Package leaflet: Information for the user

Strensiq 100 mg/ml solution for injection
(80 mg/0.8 ml)
asfotase alfa

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Strensiq is and what it is used for

What is Strensiq
Strensiq is a medicine used to treat the inherited disease hypophosphatasia that started in childhood. It contains the active substance asfotase alfa.

What is hypophosphatasia
Patients with hypophosphatasia have low levels of an enzyme called alkaline phosphatase that is important for various body functions, including the proper hardening of bones and teeth. Patients have problems with bone growth and strength, which can lead to broken bones, bone pain, and difficulty walking, as well as difficulties with breathing and a risk of seizures (fits).

What is Strensiq used for
The active substance in Strensiq can replace the missing enzyme (alkaline phosphatase) in hypophosphatasia. It is used for long-term enzyme replacement treatment to manage symptoms.

What benefits of Strensiq have been shown in clinical studies
Strensiq has shown benefits for patients' mineralization of the skeleton and growth.

2. What you need to know before you use Strensiq

Do not use Strensiq
If you are severely allergic to asfotase alfa (see section 'Warnings and precautions' below) or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before using Strensiq.

- Patients receiving asfotase alfa have had allergic reactions including life threatening allergic reactions requiring medical treatment similar to anaphylaxis. Patients who experienced anaphylaxis-like symptoms had difficulty breathing, choking sensation, nausea, swelling around the eyes, and dizziness. The reactions occurred within minutes after taking asfotase alfa, and can occur in patients who were taking asfotase alfa for more than one year. If you experience any of these symptoms, discontinue Strensiq and seek medical help immediately.
  Should you experience anaphylactic reaction, or an event with similar symptoms, your doctor will discuss with you the next steps and the possibility to restart Strensiq under medical supervision. Always follow the instructions provided by your doctor.
- The development of blood proteins against Strensiq, also called anti-drug antibodies, may occur during the treatment. Talk to your doctor if you experience decreased efficacy with Strensiq.
- Fatty lumps or decreased fatty tissue on the surface of the skin (localized lipodystrophy) have been reported at injection sites after several months in patients using Strensiq. Read section 3 carefully to know the injection recommendations. This is important to rotate the injection from among the following sites to reduce the risk of lipodystrophy: abdominal area, thigh, or deltoid.
- In studies, some eye-related side-effects (e.g. calcium buildup on the eye [conjunctival and corneal calcification]) have been reported both in patients using Strensiq and those who were not, probably associated with hypophosphatasia. Talk to your doctor in case of problems with your vision.
- Early fusion of the bones of the head (craniosynostosis) in children below 5 years of age has been reported in clinical studies of infants with hypophosphatasia, with and without use of Strensiq. Talk to your doctor if you notice any change in the shape of your infant's head.
- If you are treated with Strensiq, you may experience a reaction at the injection site (pain, nodule, rash, discoloration) during the injection of the medicine or during the hours following the injection. If you experience any severe reaction at the injection site, tell your doctor immediately.
- Increase of parathyroid hormone concentration and low calcium levels have been reported in studies. As a consequence, your doctor may ask you to take supplements of calcium and oral vitamin D if needed.
- Weight gain may occur during your treatment with Strensiq. Your doctor will provide dietary advice as necessary.

Other medicines and Strensiq
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

If you need to undergo laboratory tests (giving blood for testing), tell your doctor that you are treated with Strensiq. Strensiq may cause some tests to show wrongly higher or lower results.
Therefore another type of test may need to be used if you are treated with Strensiq.

Pregnancy
Strensiq should not be used during pregnancy. The use of effective birth control during treatment should be considered in women who are able to get pregnant.

Breast-feeding
It is not known whether Strensiq can pass into breast milk. Tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Strensiq, considering the benefit of breast-feeding to the baby and the benefit of Strensiq to the mother.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
This medicine is not expected to have any effect on the ability to drive or use machines.

Important information about some of the ingredients of Strensiq
This medicine contains less than 1 mmol sodium (23 mg) per vial, which means it is essentially ‘sodium-free’.

3. How to use Strensiq

Always use this medicine exactly as described in this leaflet or as your doctor, or pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.
How to use Strensiq will be explained to you by a doctor who is experienced in the management of patients with metabolic or bone related diseases. After being trained by the doctor or specialized nurse, you can inject Strensiq yourself at home.

