Package leaflet: Information for the patient

Amvuttra 25 mg solution for injection in pre-filled syringe
vutrisiran

▼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 are given 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.
- 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 Amvuttra is and what it is used for

The active substance in Amvuttra is vutrisiran.

What Amvuttra is used for
Amvuttra is used for the treatment of an illness called 'hereditary ATTR' or 'hATTR amyloidosis'. This is an illness which runs in families. hATTR amyloidosis is caused by problems with a protein in the body called 'transthyretin' (TTR). This protein is made mostly in the liver and carries vitamin A and other substances around the body.

In people with this illness, small fibres of TTR protein clump together to make deposits called 'amyloid'. Amyloid can build up around or within the nerves, heart, and other places in the body, stopping them from working normally. This causes the symptoms of the illness.

How Amvuttra works
Amvuttra works by lowering the amount of TTR protein made by the liver which means there is less TTR protein in the blood that can form amyloid. This can help to reduce the effects of this illness.

Amvuttra is used in adults only.

2. What you need to know before you are given Amvuttra

You must not be given Amvuttra
- If you have ever had a severe allergic reaction to vutrisiran, or any of the other ingredients of this medicine (listed in section 6).

If you are not sure, talk to your doctor, pharmacist or nurse before you are given this medicine.

Warnings and precautions

Lowered vitamin A levels in the blood and vitamin supplements

Amvuttra lowers the amount of vitamin A in your blood.
Your doctor will ask you to take a daily vitamin A supplement. Please follow the vitamin A dose recommended by your doctor.
Signs of low vitamin A may include: sight problems especially at night, dry eyes, hazy, or cloudy vision.

- If you notice a change in your vision or any other eye problems whilst using Amvuttra, talk to your doctor. Your doctor may send you to an eye specialist for a check-up.

Both too high and too low levels of vitamin A can harm the development of your unborn child. Therefore, women of childbearing age should exclude any pregnancy before starting treatment with Amvuttra and practise effective contraception (see section "Pregnancy, breast-feeding and contraception" below).

- Vitamin A levels may remain low for more than 12 months after the last dose of Amvuttra.
- Tell your doctor if you are planning to become pregnant. Your doctor will tell you to stop taking Amvuttra and vitamin A supplementation. Your doctor will also ensure that your vitamin A levels have returned to normal before conception is attempted.
- Tell your doctor if you have an unplanned pregnancy. Your doctor will tell you to stop taking Amvuttra. In the first 3 months of your pregnancy, your doctor may tell you to stop taking vitamin A supplementation. During the last 6 months of your pregnancy, you doctor may tell you to resume the vitamin A supplementation if your vitamin A levels have not yet returned to normal, because of the increased risk of vitamin A deficiency during the last 3 months of your pregnancy.

Children and adolescents
Amvuttra is not recommended in children and adolescents under 18 years of age.

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

Pregnancy, breast-feeding and contraception
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 starting this medicine.

Pregnancy

You should not use Amvuttra if you are pregnant.

Women of childbearing age

Amvuttra will reduce the level of vitamin A in your blood and vitamin A is important for normal development of your unborn child (see "Warnings and precautions" above).

- You should use effective contraception during treatment with Amvuttra - if you are a woman who is able to become pregnant.
- Talk to your doctor or nurse about suitable methods of contraception.
- Pregnancy should be excluded before starting treatment with Amvuttra.
- Tell your doctor if you are planning to become pregnant or if you have an unplanned pregnancy. Your doctor will tell you to stop taking Amvuttra.

Breast-feeding

It is not known if vutrisiran passes into breast milk. Your doctor will consider the potential benefits of treatment for you - compared with the risks of breast-feeding for your baby.

Driving and using machines
Amvuttra is unlikely to affect your ability to drive or use machines. Your doctor will tell you whether your condition allows you to drive vehicles and use machines safely.

Amvuttra contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially 'sodium-free'.

