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

Common Assessments for STRENSIQ Prior Authorizations and Reauthorizations

INDICATION

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

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Initiate STRENSIQ under the supervision of a healthcare provider with appropriate medical monitoring and support measures. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue STRENSIQ and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur *[see Warnings and Precautions (5.1)]*.

Please see Important Safety Information on pages 1, 16, and 17 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

Introduction

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

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

Table of Contents

Validated functional assessments and calculations used in STRENSIQ clinical trials or clinical practice to measure HPP baseline and/or progress

Test[a]	Perinatal/Infantile[b]	Childhood/Adolescents	Adult
6-Minute Walk Test (6MWT)[1]		✓	✓
Timed Up & Go (TUG) Test[2]			✓
Chair Rise Test[3]			✓
Lower Extremity Function Scale (LEFS)[4]			✓
Weight-for-Height Z-score (WHZ)[5]	✓	✓	

The Modified Performance Oriented Mobility Assessment-Gait (mPOMA-G) and Radiographic Global Impression of Change (RGI-C) scales are probably not routinely used in clinical practice by healthcare providers who treat HPP; therefore, they are not present in this guide.
a. The 6MWT is a validated test for use in patients with HPP. All other tests listed above are not validated specifically for use in patients with HPP.
b. Monitor for skeletal and respiratory improvements.

6 Minute Walk Test (6MWT)

Appropriate age group: Adults >18 years and children/adolescents ≥5 years[1]

- The 6MWT has been clinically validated[a] and is utilized in clinical practice.

What is the 6MWT?

- The 6MWT is a self-paced walking test that measures the distance of one's ability to walk on a hard, flat surface for 6 minutes; the goal is to walk as far as possible in 6 minutes.[1,6]
- Originally developed for assessment of aerobic activity in patients with respiratory disease, the 6MWT is now validated in other patient populations such as those with musculoskeletal disease. The 6MWT has been used in clinical studies as a measure for patients with muscular and metabolic disorders and rare diseases.[1]

Why is the 6MWT used for patients who have been prescribed STRENSIQ?

- The 6MWT is a reliable and valid measure in children, adolescents, and adults with hypophosphatasia (HPP) signs and symptoms first occurring before 18 years of age.[1]
- This test can be used to monitor a patient's response to treatments for cardiovascular, pulmonary, musculoskeletal, and other health problems reflecting the exercise level required to perform activities of daily living.[1]
- The 6MWT has also been used as a one-time measure of functional status for patients and as a predictor of morbidity and mortality for patients with moderate to severe cardiovascular or pulmonary disease.[7]

How is the 6MWT conducted?

- **Select equipment/space requirements:** Stopwatch or timer, chair if patient needs to rest during the 6MWT, 30 meters (~100 feet) of hard, flat walking area, and two small cones or bright tape to mark turnaround points.[6,7]
- **Patient instructions:** Patients are instructed to walk as far as possible for 6 minutes. Walking at a normal pace to a chair or cone, then turning around and continuing for 6 minutes is acceptable (See Figure A on page 4). It is acceptable to slow down, rest, or stop.[7,8]
- **HCP instructions:** Begin your timer when the patient starts walking and stop the timer at 6 minutes. Give an update after every passing minute interval.[7,8]
- Conducive outdoor areas may be used if deemed appropriate by medical staff.[6,7]

Examples of 6MWT prior authorization criteria for STRENSIQ:

- Gait disturbance, such as delayed walking or waddling gait:
  - Must provide results of a recent (within 12 months) 6MWT showing lower-than-expected results.[9,10]

Examples of reauthorization/continuation of therapy 6MWT criteria for STRENSIQ:

- Has the patient experienced an improvement in the 6MWT compared to baseline?
  - If yes, please submit medical record of distance walked in the 6MWT.[9,10]
- Improvement in the 6MWT.[9,11]
- Member has experienced an improvement in the 6MWT compared to baseline.[9,11]

Coding and billing information:

- The following CPT code and modifiers may be appropriate to report administration of the 6MWT in physician office and hospital outpatient facilities.

CPT[12]	Description
94618	Pulmonary stress testing (eg, 6 Minute Walk Test), including measurement of heart rate, oximetry, and oxygen titration, when performed

- Please note that Medicare has a Local Coverage Determination (LCD) for 6MWT.[13] If billing Medicare, the LCD should be reviewed prior to submitting a claim to ensure all LCD requirements are met.

a. Test specifically validated in patients with HPP.

Please see Important Safety Information on pages 1, 16, and 17 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

6 Minute Walk Test (6MWT) (cont.)

Coding and billing information (cont.):