Dose
- The dose you receive is based on your body weight.
- The correct dose will be calculated by your doctor and consists of a total of 6 mg of asfotase alfa per kg of body weight every week, given either as an injection of 1 mg/kg asfotase alfa 6 times per week or as 2 mg/kg asfotase alfa 3 times per week depending on the recommendation of your doctor. Each dose will be administered by injection under the skin (subcutaneous), (see the dosing chart below for detailed information on the volume to be injected, and the type of vials to be used, based on your weight).
- Doses will need to be adjusted regularly by your doctor as the body weight changes.
- The maximum volume per injection should not exceed 1 ml. If more than 1 ml is required, you need to do multiple injections immediately one after the other.

If injecting 3x per week

Body Weight (kg)	Volume to be injected	Color code of the vial to be used
3	0.15 ml	Dark blue
4	0.20 ml	Dark blue
5	0.25 ml	Dark blue
6	0.30 ml	Dark blue
7	0.35 ml	Orange
8	0.40 ml	Orange
9	0.45 ml	Orange
10	0.50 ml	Light blue
11	0.55 ml	Light blue
12	0.60 ml	Light blue
13	0.65 ml	Light blue
14	0.70 ml	Light blue
15	0.75 ml	Pink
16	0.80 ml	Pink
17	0.85 ml	Pink
18	0.90 ml	Pink
19	0.95 ml	Pink
20	1 ml	Pink
25	0.50 ml	Green
30	0.60 ml	Green
35	0.70 ml	Green
40	0.80 ml	Green

If injecting 6 x per week

Body Weight (kg)	Volume to be injected	Color code of the vial to be used
6	0.15 ml	Dark blue
7	0.18 ml	Dark blue
8	0.20 ml	Dark blue
9	0.23 ml	Dark blue
10	0.25 ml	Dark blue
11	0.28 ml	Dark blue
12	0.30 ml	Dark blue
13	0.33 ml	Orange
14	0.35 ml	Orange
15	0.38 ml	Orange
16	0.40 ml	Orange
17	0.43 ml	Orange
18	0.45 ml	Orange
19	0.48 ml	Light blue
20	0.50 ml	Light blue
25	0.63 ml	Light blue
30	0.75 ml	Pink
35	0.88 ml	Pink
40	1 ml	Pink
50	0.50 ml	Green
60	0.60 ml	Green
70	0.70 ml	Green
80	0.80 ml	Green
90	0.90 ml	Green (x2)
100	1 ml	Green (x2)

Injection recommendations

- You may experience a reaction at the injection site. Read section 4 carefully to know what side effects can occur before using this medicine
- When injecting regularly, the injection site should be changed between different areas of the body to help reduce potential pain and irritation
- Areas with a good amount of fat below the skin (thighs, arms (deltoids), abdomen, and buttocks) are the most suitable areas to inject. Please discuss with you doctor or nurse the best sites for you.

Before injecting Strensiq, please read the following instructions carefully

- Each vial is for single use and should only be punctured once. Only clear and colourless to slightly yellow aqueous solution without visible signs of deterioration should be used. Any unused medicinal product or waste material should be disposed of immediately.

- If you are injecting this medicine yourself, you will be shown how to prepare and inject the medicine by your doctor, pharmacist or nurse. Do not inject this medicine yourself unless you have received training and you understand the procedure.

How to inject Strensiq:

Step 1: Preparing the Strensiq dose

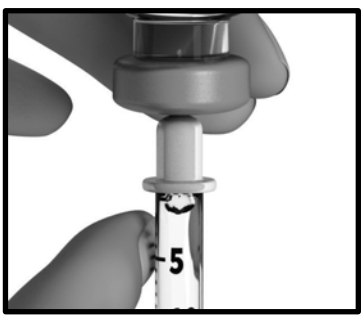
1. Wash your hands thoroughly with soap and water.
2. Take the unopened Strensiq vial(s) out of the refrigerator 15 to 30 minutes before injecting to allow the liquid to reach room temperature. Do not warm Strensiq in any other way (for example, do not warm it in a microwave or in hot water). Upon removal of the vial(s) from refrigeration, Strensiq should be used within 3 hours maximum (see section 5. How to store Strensiq).
3. Remove the protective cap from the Strensiq vial. Remove the protective plastic from the syringe to be used.
4. Always use a new syringe contained in a protective plastic.
5. Place a larger bore needle (e.g. 25G) on the empty syringe and with the protective cap on, push down and turn clockwise the needle onto the syringe until it is tight.
6. Remove the plastic cap covering the syringe needle. Pay attention not to hurt yourself with the needle.
7. Pull the plunger back to draw air into the syringe equal to your dose.

