per week based on PK data.

Study 2 was a prospective open-label study in 59 patients with perinatal/infantile-onset HPP. In this study, 32/59 (54%) were female, 46/59 (78%) were white, and age ranged from 1 day to 78 months. Patients received subcutaneous STRENSIQ at 6 mg/kg per week for the first 4 weeks. Ten patients received dose increases higher than 6 mg/kg per week due to suboptimal clinical response, with dose increases occurring between 8 and 24 weeks after starting treatment. The recommended dosage regimen of STRENSIQ for the treatment of perinatal/infantile-onset HPP is up to 9 mg/kg per week administered subcutaneously as 3 mg/kg three times per week *[see Dosage and Administration (2.2)]*.

Forty-one patients were treated for at least 24 weeks (6 months) and 15 patients were treated for at least 96 weeks (24 months).

Survival and Ventilation-Free Survival in Perinatal/Infantile-Onset HPP

Survival and invasive ventilation-free survival were compared in STRENSIQ-treated patients (Studies 1 and 2) with a historical cohort of untreated patients with similar clinical characteristics (Table 7 and Figure 1).

**Table 7: Survival and Invasive Ventilation-Free Survival in STRENSIQ-Treated versus Historical Control Patients with Perinatal/Infantile-Onset HPP (Pooled Studies 1 and 2)**

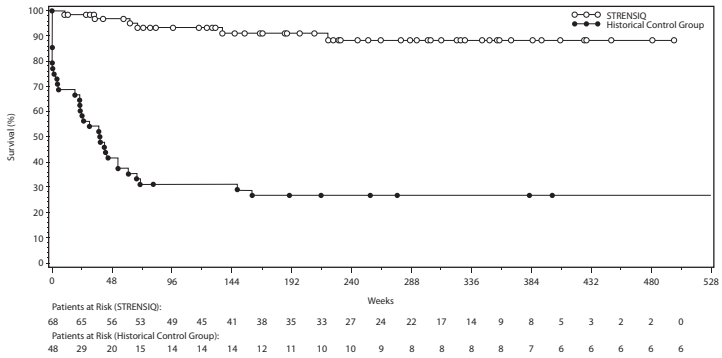
| | STRENSIQ-Treated | Historical Controls |
|---|---|---|
| Survival | n = 68 | n = 48 |
| Alive at Point of Last Contact (%) | 91 | 27 |
| Hazard Ratio (STRENSIQ/Historical Control), 95% Confidence Interval* | 0.14 (0.05, 0.39) | |
| Kaplan-Meier Estimate and Alive at Age 1 Year (Week 48) (%) | 97 | 42 |
| Invasive Ventilation-Free Survival** | n = 54 | n = 48 |
| Alive and Not on Ventilation at Point of Last Contact (%) | 85 | 25 |
| Hazard Ratio (STRENSIQ/Historical Control), 95% Confidence Interval* | 0.21 (0.09, 0.51) | |
| Kaplan-Meier Estimate of Alive and Not on Ventilation at Age 1 Year (Week 48) (%) | 96 | 31 |

* Adjusted for year of diagnosis.

** Alive and not initiating invasive ventilation after start of STRENSIQ treatment. STRENSIQ-treated patients on invasive ventilation at baseline were excluded from this analysis.

In patients who required any form of respiratory support, 21 of 26 (81%) of the treated patients survived through their last assessment (median age at last assessment was 3.2 years of age), versus 1 of 20 (5%) of historical controls.

**Figure 1: Overall Survival in STRENSIQ-Treated versus Historical Control Patients with Perinatal/Infantile-Onset HPP (Pooled Studies 1 and 2)**




x – axis truncated at Week 528; there were 6 historical control patients censored after truncation with censored times ranging from 538 to 1030 weeks

Skeletal Manifestations in Perinatal/Infantile-Onset HPP

Radiographs from 68 STRENSIQ-treated perinatal/infantile-onset HPP patients, including 64 patients in Studies 1 and 2, and 4 patients in Study 3 *[see Clinical Studies (14.2)]*, were examined to assess HPP-related rickets using the 7-point Radiographic Global Impression of Change (RGI-C) scale. Patients with a minimum RGI-C score of +2 were defined as "responders". Radiologic improvements could be seen by Month 24; at last assessment, 50/68 [74%] treated patients were rated as RGI-C responders. No comparative data were available from historical controls. The mean time interval between the baseline and last RGI-C assessment was 24 months (range was 1 month to 67 months).