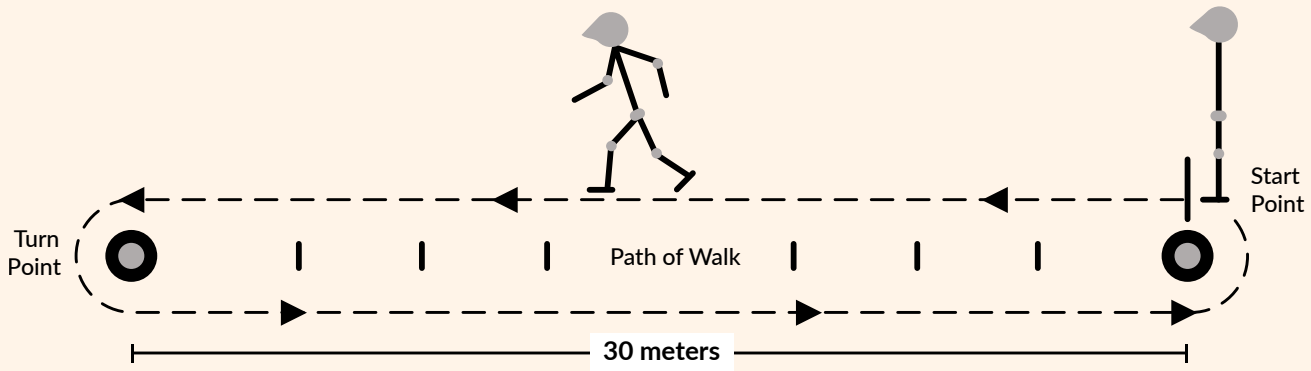
CPT Modifiers

- The 6MWT CPT, 94618, is considered a diagnostic test and, as such, has both a technical and professional component. If only one component needs to be reported, the appropriate modifier should be added:

CPT Modifier[12,14]	Description	Appropriate Use[15]
26	Professional Component	The professional component consists of the interpretation of the test and the report subsequently generated by the physician
TC	Technical Component	The technical component which captures the expenses related to the performance of the test, including the cost of technicians, equipment, and space. The technical component charges are institutional charges and not billed separately by physicians

You can find more information regarding the administration of the 6MWT Test in the official guidelines published by the American Thoracic Society.

Figure A: Visualization of a 6MWT on a Hard, Flat Surface[16]



6 Minute Walk Test (6MWT) (cont.)

Example of a 6MWT Report[7,17]:

Patient name: Patient ID #:

Walk #: Tech ID: Date:

Gender: Male Female Age: Race:

Weight: lbs, kgs Height: feet inch(s), meters

Medications taken before the test (dose and time):

Use of supplemental oxygen during the test: No Yes, flow L/minute, type:

Fall risk assessment *(Check all that apply)*:

- ☐ Unsteady gait/dizziness/imbalance
- ☐ History of falls
- ☐ Weakness
- ☐ Uses ambulatory assistance (eg, cane, walker)
- ☐ Impaired memory or judgment

	Baseline	End of Test	
Time	:	:	
Heart Rate			
Blood Pressure			
Dyspnea			(Borg scale)
Fatigue			(Borg scale)
SpO2	%	%	

Borg Scale	
0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

The Borg Scale may be shown to the patient to self-grade their level of 1) dyspnea and 2) fatigue both prior to and following the 6MWT.

Stopped or paused before 6 minutes? No Yes, reason:

Other symptoms at end of exercise: ☐ angina ☐ dizziness ☐ hip, leg, or calf pain ☐ other:

Number of laps: (x60 meters) + final partial lap: meters:

Total distance walked in 6 minutes: meters:

Medical staff comments:

Timed Up & Go (TUG) Test

Appropriate age group: Adults ≥20 years[2,18]

- The TUG Test has been clinically validated[a] and is utilized in clinical practice.

What is the TUG Test?

- The TUG Test is a reliable, cost-effective, safe, and time-efficient way to evaluate overall functional mobility.[18]
- The TUG Test requires patients to stand up out of the chair, walk 3 meters, turn around, walk back to the chair, and sit down.[18]

Why is the TUG Test used for patients who have been prescribed STRENSIQ?

- Patients with hypophosphatasia (HPP) who have chronic muscle pain and weakness may have associated reduced mobility and physical activity.[19]
- The TUG Test is highly correlated with other proven tests—such as the 10-meter walk—that measure pure gait speed for longer distances.[18]
- This test may be used as a baseline to assess patients at risk for health decline to measure treatment progress toward improved function or to review a patient's physical activity program.[18]

How is the TUG Test conducted?

- **Select equipment/space requirements:** Chair, stopwatch or timer, and 3 meters of walking area.[18]
- **Patient instructions:** Patients are instructed to stand up out of a chair, walk 3 meters, turn around, walk back to the chair, and sit down.[18]
- **HCP instructions:** Begin your timer when the patient stands up out of the chair and end the timing when the patient sits back down.[18]
- A TUG score ≥10 seconds indicates reduced physical capacity whether compared with healthy older people or younger adults attending a primary care visit.[18]
- A TUG Test may be performed in any primary care setting.[18]

Example of reauthorization/continuation of therapy TUG Test criteria for STRENSIQ:

- Member has experienced an improvement in Timed Up & Go (TUG) Test compared to baseline.[20]

Coding and billing information:

- The following CPT code and modifiers may be appropriate to report administration of the TUG in physician office and hospital outpatient facilities.

CPT[12]	Description
97750	Physical performance test or measurement (eg, musculoskeletal, functional capacity), with written report, each 15 minutes

You can find more information regarding the administration of the TUG Test in the CDC.gov STEADI tools.

a. Test not specifically validated in patients with HPP.

Timed Up & Go (TUG) Test (cont.)

Example of a TUG Test[21]:

Purpose: To assess mobility

Equipment: A stopwatch

Directions: Patients wear their regular footwear and can use a walking aid, if needed. Begin by having the patient sit back in a standard arm chair and identify a line 3 meters, or 10 feet away, on the floor.

Instructions:

1) Instruct patient:

- When I say "Go," I want you to:
  1. Stand up from the chair.
  2. Walk to the line on the floor at your normal pace.
  3. Turn.
  4. Walk back to the chair at your normal pace.
  5. Sit down again.

2) On the word "Go," begin timing.

3) Stop timing after the patient sits back down.

4) Record time.

Time in seconds: _____

An older adult who takes ≥12 seconds to complete the TUG is at risk for falling.