Step 2: Withdrawing Strensiq solution from the vial

1. Holding the syringe and vial, insert the needle through the sterile rubber seal and into the vial.

2. Push the plunger in completely to inject air into the vial.

3. Invert the vial and syringe. With the needle in the solution, pull the plunger to withdraw the correct dose into the syringe.



4. Before removing the needle from the vial, check the syringe for air bubbles. In the event that bubbles appear in the syringe, hold the syringe with the needle pointing upwards and gently tap the side of the syringe until the bubbles rise to the top.

5. Once all the bubbles are at the top of the syringe, gently push on the plunger to force the bubbles out of the syringe and back into the vial.

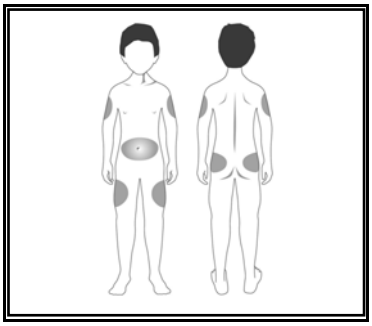
6. After removing the bubbles, check the dose of medication in the syringe to be sure you have drawn up the correct amount. You may need to use several vials to withdraw the complete amount needed to reach the correct dose.

Step 3: Placing the needle for injection on the syringe

1. Remove the needle from the vial and place back the protective cap over the needle.
2. Remove the larger bore needle pushing down and turning counterclockwise. Dispose the needle with the protective cap in your sharps container.
3. Place a smaller bore needle (e.g. 27 or 29G) on the filled syringe and with the protective cap on, push down and turn clockwise the needle onto the syringe until it is tight. Pull the cap straight off the needle.
4. Hold the syringe with the needle pointing up and tap the barrel of the syringe with your finger to remove any air bubbles.

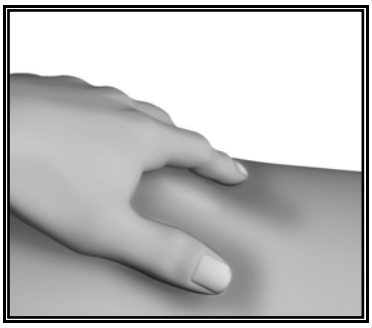
Control visually that the volume contained into the syringe is correct.
The volume per injection should not exceed 1 ml. If it is the case, multiple injections should be done at different sites.
You are now ready to inject the correct dose.

Step 4: Injecting Strensiq

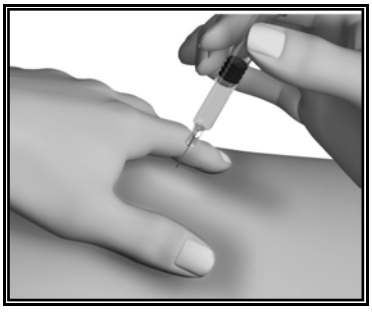


1. Choose an injection site (thighs, abdomen, arms (deltoids), buttocks). Most suitable areas for injection are marked grey in the picture. Your doctor will advise you on the possible injection sites.

NOTE: do not use any areas in which you feel lumps, firm knots, or pain; talk to your doctor about anything you find.

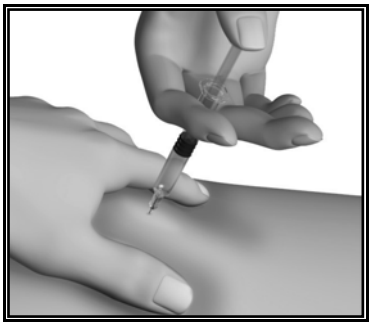


2. Gently pinch the skin of the chosen injection area between your thumb and index finger.



3. Holding the syringe like a pencil or a dart, insert the needle into the raised skin so it is at an angle of between 45º and 90º to the skin surface.

