STRENSIQ® (ASFOTASE ALFA)

STRENSIQ® (ASFOTASE ALFA) OVERVIEW

Strensiq (asfotase alfa) is a highly innovative, first-in-class enzyme replacement therapy approved in the United States for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP). Strensiq is also approved in the European Union, Japan, and Canada.

HPP is a genetic, chronic, progressive, and life-threatening metabolic disease in which patients experience devastating effects on multiple systems of the body, leading to debilitating or life-threatening complications.[1] It is an ultra-rare disease, which is defined as a disease that affects fewer than 20 patients per one million in the general population.[2] HPP is characterized by low alkaline phosphatase (ALP) activity and defective bone mineralization that can lead to deformity of bones and other skeletal abnormalities, as well as systemic complications such as muscle weakness and respiratory failure leading to premature death in infants.[1,3,4]

MECHANISM OF ACTION

HPP is caused by a defect (mutation) in the gene that makes an enzyme known as tissue non-specific alkaline phosphatase (TNSALP), resulting in low levels of ALP activity.[1,5,6] When ALP is functioning normally, it allows two key minerals—calcium and phosphate—to bind together to form healthy, mineralized bones.[5,7] In patients with HPP, however, ALP activity is low, leading to insufficient mineralization of bone and altered calcium and phosphate metabolism.[8]

Strensiq is the first therapy to treat the underlying cause of HPP—deficient ALP. By replacing the deficient ALP, Strensiq aims to reduce the elevated enzyme substrate levels and improve the body's ability to mineralize bone. Strensiq is administered via subcutaneous injection (injection under the skin).

CONSEQUENCES OF HPP

The signs and symptoms of HPP can vary from patient to patient, and can include problems in the bones, muscles, and lungs.[1,7]

Many patients with HPP have weak, soft, or brittle bones, as well as skeletal deformities, including HPP-related rickets and bowed legs.[1,3,4,10] These abnormalities can impede growth in children and can continue to impair a person's mobility.[11,12]

Infants and young children may experience severe symptoms of HPP that can lead to premature death, such as severe breathing complications that may require an assistive breathing device or cause respiratory failure.[1,12] In a retrospective natural history study of infants with severe HPP, those who experienced their first symptom of HPP within the first six months of life had a very high mortality rate.[12]

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CLINICAL TRIAL DATA[9]

The safety and efficacy of Strensiq in the U.S. was based on data from four prospective, open-label clinical trials and supporting extension trials comprising 99 patients with perinatal/infantile (n=79) and juvenile-onset (n=20) HPP (ages 1 day to 58 years) who received treatment with Strensiq for up to 24 months or more. The efficacy evaluation of Strensiq also included data from two retrospective natural history studies that were used as control cohorts.

Strensiq in Patients with Perinatal/Infantile-Onset HPP

- Patients with perinatal/infantile-onset HPP treated with Strensiq had significantly improved survival compared with a historical cohort of untreated patients with similar clinical characteristics.
  - At 48 weeks, estimated survival was 97% for Strensiq-treated patients compared with 42% for historical control patients (Hazard Ratio [95% CI]: 0.14 [0.05, 0.39]).
  - Estimated survival without invasive ventilator support was 96% for Strensiq-treated patients compared with 31% for historical control patients (Hazard Ratio [95% CI]: 0.21 [0.09, 0.51]).
- Radiographs were examined to assess the treatment effect of Strensiq on HPP-related rickets using a 7-point Radiographic Global Impression of Change (RGI-C) score to measure change. In patients treated with Strensiq, 74% (50/68) were rated as RGI-C responders at last assessment (mean time from baseline was 24 months; range was 1 to 67 months).
- Improvements were also observed in mean weight and height z-scores for Strensiq-treated patients, reflecting improvements in growth relative to healthy, same-aged peers.

Strensiq in Patients with Juvenile-Onset HPP

- In patients with juvenile-onset HPP, 100% of Strensiq-treated patients (8/8) were rated as RGI-C responders by 54 months of treatment. Comparatively, 6% (2/32) of untreated historical control patients were rated as responders at last assessment.
- Gait performance (walking ability) was assessed using a modified Performance Oriented Mobility Assessment-Gait (mPOMA-G) scale. Seventy-five percent of patients (6/8) treated with Strensiq demonstrated at least a 1 point improvement in step length in either foot compared with 17% (1/6) of historical control patients.
- Improvements in mobility were demonstrated in patients treated with Strensiq, as measured by improvements in the Six Minute Walk Test (6MWT) compared to baseline.
  - By 4 years of treatment, 100% of patients assessed (6 of 6) achieved the 6MWT within the normal range for age-, sex- and height-matched peers, whereas no patients were in the normal range at baseline, and all 6 were able to walk longer distances at this time point compared to baseline.
- Improvements were also observed in mean weight and height z-scores for Strensiq-treated patients compared with untreated historical controls, reflecting improvements in growth relative to healthy, same-aged peers.

PATIENT SUPPORT

At Alexion, we recognize our obligation to the HPP community. Our objective is that every patient with HPP who can benefit from Strensiq will have access to it. As part of this commitment, Alexion offers OneSource™, a comprehensive program that pairs each HPP patient and family with a dedicated Alexion Nurse Case Manager who will be a single point of contact for all treatment support, disease education and access information. Since Strensiq is administered in the patient's home, Nurse Case Managers can help coordinate in-home injection training as well as services to assist with proper medication use. Nurse Case Managers can also help answer questions about insurance coverage and reimbursement and can refer families to foundations that provide additional physical and emotional support, as well as equipment for patients with HPP.

For patients whose insurance is not adequate, Alexion Nurse Case Managers will provide information about resources for alternative coverage or funding. Through OneSource, patients and families can obtain further information regarding third-party foundations and co-pay assistance programs, which help patients meet out-of-pocket expenses related to the treatment of HPP. For uninsured patients who have no access to insurance, the Alexion Access Foundation, a charitable entity, provides Strensiq free of charge for patients.

Patients and caregivers in the United States can call 1.888.765.4747 to speak with an Alexion Nurse Case Manager and learn about support options.

INDICATION

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

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IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been reported in STRENSIQ-treated patients. In clinical trials, 1 out of 99 treated patients (1%) experienced signs and symptoms consistent with anaphylaxis, including difficulty breathing, nausea, periorbital edema, and dizziness. Other reported hypersensitivity reactions include vomiting, fever, headache, flushing, irritability, chills, skin erythema, rash, pruritus, and oral hypoesthesia. If a severe hypersensitivity reaction occurs, discontinue STRENSIQ and initiate appropriate medical treatment. Consider the risks and benefits of re-administering STRENSIQ following a severe reaction. If the decision is made to re-administer STRENSIQ, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.

Localized lipodystrophy, including lipoatrophy and lipohypertrophy, has been reported at injection sites after several months in patients treated with STRENSIQ. Advise patients to follow proper injection technique and to rotate injection sites.

Patients with HPP are at increased risk for developing ectopic calcifications. In clinical trials, 14 cases (14%) of ectopic calcification of the eye including the cornea and conjunctiva, and the kidneys (nephrocalcinosis) were reported. 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. 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.

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

Please see full prescribing information for Strensiq.

References

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