Eighteen perinatal/infantile-onset HPP patients experienced fractures during the course of treatment. There were insufficient data to determine the effect of STRENSIQ on fractures.

Growth in Perinatal/Infantile-Onset HPP

Height and weight measurements (as measured by Z-scores) were available post-treatment for 72 perinatal/infantile-onset HPP patients, including 68 patients enrolled in Studies 1 and 2, and 4 patients enrolled in Study 3 (Table 8).

**Table 8: Perinatal/Infantile-Onset Height and Weight Measurements as Measured by Z-Score (Studies 1 and 2)**

| | Height Z-score | | | | Weight Z-score | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | | Last Assessment | | Baseline | | Last Assessment | |
| | Mean | Min, Max | Mean | Min, Max | Mean | Min, Max | Mean | Min, Max |
| Studies 1 and 2* (N=68) | -3.3 | -10.1, 0.9 | -2.9 | -10.6, 0.4 | -3.2 | -23.8, 0 | -2.4 | -20.9, 1.1 |
| Study 3 (N=4)** | -2.6 | -6.6, -0.7 | -1.5 | -5.8, 0.4 | -2.5 | -8.2, -1.0 | -1.5 | -5.4, 0.5 |

* The mean time interval between baseline and last assessment was 21 months (range was 1 month to 72 months).

** The mean time between baseline and last assessment was 56 months (range was 53 months to 60 months).

Long-Term Extension Trials in Perinatal/Infantile-Onset HPP

Long-term data were collected in 68 STRENSIQ-treated patients with perinatal/infantile onset HPP in Studies 1 and 2 and an additional 10 patients enrolled in Study 2. The longest duration of follow-up in the 78 patients was 7 years (84 months). At point of last contact, 69/78 (88%) STRENSIQ-treated patients had survived.

### 14.2 Juvenile-Onset HPP

Study 3 was a prospective open-label 24-week trial that included 8 juvenile-onset HPP patients and 5 perinatal/infantile-onset HPP patients; 11/13 (85%) were male and 12/13 (92%) were white *[see Clinical Studies (14.1)]*. On study entry, patients were 6 to 12 years of age. All 8 juvenile-onset patients entered the extension study and were treated for at least 48 months. At trial entry, patients were randomized to receive subcutaneous STRENSIQ 6 mg/kg per week or 9 mg/kg per week. Two patients received dose reductions during the primary treatment period, including one patient who experienced a decrease in vitamin B6 levels and one patient who experienced recurrent injection site reactions. During the extension phase, the dosing regimen for all patients was initially changed to 3 mg/kg per week. Dosing was subsequently increased to 6 mg/kg per week, with no patients requiring doses higher than 6 mg/kg per week. The recommended dosage regimen of STRENSIQ for the treatment of juvenile-onset HPP is 6 mg/kg per week *[see Dosage and Administration (2.2)]*.

Growth in Juvenile-Onset HPP

Height and weight measurements (as measured by Z-scores) in 8 STRENSIQ-treated juvenile-onset HPP patients were compared with a historical cohort of 32 untreated patients with similar clinical characteristics (Table 9). Height and weight data for historical patients were collected from medical records.

**Table 9: Juvenile-Onset Height and Weight Measurements as Measured by Z-Score (Study 3)**

| | Height Z-score | | | | Weight Z-score | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | | Last Assessment | | Baseline | | Last Assessment | |
| | Mean | Min, Max | Mean | Min, Max | Mean | Min, Max | Mean | Min, Max |
| STRENSIQ (N=8)* | -1.5 | -3.8, 0 | -0.9 | -2, 0 | -1.1 | -3.5, 2.3 | 0 | -1.3, 2.2 |
| Control (N=32)** | -1.1 | -4.9, 2.6 | -1.1 | -4.9, 1.8 | -1.2 | -5, 2.1 | -1 | -5.7, 2.1 |

* The mean time interval between baseline and last assessment was 55 months (range was 53 months to 60 months).

