LOUISIANA BLUE

asfotase alfa (Strensiq®)

Policy # 00499
Original Effective Date: 02/17/2016
Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider asfotase alfa (Strensiq®‡) for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for asfotase alfa (Strensiq) for the treatment of patients with perinatal/infantile- and juvenile-onset HPP will be considered when the following criteria are met:

- Patient has a diagnosis of perinatal/infantile- or juvenile onset hypophosphatasia; AND
- Patient has hallmark skeletal and/or dental manifestations representative of hypophosphatasia (e.g., Skeletal manifestations include: rickets, osteomalacia, nonhealing fractures, osteopenia, osteoporosis, and craniosynostosis. Dental manifestations include: premature tooth loss or periodontal disease.); AND
- Patient has a LOW alkaline phosphatase (ALP) level (age adjusted).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of asfotase alfa (Strensiq) when patient selection criteria are not met to be **investigational.***

Background/Overview

Strensiq is a tissue nonspecific ALP approved for the treatment of patients with perinatal/infantile- and juvenile-onset HPP. Strensiq is administered by subcutaneous injection. The dosing of Strensiq is weight based and can be given either three times per week or six times per week.

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Hypophosphatasia
HPP is caused by a deficiency in TNSALP (tissue-nonspecific alkaline phosphatase) enzyme activity, which leads to elevations in many TNSALP substrates, including inorganic pyrophosphate (PPi). Elevated levels of PPi block hydroxyapatite crystal growth, which in turn inhibits bone mineralization and causes an accumulation of unmineralized bone matrix. The unmineralized bone matrix manifests as rickets and bone deformation in infants and children. It can then manifest 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.

Hallmark manifestations of HPP include skeletal and/or dental issues. Skeletal manifestations include: rickets, osteomalacia, nonhealing fractures, osteopenia, osteoporosis, and craniosynostosis. Dental manifestations include: premature tooth loss or periodontal disease. These hallmark manifestations combined with a low age adjusted ALP steer in the direction of a HPP diagnosis.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Strensiq was approved in October of 2015 for the treatment of patients with perinatal/infantile- and juvenile-onset HPP. Strensiq is the only drug FDA approved for this indication.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Strensiq was studied in three open-label, multicenter studies in patients with perinatal/infantile- and juvenile-onset HPP. The primary endpoint of the studies included the change in skeletal manifestations of HPP [using the 7 point Radiographic Global Impression of Change (RGI-C) scale (from -3 to +3) and the 10 point Rickets Severity Scale (RSS)]. For the RGI-C scale, a reduction of 3 points represented severe worsening and an increase of 3 points indicated complete healing of the skeletal disease. For the RSS score, higher scores represented more severe rickets.

In the first study (n=11), the RGI-C improved from baseline to week 24 in 90% of perinatal/infantile onset patients (n=9/10) treated with Strensiq. The RGI-C also improved from baseline to week 48 in 89% of patients (n=8/9). The RSS score improved significantly from baseline at weeks 24, 72, and 240. In the second study (n=13), at week 24, the RGI-C sore was increased by 2 points for the infantile and juvenile onset Strensiq treated patients, whereas there was no increase noted in the historical control patients. The RSS scores also improved in Strensiq treated patients. The mean change from baseline was statistically significant at all time points when compared to the historical

controls. At 5 years, the median RGI-C was 2.2. In the third study (n=59), the median RGI-C score showed statistically significant improvement in all Strensiq treated patients (perinatal/infantile onset). Nearly 82% of patients (n=37/45) achieved RGI-C scores of ≥1 (minimal healing of rickets); 49% of patients (n=22/45) had RGI-C scores of ≥2; 9% (n=4/45) achieved scores of 3. Of the 33 patients with week 48 data, 70% of patients demonstrated at least "substantial healing" of HPP associated rickets (RGI-C score ≥2) and were considered responders.

References

1. Strensiq injection [prescribing information]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; October 2015.
2. Strensiq Drug Evaluation. Express Scripts. Updated November 2015.
3. Hypophosphatasia.www.hyposphatasia.com/hcp/diagnostic-pathway. Alexion Pharmaceuticals.

Policy History

Original Effective Date: 02/17/2016
Current Effective Date: 03/10/2025

02/04/2016	Medical Policy Committee review
02/17/2016	Medical Policy Implementation Committee approval. New policy.
02/02/2017	Medical Policy Committee review
02/15/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/01/2018	Medical Policy Committee review
02/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/07/2019	Medical Policy Committee review
02/20/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2020	Medical Policy Committee review
02/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/04/2021	Medical Policy Committee review
02/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/01/2024	Medical Policy Committee approval

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02/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.