Patient _____

Date _____ Time _____ ☐ AM ☐ PM

OBSERVATIONS

Observe the patient's postural stability, gait, stride length, and sway. Check all that apply.

- ☐ Slow tentative pace
- ☐ Loss of balance
- ☐ Short strides
- ☐ Little or no arm swing
- ☐ Steadying self on walls
- ☐ Shuffling
- ☐ En bloc turning
- ☐ Not using assistive device properly

These changes may signify neurological problems that require further evaluation.

Chair Rise Test

Appropriate age group: Adults >18 years[3,22]

- The Chair Rise Test has been clinically validated[a] and is utilized in clinical practice.

What is the Chair Rise Test?

- The Chair Rise Test[b] is a reliable and valid clinical tool commonly used to assess lower extremity functioning in elderly people.[23,24]
- Patients stand up from and sit down in a chair 5 times as quickly as possible without pushing off.[25]

Why is the Chair Rise Test used for patients who have been prescribed STRENSIQ?

- The Chair Rise Test is used to assess lower extremity functioning, including functional mobility or postural stability, in adults.[23]
- Hypophosphatasia (HPP) patients take longer to complete the Chair Rise Test compared to age-matched people in the general population. As such, this test may be used to assess improvements in lower extremity function in HPP patients.[22]
- Complications of HPP can impair physical function and mobility, limiting activities of daily living.[22]

How is the Chair Rise Test conducted?

- **Select equipment/space requirements:** 43 to 45-cm-tall chair and stopwatch or timer (capable of measuring tenths of a second).[23,24]
- **Patient instructions:** Patients are instructed to stand up from a seated position at the command "Go" and sit back down in a chair 5 times as quickly as possible without pushing off from the chair with their arms.[25]
- **HCP instructions:** Using a timer, record in seconds how long it takes for a patient to rise from a chair and return to a seated position 5 times.[22,25]
- A Chair Rise Test may be performed during a medical checkup in any primary care setting by an HCP.[25]

Example of reauthorization/continuation of therapy Chair Rise Test criteria for STRENSIQ:

- Member has experienced an improvement in Chair Rise Test compared to baseline.[20]

Coding and billing information:

- The following CPT code and modifiers may be appropriate to report administration of the Chair Rise Test in physician office and hospital outpatient facilities.

CPT[12]	Description
97750	Physical performance test or measurement (eg, musculoskeletal, functional capacity), with written report, each 15 minutes

You can find more information regarding the administration of the Chair Rise Test in the official Clinical Practice Guidelines published by the Academy of Neurologic Physical Therapy.

a. Test not specifically validated in patients with HPP. **b.** The test described herein is sometimes referred to as the "Five-Times-Sit-to-Stand Test" (or 5XSST). This test is related to the "Chair Rise Test" and measures similar functional capacity. Some payers will refer to the "Five-Times-Sit-to-Stand Test" as the "Chair Rise Test."

Chair Rise Test (cont.)

Example of a Chair Rise Test diagram and instructions[25-27]:

Score (seconds): _____

Instructions:

1) Instruct patient to sit in chair with arms folded across their chest and with back against chair.

- Instruct patient: "I want you to stand up and sit down five times in a row, as quickly as you can, when I say 'GO.' Be sure to stand up fully and try not to let your back touch the chair back between each repetition. Do not use the back of your legs against the chair."

2) On the word "Go," begin timing.

- A score of 0 is given when patient is unable to perform repetitions without the use of arms.

3) Score is the amount of time it takes for an patient to transfer from a seated position to standing position and back to sitting five times. Time is documented in seconds to the nearest decimal.

4) Record the time in seconds it takes the patient to complete 5 repetitions of standing and sitting.

Lower Extremity Function Scale (LEFS)

Appropriate age group: Adolescents 13-18 years old and adults >18 years[4,28]

- The LEFS has been clinically validated[a] and is utilized in clinical practice.

What is the LEFS?

- The LEFS is a patient questionnaire used to measure a patient's initial lower extremity function, ongoing progress and outcome, and set functional goals.[4]
- The LEFS assesses performance of daily activities (eg, getting out of bath, rolling over in bed, getting into or out of a car), locomotion (eg, walking, running), climbing stairs, and squatting.[28]
- The LEFS is a 1-page scale that consists of 20 items that can be filled out by most patients in <2 minutes. Final scoring can be performed without the use of a calculator or computer.[4]

Why is the LEFS used for patients who have been prescribed STRENSIQ?

- The LEFS was developed to address the need for a functional measure that is easy to administer and score while being applicable to a wide range of patients with lower-extremity orthopedic conditions.[4]
- LEFS is used during initial assessments in patients with lower-extremity musculoskeletal dysfunction, such as hypophosphatasia (HPP).[4] In the phase 2, open-label, STRENSIQ clinical study, the LEFS was measured at baseline, at month 6, and then annually.[29]

How is the LEFS questionnaire applied?

- **Recommended equipment:** The LEFS questionnaire.[4]
- **Patient instructions:** Patients should fill out the LEFS questionnaire and answer how difficult it is for them to perform specific activities by giving a score to each activity.[4]
- **HCP instructions:** Give the patient the LEFS questionnaire to fill out and calculate the total score by totaling all points and recording the final score.[4] The maximum score is 80, with higher scores indicating better functioning and lower scores indicating greater disability.[4,30]
- The LEFS questionnaire can be given by any healthcare provider.[4]

Example of reauthorization/continuation of therapy LEFS criteria for STRENSIQ:

- Member has experienced an improvement in LEFS compared to baseline.[20]

Coding and billing information:

CPT[12]	Description
97755	Assistive technology assessment (eg, to restore, augment or compensate for existing function, optimize functional tasks and/or maximize environmental accessibility), direct one-on-one contact, with written report, each 15 minutes

You can find more information regarding the application of the LEFS on the Emoryhealthcare.org website.

a. Test not specifically validated in patients with HPP.