** The mean time interval between baseline and last assessment was 61 months (range was 19 months to 109 months).

Skeletal Manifestations in Juvenile-Onset HPP

Radiographs from 8 STRENSIQ-treated juvenile-onset HPP patients and 32 historical controls were compared to assess HPP-related rickets using the 7-point RGI-C (Radiographic Global Impression of Change) scale. Patients who achieved a RGI-C score of 2 or higher (corresponding to substantial healing of rickets) were classified as being responders to treatment. All 8 treated patients were rated as responders by Month 54 of treatment. The mean duration between the baseline and last RGI-C assessments for control patients was 56

months (range was 8 to 95 months). At last assessment, 2/32 (6%) of control patients were rated as responders.

Eight of 20 (40%) patients with juvenile-onset HPP experienced new fractures during the course of treatment. There were insufficient data to assess the effect of STRENSIQ on fractures.

Gait/Mobility in Juvenile-Onset HPP

Gait was assessed using a modified Performance Oriented Mobility Assessment-Gait (MPOMA-G) scale in 8 STRENSIQ-treated juvenile-onset HPP patients at 6-month intervals out to 36 months. Mobility was also assessed using the 6 Minute Walk Test (6MWT) in 7 of the 8 patients. Step length improved by at least 1 point in either foot in 6/8 patients compared to 1/6 (17%) control patients. The proportion of patients who had 6MWT percent predicted values within the normal range for age, sex, and height-matched peers increased from 0/8 patients at baseline to 6/6 patients (100%) by Month 48 and all 6 were also able to walk longer distances at this time point compared to baseline.

Long-Term Extension Trials in Juvenile-Onset HPP

Long-term data were collected in 8 patients with juvenile-onset HPP treated with STRENSIQ for at least 6 years (72 months). At last assessment, 7 patients with available 6MWT results had maintained improvements in gait/mobility.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

STRENSIQ is supplied as a sterile, nonpyrogenic, preservative-free, clear, slightly opalescent or opalescent, colorless to slightly yellow aqueous solution; a few small translucent or white particles may be present. The product is available as single-dose vials in a carton of one (1) or twelve (12) vials at the following strengths:

**Table 10: STRENSIQ Vial Presentations**

| Strength | National Drug Code (NDC) | Quantity of Vials in Carton |
|---|---|---|
| 18 mg/0.45 mL | NDC 25682-010-01 | 1 |
| | NDC 25682-010-12 | 12 |
| 28 mg/0.7 mL | NDC 25682-013-01 | 1 |
| | NDC 25682-013-12 | 12 |
| 40 mg/mL | NDC-25682-016-01 | 1 |
| | NDC-25682-016-12 | 12 |
| For pediatric patients 40 kg and greater | | |
| 80 mg/0.8 mL | NDC 25682-019-01 | 1 |
| | NDC 25682-019-12 | 12 |

STRENSIQ vials must be stored in the original carton until the time of use under refrigerated conditions at 2°C to 8°C (36°F to 46°F) and protected from light.

Once removed from refrigeration, STRENSIQ should be administered within 3 hours.

Do not use beyond the expiration date stamped on the carton.

DO NOT FREEZE OR SHAKE.