3. How Amvuttra is given

This medicine will be given to you by a doctor, pharmacist, or nurse.

How much Amvuttra you are given
The recommended dose is 25 mg once every 3 months.

Where the injection is given
Amvuttra is given by injection under the skin ('subcutaneous injection') into your stomach area (abdomen), upper arm or thigh.

How long to use Amvuttra
Your doctor will tell you how long you need to receive Amvuttra. Do not stop treatment with Amvuttra unless your doctor tells you to.

If you receive more Amvuttra than you should
In the unlikely event that you are given too much (an overdose), your doctor will check you for side effects.

If you miss your dose of Amvuttra
If you miss an appointment for your Amvuttra injection, contact your doctor, pharmacist or nurse as soon as you can to arrange to have the injection you missed.

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.

Tell your doctor, pharmacist, or nurse if you notice any of the following side effects:
Very common: may affect more than 1 in 10 people
- Pain in the joints
- Pain in arms and legs

Common: may affect up to 1 in 10 people
- Being short of breath
- Redness, pain, itching, bruising, or warmth where the injection was given
- Blood tests showing increases in a liver enzyme called alkaline phosphatase

Reporting of side effects
If you get any side effects, talk to your doctor, 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:

United Kingdom
Yellow Card Scheme

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

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Amvuttra

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 label, tray lid and carton after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 30 °C. Do not freeze.

Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What Amvuttra contains

- The active substance is vutrisiran.
  Each pre-filled syringe contains vutrisiran sodium equivalent to 25 mg vutrisiran in 0.5 mL solution.
- The other ingredients are: sodium dihydrogen phosphate dihydrate, disodium phosphate dihydrate, sodium chloride and water for injections. Sodium hydroxide and phosphoric acid may be used to adjust the pH (see "Amvuttra contains sodium" in section 2).

What Amvuttra looks like and contents of the pack
This medicine is a clear, colourless-to-yellow solution for injection (injection). Each pack contains one single-use pre-filled syringe.

Marketing Authorisation Holder and Manufacturer
Alnylam Netherlands B.V.
Antonio Vivaldistraat 150
1083 HP Amsterdam
Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Alnylam UK Ltd.
Tel: 08001412569 (+44 1628 878592)
medinfo@alnylam.com

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The following information is intended for healthcare professionals only:

Amvuttra 25 mg solution for injection in pre-filled syringe
vutrisiran

Healthcare professionals should refer to the Summary of Product Characteristics for full prescribing information.

Posology and method of administration
Therapy should be initiated under the supervision of a physician knowledgeable in the management of amyloidosis.

Posology
The recommended dose is 25 mg vutrisiran administered by subcutaneous injection once every 3 months.

Missed dose
If a dose is missed, administer Amvuttra as soon as possible. Resume dosing every 3 months, from the most recently administered dose.

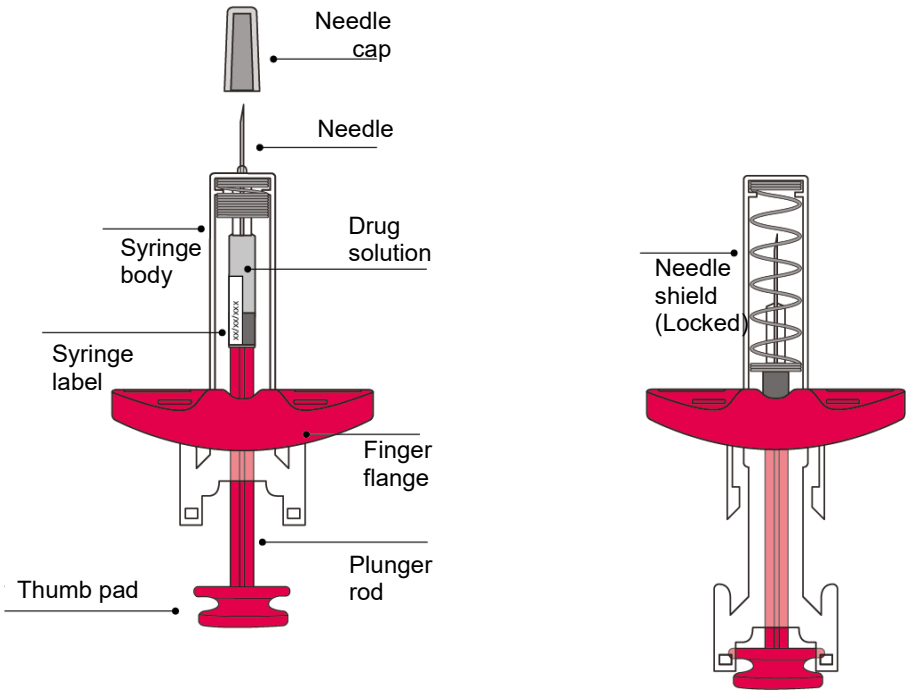
Method of administration
Amvuttra is for subcutaneous use only and should be administered by a healthcare professional.