Please see Important Safety Information on pages 1, 16, and 17 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

Lower Extremity Function Scale (LEFS) (cont.)

Example of a LEFS questionnaire[4]:

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb problem for which you are currently seeking attention. Please provide an answer for **each** activity.

Today, do you or would you have any difficulty at all with:

(Circle one number on each line)

Activities	Extreme difficulty or unable to perform activity	Quite a bit of difficulty	Moderate difficulty	A little bit of difficulty	No difficulty
1. Any of your usual work, housework, or school activities.	0	1	2	3	4
2. Your usual hobbies, recreational, or sporting activities.	0	1	2	3	4
3. Getting into or out of the bath.	0	1	2	3	4
4. Walking between rooms.	0	1	2	3	4
5. Putting on your shoes or socks.	0	1	2	3	4
6. Squatting.	0	1	2	3	4
7. Lifting an object, like a bag of groceries from the floor.	0	1	2	3	4
8. Performing light activities around your home.	0	1	2	3	4
9. Performing heavy activities around your home.	0	1	2	3	4
10. Getting into or out of a car.	0	1	2	3	4
11. Walking 2 blocks.	0	1	2	3	4
12. Walking a mile.	0	1	2	3	4
13. Going up or down 10 stairs (about 1 flight of stairs).	0	1	2	3	4
14. Standing for 1 hour.	0	1	2	3	4
15. Sitting for 1 hour.	0	1	2	3	4
16. Running on even ground.	0	1	2	3	4
17. Running on uneven ground.	0	1	2	3	4
18. Making sharp turns while running fast.	0	1	2	3	4
19. Hopping.	0	1	2	3	4
20. Rolling over in bed.	0	1	2	3	4
Column totals:	0	1	2	3	4

SCORE: /80

Weight-for-Height Z-Score (WHZ)

Appropriate age group: Pediatric patients 0-59 months[5]

- The Weight-for-Height Z-Score (WHZ) has been clinically validated[a] and is utilized in clinical practice.

What is the Weight-for-Height Z-Score (WHZ)?

- A Weight-for-Height Z-Score (WHZ) is a statistical measurement of how a patient's weight compares to the weight of other patients who are the same height.[30] Specifically, the z-score shows how many standard deviations a patient's height and weight are from clinically validated average height and weight from each sex to classify a patient's nutritional status.[30]
- A Weight-for-Height Z-Score (WHZ) allows healthcare providers to use a patient's height and weight to assess the nutritional status of children who are still in their growth and development phases compared to measurements published by health authorities.[30]

Why is a Weight-for-Height Z-Score (WHZ) recommended for patients prescribed STRENSIQ?

- Pediatric patients with odonto (dental) hypophosphatasia (HPP), mild childhood HPP, severe childhood HPP, and those who survive infantile HPP typically exhibit below-average heights in comparison to healthy American boys and girls. Height and weight measurements, as determined by z-scores, were documented in clinical studies of individuals with HPP.[31]

How do you calculate a Weight-for-Height Z-Score (WHZ)?

- **Recommended equipment[5,30]:**
  - Height: Tape measure or stadiometer that measures in cm.
  - Weight: Standard scale that measures in kg (to within nearest 100 g).
  - Published, clinically validated Weight-for-Height Z-Score (WHZ) tables (see pages 13 and 14).
- **HCP instructions[5]:** Measure the patient's height (cm) and weight (kg), then follow the instructions below to classify a patient's nutritional status:
  1. Use the correct table for the patient's age (0-23 months or 24-59 months) and sex (boy or girl). Measure children 0-23 months of age or less than 87 cm long lying down (length). Measure children 24-59 months of age or taller than 87 cm standing up (height). Tables can be found on pages 13 and 14.
  2. Find the number closest to the child's length/height in the left column.
  3. Move your finger to the right to find the numerical range that contains the child's weight.
  4. The label at the top of the column with the range containing the child's weight tells you the child's nutritional status.

Example of reauthorization payer policy criteria for the Weight-for-Height Z-score (WHZ) for STRENSIQ:

- Member is <18 years of age and has experienced an improvement in height and weight compared to baseline, as measured by z-scores.[20]

Coding and billing information

CPT[12]	Description	Coding & Billing Notes
99211-99215	Established patient evaluation and management (levels 1 to 5)	The assessment may be reported as a component of an established patient visit

You can find more information regarding the calculation of the height and weight z-score in module 2 of the Nutrition Assessment, Counseling, and Support: A User's Guide on the United States Agency for International Development website.

a. Test not specifically validated in patients with HPP.

Please see Important Safety Information on pages 1, 16, and 17 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

Weight-for-Height Z-Score (WHZ) (cont.)