Vials are for one time use only. Discard any unused product.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient or caregiver to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Advise patients or caregivers of the following:

Preparation

- 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.
- Take the unopened STRENSIQ vial(s) out of the refrigerator 15 to 30 minutes before injecting to allow the liquid to reach room temperature.
- Inspect the solution in the vial(s) for particulate matter and discoloration.
- Assemble injection supplies. Administer STRENSIQ using sterile disposable syringes and injection needles. The syringes should be of small enough volume that the prescribed dose can be withdrawn from the vial with reasonable accuracy. Always use a new syringe and needle.
- Remove vial cap, aseptically prepare the vial and insert the syringe into the vial to withdraw the prescribed dose for administration.
- Remove any air bubbles in the syringe and verify the correct dose.
- STRENSIQ vials are for one time use only. Discard any unused product *[see Dosage and Administration (2.4)]*.

Administration

- Administer STRENSIQ within 3 hours upon removal of the vial(s) from refrigeration.
- Rotate the injection site to reduce the risk of lipohypertrophy and injection site atrophy.
- Do NOT administer injections in areas that are reddened, inflamed, or swollen.
- Inject STRENSIQ subcutaneously into the determined site and properly dispose of the syringe and needle *[see Dosage and Administration (2.5)]*.

Hypersensitivity Reactions Including Anaphylaxis

- Life-threatening hypersensitivity reactions, including anaphylaxis may occur with STRENSIQ treatment.
- Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.
- Symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur *[see Warnings and Precautions (5.1)]*.

Lipodystrophy

- Lipohypertrophy (enlargement or thickening of tissue) and localized atrophy (depression in the skin) have been reported at injection sites after several months. Follow proper injection technique and rotate injection sites *[see Warnings and Precautions (5.2)]*.

Possible Immune-Mediated Clinical Effects

- Anti-drug antibodies may develop during treatment which may interfere with STRENSIQ's pharmacologic action. Inform patients or their caregivers to contact their healthcare provider if they experience worsening symptoms of HPP (e.g., increased respiratory support, increased difficulty walking, new fractures) *[see Warnings and Precautions (5.4)]*.

Hypophosphatasia (HPP) Registry

- A registry has been established in order to better understand HPP in the population, and to monitor and evaluate long-term treatment effects of STRENSIQ. Patients and their caregivers should be encouraged to participate and advised that their participation is voluntary and may involve long-term follow-up. For more information, visit www.hppregistry.com

Manufactured by:
Alexion Pharmaceuticals, Inc.
121 Seaport Boulevard
Boston, MA 02210 USA

U.S. License Number: 1743

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US/STQ-H/0604 V1 07/2024

# PATIENT INFORMATION
# STRENSIQ® [stren sik]
## (asfotase alfa)
## injection, for subcutaneous use

**What is the most important information I should know about STRENSIQ?**

**STRENSIQ may cause serious side effects, including:**

- **severe allergic (hypersensitivity) reactions.** Allergic reactions are common with STRENSIQ treatment and can be severe and life-threatening. Severe allergic reactions have happened in some people within minutes after receiving STRENSIQ and more than 1 year after starting treatment with STRENSIQ. Stop using STRENSIQ and go to the nearest hospital emergency room right away if you get any of the following signs and symptoms of a serious allergic reaction:
  - difficulty breathing
  - choking sensation
  - swelling of your eyes, lips, or tongue
  - dizziness
  - nausea or vomiting
  - fever
  - headache
  - sweating
  - feeling irritable
  - chills
  - skin redness
  - skin rash or hives
  - itching or numbness of the tongue, lips, cheeks, or gums

**What is STRENSIQ?**

STRENSIQ is a prescription medicine used to treat people with perinatal, infantile, and juvenile onset hypophosphatasia (HPP).

**Before using STRENSIQ, tell your healthcare provider about all of your medical conditions, including if you:**

- have had an allergic reaction to STRENSIQ.
- are pregnant or plan to become pregnant. It is not known if STRENSIQ will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if STRENSIQ passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you use STRENSIQ.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

There is a registry for people who use STRENSIQ. The purpose of this registry is to collect information about HPP and about what happens when you use STRENSIQ for a long time. For more information about this registry, talk with your healthcare provider or go to www.hppregistry.com.