For patients who have little fat under the skin or thin skin, a 45º angle may be preferable.



4. While continuing to hold the skin, push the syringe plunger to inject the medicine slowly, and steadily all the way in.

5. Remove the needle, release the skin fold and gently place a piece of cotton wool or gauze over the injection site for a few seconds.

This will help seal the punctured tissue and prevent any leakage. Do not rub the injection site after injection.

If you need a second injection for your prescribed dose, get another Strensiq vial and repeat steps 1 through 4.

Step 5: Disposing of supplies

Please collect your syringes, vials and needle in a sharps container. Your doctor, pharmacist or nurse will advise you on how you can obtain a sharps container.

If you use more Strensiq than you should
If you suspect that you have been accidently administered a higher dose of Strensiq than prescribed, please contact your doctor for advice.

If you forget to use Strensiq
Do not inject a double dose to make up for a forgotten dose and contact your doctor for advice.

For more information, please consult:

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you are not sure what the side effects below are, ask your doctor to explain them to you.

The most serious side effects seen in patients receiving asfotase alfa have been allergic reactions including life threatening allergic reactions requiring medical treatment similar to anaphylaxis. This side effect is common [may affect up to 1 in 10 people]). Patients who experienced these serious allergic reactions had difficulty breathing, choking sensation, nausea, swelling around the eyes, and dizziness. The reactions occurred within minutes after using asfotase alfa and can occur in patients who were using asfotase alfa for more than one year. **If you experience any of these symptoms, discontinue Strensiq and seek medical help immediately.**

Additionally, other allergic reactions (hypersensitivity) which may appear as redness (erythema), fever (pyrexia), rash, itchiness (pruritis), irritability, feeling sick (nausea), throwing up (vomiting), pain, chills (rigor), numbness of the mouth (hypoaesthesia oral), headache, blushing (flushing), fast beating of the heart (tachycardia), and cough may occur commonly. **If you experience any of these symptoms, discontinue Strensiq and seek medical help immediately.**

Very common: may affect more than 1 in 10 people
Reactions at the injection site during the injection of the medicine or during the hours following the injection (which can lead to redness, discolorations, itching, pain, fatty lumps or decreased fatty tissue on the surface of the skin, skin hypopigmentation, and/or swelling)
Fever (pyrexia)
Irritability
Skin redness (erythema)
Pain in hands and feet (pain in extremity)
Bruise (contusion)
Headache

Common: may affect up to 1 in 10 people
Stretched skin, skin discolouration
Feeling sick (nausea)
Numbness of the mouth (hypoaesthesia oral)
Aching muscles (myalgia)
Scar
Increased tendency to bruise
Hot flush
Infection of skin at injection site (injection site cellulitis)
Reduced levels of calcium in the blood (hypocalcaemia)
Kidney stones (nephrolithiasis)

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed below:

United Kingdom:

via theYellow Card Scheme

Website: https://yellowcard.mhra.gov.uk/
or search for MHRA Yellow Card in the Google Play or Apple App Store.

Ireland:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

5. How to store Strensiq

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C-8°C).
Do not freeze.
Store in the original package in order to protect from light.

After opening the vial, the product should be used immediately (within 3 hours maximum at room temperature, between 23°C and 27°C).

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Strensiq contains
The active substance is asfotase alfa. Each ml of solution contains 100 mg of asfotase alfa.
Each vial of 0.8 ml solution (100 mg/ml) contains 80 mg of asfotase alfa.

The other ingredients are sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate and water for injections.

What Strensiq looks like and contents of the pack
Strensiq is presented as a clear colourless to slightly yellow aqueous solution for injection in vials containing 0.8 ml of solution.

Pack sizes of 1 or 12 vials.
Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder
Alexion Europe SAS
103-105 rue Anatole France
92300 Levallois-Perret
France

Manufacturer
Alexion Pharma International Operations Unlimited Company
College Business and Technology Park, Blanchardstown
Dublin 15
Ireland

This leaflet was last revised in April 2020

This medicine has been authorised under ‘exceptional circumstances’.
This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.