Prior to administration, if stored cold, allow Amvuttra to warm by leaving carton at room temperature for about 30 minutes.

- Administer subcutaneous injection into one of the following sites: the abdomen, thighs, or upper arms. Do not inject into scar tissue or areas that are reddened, inflamed, or swollen.
- If injecting into the abdomen, avoid the area around the navel.
- Each 25 mg dose is administered using a single pre-filled syringe. Each pre-filled syringe is for single-use only.

How the syringe looks before and after use:

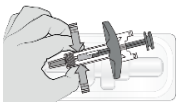
Before Use **After Use**



1. Prepare syringe

If stored cold, allow the syringe to warm to room temperature for 30 minutes prior to use.

Remove the syringe from the packaging by gripping the syringe body.



Do not touch plunger rod until ready to inject.

Amvuttra is a sterile, preservative-free, clear, colourless-to-yellow solution. Visually inspect the solution. **Do not** use if it contains particulate matter or if it is cloudy or discoloured.

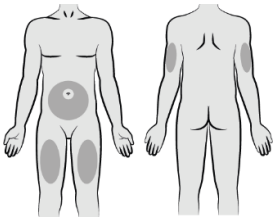
Check:

- Syringe is not damaged, such as cracked or leaking
- Needle cap is attached to the syringe
- Expiry date on syringe label.

Do not use the syringe if any issues are found while checking the syringe.

2. Choose injection site

Choose an injection site from the following areas: the abdomen, thighs, or upper arms.



Avoid:

- Area around the navel
- Scar tissue or areas that are reddened, inflamed, or swollen.

Clean the chosen injection site.

3. Prepare for injection

Hold the syringe body with one hand. Pull the needle cap straight off with other hand and dispose of needle cap immediately. It is normal to see a drop of liquid at the tip of the needle.

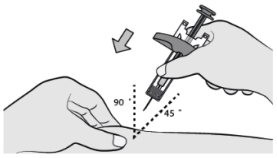
Do not touch the needle or let it touch any surface.

Do not recap the syringe.

Do not use the syringe if it is dropped.

4. Perform Injection

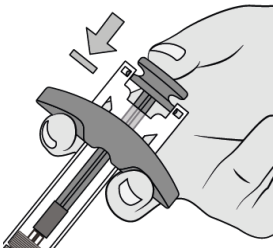
Pinch the cleaned skin.



Fully insert the needle into the pinched skin at a 45-90° angle.

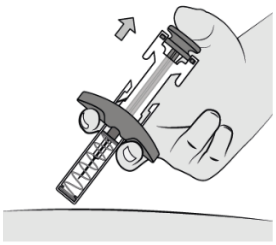
Inject all of the medicine

Push the plunger rod as far as it will go to administer the dose and activate the needle shield.



Release the plunger rod to allow the needle shield to cover the needle.

Do not block plunger rod movement.



5. Dispose of syringe

Immediately dispose of the used syringe into a sharps container.