**How should I use STRENSIQ?**

- Use STRENSIQ exactly as your healthcare provider tells you to.
- You will begin receiving STRENSIQ under the supervision of a healthcare provider.
- **See the "Instructions for Use" at the end of the Patient Information for instructions about:**
  - **How to prepare and inject STRENSIQ**
  - **How to properly throw away (dispose of) any unused STRENSIQ**
  - **How to dispose of used syringes and needles.**
- Your healthcare provider will tell you how much STRENSIQ to use and when to use it.
- Your healthcare provider may change your dose, if needed.

**What are the possible side effects of STRENSIQ?**

**STRENSIQ may cause serious side effects, including:**

- **severe allergic (hypersensitivity) reactions. See "What is the most important information I should know about STRENSIQ?"**
- **skin thickening or pits at the injection site (lipodystrophy).** Lipodystrophy is common and has happened after several months in people treated with STRENSIQ.
- **calcium build-up in your eyes and kidneys.** People with HPP are at increased risk for developing calcium build-up in the body. Calcium build-up in the eyes and kidneys has happened and is a common side effect of STRENSIQ. Calcium build-up in the eyes and kidneys may also happen in people with HPP who are not treated with STRENSIQ. Your healthcare provider should check your eyes and kidneys before and during treatment with STRENSIQ.

- **immune-related effects.** You may develop antibodies during treatment that may decrease how well STRENSIQ works. Tell your healthcare provider right away if you get worsening symptoms of HPP including:
  - difficulty breathing
  - difficulty walking
  - feeling tired
  - bone pain
  - stiff joints
  - loss of appetite

**The most common side effects of STRENSIQ include** local skin injection site reactions such as skin redness, bruising, color change, pain, itching, hardening of the skin (induration), swelling, and bumps.

These are not all of the possible side effects of STRENSIQ. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of STRENSIQ.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use STRENSIQ for a condition for which it was not prescribed. Do not give STRENSIQ to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about STRENSIQ that is written for health professionals.

**What are the ingredients in STRENSIQ?**

**Active ingredient:** asfotase alfa.

**Inactive ingredients:** dibasic sodium phosphate, heptahydrate; monobasic sodium phosphate, monohydrate and sodium chloride.

Manufactured by: Alexion Pharmaceuticals, Inc., Boston, MA 02210 USA
U.S. License Number: 1743
For more information, go to www.strensiq.com or call 888-765-4747.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 7/2024

# INSTRUCTIONS FOR USE
# STRENSIQ® [stren' sik]
## (asfotase alfa)
## injection, for subcutaneous use vial

Read this "Instructions for Use" before you start using STRENSIQ and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

**Do not share your syringes or needles with anyone else. You may give an infection to them or get an infection from them.**

**Supplies needed to give your STRENSIQ injection (See Figure A):**

- 1 or 2 STRENSIQ vial(s).
- 1 or 2 sterile disposable 1 mL syringes for injection with 25 to 29 gauge (G), ½ inch needles.
  - The use of two different gauge needles is recommended, a larger bore needle (e.g. 25 gauge) for withdrawal of the medication, and a smaller bore needle (e.g. 29 gauge) for the injection.
  - Always use a new syringe and needle for each injection.
- 2 alcohol wipes
- 1 gauze or cotton ball
- a clean flat surface, like a table
- 1 sharps container for throwing away used needles and syringes. See **"Disposing of used needles and syringes"** at the end of these instructions.

**Figure A**

**Storing your STRENSIQ dose:**

- Store STRENSIQ in the original carton in the refrigerator between 36°F to 46°F (2°C to 8°C) until you are ready to use it.
- Do not freeze your STRENSIQ vials. Do not use STRENSIQ if it has been frozen.
- Do not shake your STRENSIQ vials.
- Protect STRENSIQ from light until you are ready to use it.
- Do not use STRENSIQ after the expiration date printed on the carton.
- STRENSIQ vials are for 1 time use only. Throw away any unused STRENSIQ left in the vial.