Example of a Weight-for-Height Z-Score (WHZ) table for patients 0-23 months old[5]:

BOYS 0–23 months, weight-for-length

Length (cm)	SAM < –3	MAM ≥ –3 to < –2	Normal ≥ –2 to ≤ +2	Overweight ≥ +2 to < +3	Obesity > +3
	Weight (kg)				
45	0–1.8	1.9	2.0–3.0	3.1–3.3	> 3.3
46	0–1.9	2.0–2.1	2.2–3.1	3.2–3.5	> 3.5
47	0–2.0	2.1–2.2	2.3–3.3	3.4–3.7	> 3.7
48	0–2.2	2.3–2.4	2.5–3.6	3.7–3.9	> 3.9
49	0–2.3	2.4–2.5	2.6–3.8	3.9–4.2	> 4.2
50	0–2.5	2.6–2.7	2.8–4.0	4.1–4.4	> 4.4
51	0–2.6	2.7–2.9	3.0–4.2	4.3–4.7	> 4.7
52	0–2.8	2.9–3.1	3.2–4.5	4.6–5.0	> 5.0
53	0–3.0	3.1–3.3	3.4–4.8	4.9–5.3	> 5.3
54	0–3.2	3.3–3.5	3.6–5.1	5.2–5.6	> 5.6
55	0–3.5	3.6–3.7	3.8–5.4	5.5–6.0	> 6.0
56	0–3.7	3.8–4.0	4.1–5.8	5.9–6.3	> 6.3
57	0–3.9	4.0–4.2	4.3–6.1	6.2–6.7	> 6.7
58	0–4.2	4.3–4.5	4.6–6.4	6.5–7.1	> 7.1
59	0–4.4	4.5–4.7	4.8–6.8	6.9–7.4	> 7.4
60	0–4.6	4.7–5.0	5.1–7.1	7.2–7.8	> 7.8
61	0–4.8	4.9–5.2	5.3–7.4	7.5–8.1	> 8.1
62	0–5.0	5.1–5.5	5.6–7.7	7.8–8.5	> 8.5
63	0–5.2	5.3–5.7	5.8–8.0	8.1–8.8	> 8.8
64	0–5.4	5.5–5.9	6.0–8.3	8.4–9.1	> 9.1
65	0–5.6	5.7–6.1	6.2–8.6	8.7–9.4	> 9.4
66	0–5.8	5.9–6.3	6.4–8.9	9.0–9.7	> 9.7
67	0–6.0	6.1–6.5	6.6–9.2	9.3–10.0	> 10.0
68	0–6.2	6.3–6.7	6.8–9.4	9.5–10.3	> 10.3
69	0–6.4	6.5–6.9	7.0–9.7	9.8–10.6	> 10.6
70	0–6.5	6.6–7.1	7.2–10.0	10.1–10.9	> 10.9
71	0–6.7	6.8–7.3	7.4–10.2	10.3–11.2	> 11.2
72	0–6.9	7.0–7.5	7.6–10.5	10.6–11.5	> 11.5
73	0–7.1	7.2–7.6	7.7–10.8	10.9–11.8	> 11.8
74	0–7.2	7.3–7.8	7.9–11.0	11.1–12.1	> 12.1
75	0–7.4	7.5–8.0	8.1–11.3	11.4–12.3	> 12.3
76	0–7.5	7.6–8.2	8.3–11.5	11.6–12.6	> 12.6
77	0–7.7	7.8–8.3	8.4–11.7	11.8–12.8	> 12.8
78	0–7.8	7.9–8.5	8.6–12.0	12.1–13.1	> 13.1
79	0–8.0	8.1–8.6	8.7–12.2	12.3–13.3	> 13.3
80	0–8.1	8.2–8.8	8.9–12.4	12.5–13.6	> 13.6
81	0–8.3	8.4–9.0	9.1–12.6	12.7–13.8	> 13.8
82	0–8.4	8.5–9.1	9.2–12.8	12.9–14.0	> 14.0
83	0–8.6	8.7–9.3	9.4–13.1	13.2–14.3	>14.3
84	0–8.8	8.9–9.5	9.6–13.3	13.4–14.6	> 14.6
85	0–9.0	9.1–9.7	9.8–13.6	13.7–14.9	> 14.9
86	0–9.2	9.3–9.9	10.0–13.9	14.0–15.2	> 15.2
87	0–9.4	9.5–10.1	10.2–14.2	14.3–15.5	> 15.5
88	0–9.6	9.7–10.4	10.5–14.5	14.6–15.8	> 15.8
89	0–9.8	9.9–10.6	10.7–14.7	14.8–16.1	> 16.1
90	0–10.0	10.1–10.8	10.9–15.0	15.1–16.4	> 16.4
91	0–10.2	10.3–11.0	11.1–15.3	15.4–16.7	> 16.7
92	0–10.4	10.5–11.2	11.3–15.6	15.7–17.0	> 17.0
93	0–10.6	10.7–11.4	11.5–15.8	15.9–17.3	> 17.3
94	0–10.7	10.8–11.6	11.7–16.1	16.2–17.6	> 17.6
95	0–10.9	11.0–11.8	11.9–16.4	16.5–17.9	> 17.9
96	0–11.1	11.2–12.0	12.1–16.7	16.8–18.2	> 18.2
97	0–11.3	11.4–12.2	12.3–17.0	17.1–18.5	> 18.5
98	0–11.5	11.6–12.4	12.5–17.3	17.4–18.9	> 18.9
99	0–11.7	11.8–12.6	12.7–17.6	17.7–19.2	> 19.2
100	0–11.9	12.0–12.8	12.9–18.0	18.1–19.6	> 19.6