**Preparing your STRENSIQ dose and giving your STRENSIQ injection:**

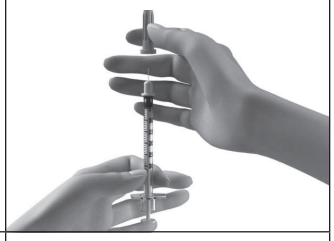
- Prepare a clean flat surface, like a table or counter top.
- Remove the unopened STRENSIQ vial(s) out of the refrigerator and allow it to sit at room temperature for at least 15 to 30 minutes. Injecting STRENSIQ when cold can make the injection feel uncomfortable.
  - Do not warm STRENSIQ in any way other than letting it sit at room temperature (for example, do not warm it in a microwave or in hot water).
- Gather all the supplies you will need to give your STRENSIQ injection.
- Wash your hands with soap and water.
- Utilize STRENSIQ within 3 hours after removing it from the refrigerator.
- Inject STRENSIQ exactly as your healthcare provider has shown you.

| | |
|---|---|
| **Step 1:** Check the liquid in the STRENSIQ vial. STRENSIQ liquid should look clear or slightly yellow and may have a few small white particles in it. Do not use it if the liquid is discolored or contains any lumps or large particles in it. Throw it away and get a new vial. | |
| **Step 2:** Using your thumb, flip the plastic cap off the STRENSIQ vial. | |
| **Step 3:** Remove the larger bore needle (e.g., 25 G) from the package. Pick up the syringe and place the needle on the tip of the syringe. Push down and twist the needle onto the syringe until it is tight. | |

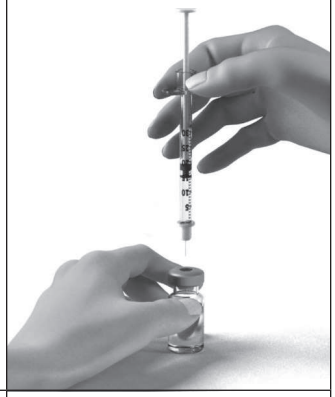
**Step 4:** Hold the syringe with the needle pointing up and pull back the plunger until the top of the plunger reaches the line for your prescribed dose.

**Step 5:** Pull the cap straight off of the needle.

- **Do not** touch the needle or let the needle touch any surface.



**Step 6:** Hold the STRENSIQ vial firmly on a flat surface, then push the needle through the rubber stopper of the STRENSIQ vial.



**Step 7:** Keeping the needle in the STRENSIQ vial, lift the vial and turn it upside down with the needle pointing toward the ceiling. Slowly push the plunger all the way in.

**Step 8:** With the needle tip still in the liquid, slowly pull back the plunger until the top of the plunger reaches the line slightly past the line for your prescribed dose. Do not pull the needle out of the STRENSIQ vial. Slowly push the plunger up until the top of the plunger reaches the line for your prescribed dose.

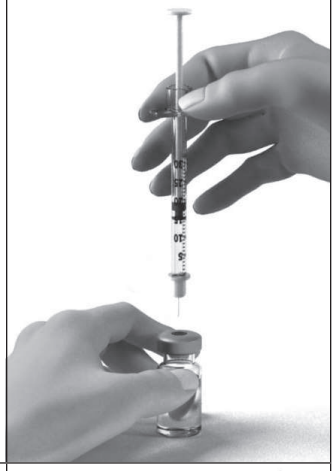
- Check the syringe to make sure that you have the right dose.

**Step 9:** Turn the STRENSIQ vial upright and pull the syringe straight out of the vial's rubber stopper.

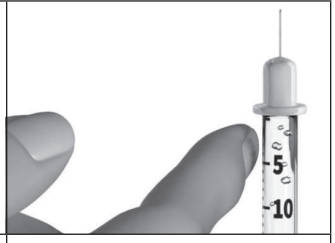
- **Do not** touch the needle or allow the needle to touch any surface.

Carefully remove the larger bore needle (e.g., 25 G) you withdrew the STRENSIQ dose with and dispose of properly (as noted at the end of these instructions).

Replace with a new, smaller bore needle (e.g., 29 G) prior to injection.

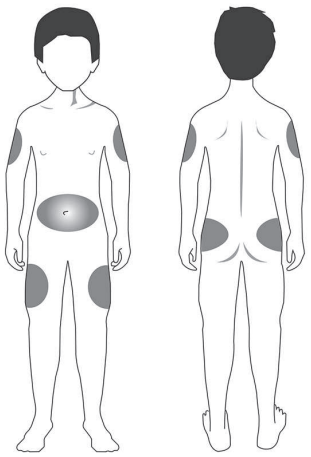


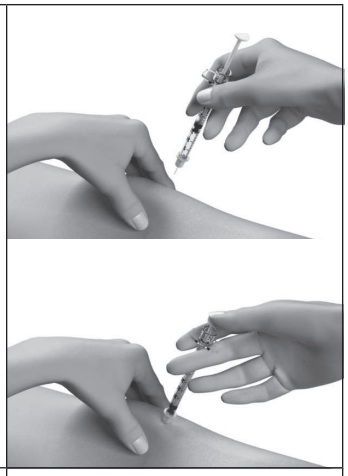
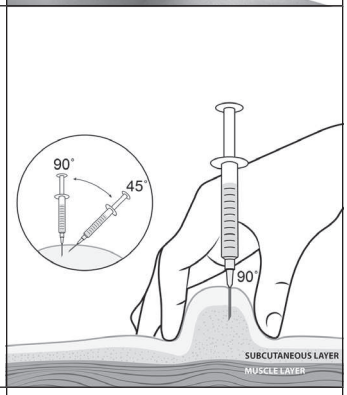
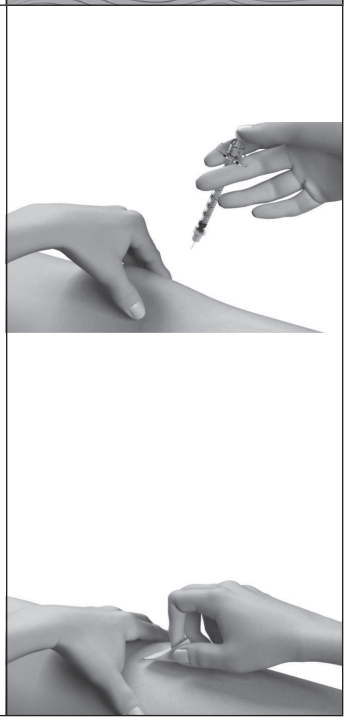
**Step 10:** Hold the syringe with the needle pointing up and tap the barrel of the syringe with your finger to remove any air bubbles.



**Step 11** Choose your injection site. STRENSIQ is injected under the skin (subcutaneously) of your stomach-area (abdomen), upper arms, upper legs, or buttocks.

- **Do not** inject STRENSIQ into the buttocks for infants.
- **Change (rotate) your injection site with each injection.** Do not use the same injection site for each injection.
- **Do not** inject STRENSIQ into skin that is red, hot, or swollen.
- Wipe your skin with an alcohol wipe. Let the site dry before you inject your dose.



| | | |
|---|---|---|
| **Step 12:** | Pinch the skin. Hold the syringe at a 90° angle (straight up and down) and insert the needle into your skin. For patients with little fat, hold the syringe at a 45° angle and insert the needle into your skin. |  |
| **Step 13:** | Push the plunger slowly and steadily all the way in to give your dose. |   |
| **Step 14:** | Pull the needle out of your skin.<br>• If you see blood after you take the needle out of your skin, press your injection site with a piece of gauze or alcohol wipe.<br>• **Do not** recap the needle. Recapping the needle can lead to a needle stick injury.<br>If you need a second injection for your prescribed dose, get another STRENSIQ vial and repeat steps 1 through 14. |  |

**Disposing of used needles and syringes:**

- Put your used needles in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid,
  - without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

**Keep STRENSIQ and all medicines, needles and syringes out of the reach of children.**

This "Instructions for Use" has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Alexion Pharmaceuticals, Inc.
Boston, MA 02210 USA
U.S. License Number: 1743

Approved: 6/2020

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