GIRLS 0–23 months, weight-for-length

Length (cm)	SAM < –3	MAM ≥ –3 to < –2	Normal ≥ –2 to ≤ +2	Overweight ≥ +2 to < +3	Obesity > +3
	Weight (kg)				
45	0–1.8	1.9–2.0	2.1–3.0	3.1–3.3	> 3.3
46	0–1.9	2.0–2.1	2.2–3.2	3.3–3.5	> 3.5
47	0–2.1	2.2–2.3	2.4–3.4	3.5–3.7	> 3.7
48	0–2.2	2.3–2.4	2.5–3.6	3.7–4.0	> 4.0
49	0–2.3	2.4–2.5	2.6–3.8	3.9–4.2	> 4.2
50	0–2.5	2.6–2.7	2.8–4.0	4.1–4.5	> 4.5
51	0–2.7	2.8–2.9	3.0–4.3	4.4–4.8	> 4.8
52	0–2.8	2.9–3.1	3.2–4.6	4.7–5.1	> 5.1
53	0–3.0	3.1–3.3	3.4–4.9	5.0–5.4	> 5.4
54	0–3.2	3.3–3.5	3.6–5.2	5.3–5.7	> 5.7
55	0–3.4	3.5–3.7	3.8–5.5	5.6–6.1	> 6.1
56	0–3.6	3.7–3.9	4.0–5.8	5.9–6.4	> 6.4
57	0–3.8	3.9–4.2	4.3–6.1	6.2–6.8	> 6.8
58	0–4.0	4.1–4.4	4.5–6.5	6.6–7.1	> 7.1
59	0–4.2	4.3–4.6	4.7–6.8	6.9–7.5	> 7.5
60	0–4.4	4.5–4.8	4.9–7.1	7.2–7.8	> 7.8
61	0–4.6	4.7–5.0	5.1–7.4	7.5–8.2	> 8.2
62	0–4.8	4.9–5.2	5.3–7.7	7.8–8.5	> 8.5
63	0–5.0	5.1–5.4	5.5–8.0	8.1–8.8	> 8.8
64	0–5.2	5.3–5.6	5.7–8.7	8.4–9.1	> 9.1
65	0–5.4	5.5–5.8	5.9–8.6	8.7–9.5	> 9.5
66	0–5.5	5.6–6.0	6.1–8.8	8.9–9.8	> 9.8
67	0–5.7	5.8–6.2	6.3–9.1	9.2–10.0	> 10.0
68	0–5.9	6.0–6.4	6.5–9.4	9.5–10.3	> 10.3
69	0–6.0	6.1–6.6	6.7–9.6	9.7–10.6	> 10.6
70	0–6.52	6.3–6.8	6.9–9.9	10.0–10.9	> 10.9
71	0–6.4	6.5–6.9	7.0–10.1	10.2–11.1	> 11.1
72	0–6.5	6.6–7.1	7.2–10.3	10.4–11.4	> 11.4
73	0–6.7	6.8–7.3	7.4–10.6	10.7–11.7	> 11.7
74	0–6.8	6.9–7.4	7.5–10.8	10.9–11.9	> 11.9
75	0–7.0	7.1–7.6	7.7–11.0	11.1–12.2	> 12.2
76	0–7.1	7.2–7.7	7.8–11.2	11.3–12.4	> 12.4
77	0–7.3	7.4–7.9	8.0–11.5	11.6–12.6	> 12.6
78	0–7.4	7.5–8.1	8.2–11.7	11.8–12.9	> 12.9
79	0–7.6	7.7–8.2	8.3–11.9	12.0–13.1	> 13.1
80	0–7.7	7.8–8.4	8.5–12.1	12.2–13.4	> 13.4
81	0–7.9	8.0–8.6	8.7–12.4	12.5–13.7	> 13.7
82	0–8.0	8.1–8.7	8.8–12.6	12.7–13.9	> 13.9
83	0–8.2	8.3–8.9	9.0–12.9	13.0–14.2	> 14.2
84	0–8.4	8.5–9.1	9.2–13.2	13.3–14.5	> 14.5
85	0–8.6	8.7–9.3	9.4–13.5	13.6–14.9	> 14.9
86	0–8.8	8.9–9.6	9.7–13.8	13.9–15.2	> 15.2
87	0–9.0	9.1–9.8	9.9–14.1	14.2–15.5	> 15.5
88	0–9.2	9.3–10.0	10.1–14.4	14.5–15.9	> 15.9
89	0–9.4	9.5–10.2	10.3–14.7	14.8–16.2	> 16.2
90	0–9.6	9.7–10.4	10.5–15.0	15.1–16.5	> 16.5
91	0–9.8	9.9–10.6	10.7–15.3	15.4–16.9	> 16.9
92	0–10.0	10.1–10.8	10.9–15.6	15.7–17.2	> 17.2
93	0–10.1	10.2–11.0	11.1–15.9	16.0–17.5	> 17.5
94	0–10.3	10.4–11.2	11.3–16.2	16.3–17.9	> 17.9
95	0–10.5	10.6–11.4	11.5–16.5	16.6–18.2	> 18.2
96	0–10.7	10.8–11.6	11.7–16.8	16.9–18.6	> 18.6
97	0–10.9	11.0–11.9	12.0–17.1	17.2–18.9	> 18.9
98	0–11.1	11.2–12.1	12.2–17.5	17.6–19.3	> 19.3
99	0–11.3	11.4–12.3	12.4–17.8	17.9–19.6	> 19.6
100	0–11.5	11.6–12.5	12.6–18.1	18.2–20.0	> 20.0

MAM, moderate acute malnutrition; **SAM,** severe acute malnutrition.

Weight-for-Height Z-Score (WHZ) (cont.)

Example of a Weight-for-Height Z-Score (WHZ) table for patients 24-59 months old[5]:

BOYS 24–59 months, weight-for-height

Height (cm)	SAM < –3	MAM ≥ –3 to < –2	Normal ≥ –2 to ≤ +2	Overweight ≥ +2 to < +3	Obesity > +3
	Weight (kg)				
65	0–5.8	5.9–6.2	6.3–8.8	8.9–9.6	> 9.6
66	0–6.0	6.1–6.4	6.5–9.1	9.2–9.9	> 9.9
67	0–6.1	6.2–6.6	6.7–9.4	9.5–10.2	> 10.2
68	0–6.3	6.4–6.8	6.9–9.6	9.7–10.5	> 10.5
69	0–6.5	6.6–7.0	7.1–9.9	10.0–10.8	> 10.8
70	0–6.7	6.8–7.2	7.3–10.2	10.3–11.1	> 11.1
71	0–6.8	6.9–7.4	7.5–10.4	10.5–11.4	> 11.4
72	0–7.0	7.1–7.6	7.7–10.7	10.8–11.7	> 11.7
73	0–7.2	7.3–7.8	7.9–11.0	11.1–12.0	> 12.0
74	0–7.3	7.4–7.9	8.0–11.2	11.3–12.2	> 12.2
75	0–7.5	7.6–8.1	8.2–11.4	11.3–12.5	> 12.5
76	0–7.6	7.7–8.3	8.4–11.7	11.8–12.8	> 12.8
77	0–7.8	7.9–8.4	8.5–11.9	12.0–13.0	> 13.0
78	0–7.9	8.0–8.6	8.7–12.1	12.2–13.3	> 13.3
79	0–8.1	8.2–8.7	8.8–12.3	12.4–13.5	> 13.5
80	0–8.2	8.3–8.9	9.0–12.6	12.7–13.7	> 13.7
81	0–8.4	8.5–9.1	9.2–12.8	12.9–14.0	> 14.0
82	0–8.6	8.7–9.2	9.3–13.0	13.1–14.2	> 14.2
83	0–8.7	8.8–9.4	9.5–13.3	13.4–14.5	> 14.5
84	0–8.9	9.0–9.6	9.7–13.5	13.6–14.8	> 14.8
85	0–9.1	9.2–9.9	10.0–13.8	13.9–15.1	> 15.1
86	0–9.3	9.4–10.1	10.2–14.1	14.2–15.4	> 15.4
87	0–9.5	9.4–10.3	10.4–14.4	14.5–15.7	> 15.7
88	0–9.7	9.8–10.5	10.6–14.7	14.8–16.0	> 16.0
89	0–9.9	10.0–10.7	10.8–14.9	15.0–16.3	> 16.3
90	0–10.1	10.2–10.9	11.0–15.2	15.3–16.6	> 16.6
91	0–10.3	10.4–11.1	11.2–15.5	15.6–16.9	> 16.9
92	0–10.5	10.6–11.3	11.4–15.8	15.9–17.2	> 17.2
93	0–10.7	10.8–11.5	11.6–16.0	16.1–17.5	> 17.5
94	0–10.9	11.0–11.7	11.8–16.3	16.4–17.8	> 17.8
95	0–11.0	11.1–11.9	12.0–16.6	16.7–18.1	> 18.1
96	0–11.2	11.3–12.1	12.2–16.9	17.0–18.4	> 18.4
97	0–11.4	11.5–12.3	12.4–17.2	17.3–18.8	> 18.8
98	0–11.6	11.7–12.5	12.6–17.5	17.6–19.1	> 19.1
99	0–11.8	11.9–12.8	12.9–17.9	18.0–19.5	> 19.5
100	0–12.0	12.1–13.0	13.1–18.2	18.3–19.9	> 19.9
101	0–12.2	12.3–13.2	13.3–18.5	18.6–20.3	> 20.3
102	0–12.4	12.5–13.5	13.6–18.9	19.0–20.7	> 20.7
103	0–12.7	12.8–13.7	13.8–19.3	19.4–21.1	> 21.1
104	0–12.9	13.0–13.9	14.0–19.7	19.8–21.6	> 21.6
105	0–13.1	13.2–14.2	14.3–20.1	20.2–22.0	> 22.0
106	0–13.3	13.4–14.4	14.5–20.5	20.6–22.5	> 22.5
107	0–13.6	13.7–14.7	14.8–20.9	21.0–22.9	> 22.9
108	0–13.8	13.9–15.0	15.1–21.3	21.4–23.4	> 23.4
109	0–14.0	14.1–15.2	15.3–21.8	21.9–23.9	> 23.9
110	0–14.3	14.4–15.5	15.6–22.2	22.3–24.4	> 24.4
111	0–14.5	14.6–15.8	15.9–22.7	22.8–25.0	> 25.0
112	0–14.8	14.9–16.1	16.2–23.1	23.2–25.5	> 25.5
113	0–15.1	15.2–16.4	16.5–23.6	23.7–26.0	> 26.0
114	0–15.3	15.4–16.7	16.8–24.1	24.2–26.6	> 26.6
115	0–15.6	15.7–17.0	17.1–24.6	24.7–27.2	> 27.2
116	0–15.9	16.0–17.3	17.4–25.1	25.2–27.8	> 27.8
117	0–16.1	16.2–17.6	17.7–25.6	25.7–28.3	> 28.3
118	0–16.4	16.5–17.9	18.0–16.1	26.2–28.9	> 28.9
119	0–16.7	16.8–18.2	18.3–26.6	26.7–29.5	> 29.5
120	0–17.0	17.1–18.5	18.6–27.2	27.3–30.1	> 30.1

GIRLS 24–59 months, weight-for-height

Height (cm)	SAM < –3	MAM ≥ –3 to < –2	Normal ≥ –2 to ≤ +2	Overweight ≥ +2 to < +3	Obesity > +3
	Weight (kg)				
65	0–5.5	5.6–6.0	6.1–8.7	8.8–9.7	> 9.7
66	0–5.7	5.8–6.2	6.3–9.0	9.1–10.0	> 10.0
67	0–5.8	5.9–6.3	6.4–9.3	9.4–10.2	> 10.2
68	0–6.0	6.1–6.5	6.6–9.5	9.6–10.5	> 10.5
69	0–6.2	6.3–6.7	6.8–9.8	9.9–10.8	> 10.8
70	0–6.3	6.4–6.9	7.0–10.0	10.1–11.1	> 11.1
71	0–6.5	6.6–7.0	7.1–10.3	10.4–11.3	> 11.3
72	0–6.6	6.7–7.2	7.3–10.5	10.6–11.6	> 11.6
73	0–6.8	6.9–7.4	7.5–10.7	10.8–11.8	> 11.8
74	0–6.9	7.0–7.5	7.6–11.0	11.1–12.1	> 12.1
75	0–7.1	7.2–7.7	7.8–11.2	11.3–12.3	> 12.3
76	0–7.2	7.3–7.9	8.0–11.4	11.5–12.6	> 12.6
77	0–7.4	7.5–8.0	8.1–11.6	11.7–12.8	> 12.8
78	0–7.5	7.6–8.2	8.3–11.8	11.9–13.1	> 13.1
79	0–7.7	7.8–8.3	8.4–12.1	11.9–13.3	> 13.3
80	0–7.8	7.9–8.5	8.6–12.3	12.4–13.6	> 13.6
81	0–8.0	7.9–8.7	8.8–12.6	12.7–13.9	> 13.9
82	0–8.2	8.3–8.9	9.0–12.8	12.7–14.1	> 14.1
83	0–8.4	8.5–9.1	9.2–13.1	13.2–14.5	> 14.5
84	0–8.5	8.6–9.3	9.4–13.4	13.2–14.8	> 14.8
85	0–8.7	8.8–9.5	9.6–13.7	13.8–15.1	> 15.1
86	0–8.9	9.0–9.7	9.8–14.0	14.1–15.4	> 15.4
87	0–9.1	9.2–9.9	10.0–14.3	14.4–15.8	> 15.8
88	0–9.3	9.4–10.1	10.2–14.6	14.7–16.1	> 16.1
89	0–6.0	9.6–10.3	10.4–14.9	15.0–16.4	> 16.4
90	0–6.52	9.8–10.5	10.6–15.2	15.3–16.8	> 16.8
91	0–6.4	10.0–10.8	10.9–15.5	15.6–17.1	> 17.1
92	0–6.5	10.2–11.0	11.1–15.8	15.9–17.4	> 17.4
93	0–6.7	10.4–11.2	11.3–16.1	16.2–17.8	> 17.8
94	0–6.8	10.6–11.4	11.5–16.4	16.5–18.1	> 18.1
95	0–7.0	10.8–11.6	11.7–16.7	16.8–18.5	> 18.5
96	0–7.1	10.9–11.8	11.9–17.0	17.1–18.8	> 18.8
97	0–7.3	11.1–12.0	12.1–17.4	17.5–19.2	> 19.2
98	0–7.4	11.3–12.2	12.3–17.7	17.8–19.5	> 19.5
99	0–7.6	11.5–12.4	12.5–18.0	18.1–19.9	> 19.9
100	0–7.7	11.7–12.7	12.8–18.4	18.5–20.3	> 20.3
101	0–7.9	12.0–12.9	13.0–18.7	18.8–20.7	> 20.7
102	0–8.0	12.2–13.2	13.3–19.1	19.2–21.1	> 21.1
103	0–8.2	12.4–13.4	13.5–19.5	19.6–21.6	> 21.6
104	0–8.4	12.6–13.6	13.8–19.9	20.0–22.0	> 22.0
105	0–8.6	12.9–13.9	14.0–20.3	20.4–22.5	> 22.5
106	0–8.8	13.1–14.2	14.3–20.8	20.9–23.0	> 23.0
107	0–9.0	13.4–14.5	14.6–21.2	21.3–23.5	> 23.5
108	0–9.2	13.7–14.8	14.9–21.7	21.8–24.0	> 24.0
109	0–9.4	13.9–15.1	15.2–22.1	22.2–24.5	> 24.5
110	0–9.6	14.2–15.4	15.5–22.6	22.7–25.1	> 25.1
111	0–9.8	14.5–15.7	15.8–23.1	23.2–25.7	> 25.7
112	0–10.0	14.8–16.1	16.2–23.6	23.7–26.2	> 26.2
113	0–10.1	15.1–16.4	16.5–24.2	24.3–26.8	> 26.8
114	0–10.3	15.4–16.7	16.8–24.7	24.8–27.4	> 27.4
115	0–10.5	15.7–17.1	17.2–25.2	25.3–28.1	> 28.1
116	0–10.7	16.0–17.4	17.5–25.8	25.9–28.7	> 28.7
117	0–10.9	16.3–17.7	17.8–26.3	26.4–29.3	> 29.3
118	0–11.1	16.6–18.1	18.2–26.9	27.0–29.9	> 29.9
119	0–11.3	16.9–18.4	18.5–27.4	27.5–30.6	> 30.6
120	0–11.5	17.3–18.8	18.9–28.0	28.1–31.2	> 31.2

MAM, moderate acute malnutrition; **SAM,** severe acute malnutrition.

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Please see Important Safety Information on pages 1, 16, and 17 and full Prescribing Information for STRENSIQ (asfotase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

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

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

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.

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

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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