Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Amvuttra 25 mg

Solution for subcutaneous injection

Active ingredient:
Each 0.5 ml pre-filled syringe contains 25 mg vutrisiran as sodium.

Inactive ingredients and allergens in this medicine: See section 2 under '**Important information about some of this medicine's ingredients**', and section 6 '**Additional information**'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Amvuttra is indicated for the treatment of hereditary transthyretin amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy (hATTR-PN).

Amvuttra is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM).

Therapeutic group: Other nervous system drugs.

Amvuttra is used for the treatment of an illness called transthyretin amyloidosis (ATTR). This illness can run in families and may also be caused by aging. Transthyretin 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, impairing their normal function. This causes the symptoms of the illness.

Amvuttra lowers the amount of TTR protein made by the liver so that there is less of it available in the blood to form amyloid deposits. This action can help reduce the effects of the illness.

2. Before using this medicine

Do not use this medicine if:

You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6 '**Additional information**').

Special warnings about using this medicine

Lowered vitamin A levels in the blood and need to take vitamin supplements
Amvuttra lowers the amount of vitamin A in your blood. Before the start of treatment, your doctor will evaluate the levels of the vitamin as well as symptoms that can indicate a low level.
Your doctor will instruct you to take a daily vitamin A supplement. Make sure to take the dose recommended by your doctor.

Signs of a low level of vitamin A may include sight problems especially at night, dry eyes, hazy, or cloudy vision.

- If you sense a decline in your vision or have any other eye problem whilst using Amvuttra, talk to your doctor. They may send you to an ophthalmologist for a check-up.

In pregnant women, both too high and too low levels of vitamin A can harm the development of your unborn child. Therefore, women of childbearing age should rule out any pregnancy before starting treatment with Amvuttra and use effective contraception during treatment (see section 'Pregnancy, breast-feeding and contraception').

- Vitamin A levels may remain low for more than 12 months after the last dose of Amvuttra received.
- Tell your doctor if you are planning to become pregnant. Your doctor will instruct you to stop taking Amvuttra and vitamin A supplements. 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 instruct you to stop taking Amvuttra. In the first three months of your pregnancy, your doctor will instruct you on continued vitamin A supplementation. Your doctor may refer you for testing of your vitamin A and thyroid stimulating hormone (TSH) levels as well as for foetal monitoring tests. During the last six months of your pregnancy, you doctor may instruct you to resume vitamin A supplementation if the vitamin A levels in your blood have not yet returned to normal. This is because of the increased risk of vitamin A deficiency during the last three months of your pregnancy.

Children and adolescents
Amvuttra is not intended for use in children and adolescents under 18 years of age as the effectiveness and safety of Amvuttra in this population have not yet been established.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before starting treatment with Amvuttra.

Pregnancy
You should not use Amvuttra if you are pregnant (see ‘Special warnings about using this medicine’ above).

Women of childbearing age
Amvuttra reduces the level of vitamin A in your blood; this vitamin is important for the normal development of your unborn child (see ‘Special warnings about using this medicine’ above).

- If you are a woman who is able to become pregnant, you should use effective contraception during treatment with Amvuttra.
- Talk to your doctor about suitable methods of contraception.
- Pregnancy should be ruled out before starting treatment.
- Tell your doctor if you are planning to become pregnant or if you have an unplanned pregnancy. Your doctor will instruct you to stop using Amvuttra.

Breast-feeding
It is not known if the active ingredient passes into breast milk. Your doctor will help you decide whether to stop breast-feeding or refrain from treatment with Amvuttra, considering the benefit of breast-feeding to the baby compared with the benefit of the medicine to the mother.

Driving and using machines
Amvuttra has no effect, or has a negligible effect, on your ability to drive and use machines. Your doctor will tell you whether your condition allows you to drive a vehicle and use machines safely.

Important information about some of this medicine’s ingredients
Amvuttra contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially ‘sodium free’.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

The medicine will be injected by a doctor or nurse (see information for healthcare providers only at the end of the leaflet).

Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually 25 mg once every three months.

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

Duration of the treatment with Amvuttra
Your doctor will tell you the duration of the treatment with Amvuttra. Do not stop using the medicine without being explicitly instructed to do so by your doctor.

Do not exceed the recommended dose.

If you have accidentally been injected with a higher dose of Amvuttra than required
If you been injected with an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. In the event of an overdose, your doctor will monitor development of side effects or symptoms and provide you with treatment if necessary.

If you missed a dose of Amvuttra
If you missed the time for injection of Amvuttra, contact your doctor or nurse to schedule a new time as soon as possible. Resume administration of Amvuttra every 3 months from the date of the most recent injection.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, using Amvuttra may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Tell your doctor, pharmacist, or nurse if you notice any of the following side effects:

Common side effects (may affect up to 1 in 10 users):
- Redness, pain, itching, bruising, or feeling of warmth at the injection site.
- Increase in liver enzymes called alkaline phosphatase (ALP, alkaline phosphatase) and alanine transaminase in blood tests.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens to an online form for reporting side effects, or you can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Do not store above 30°C.

- Do not freeze.
- Do not throw away any medicine via wastewater or household waste. The healthcare professionals will make sure to destroy medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
sodium chloride, sodium phosphate dibasic dihydrate, sodium phosphate monobasic dihydrate, water for injection, phosphoric acid (for pH adjustment), sodium hydroxide (for pH adjustment).

What the medicine looks like and contents of the pack:
Amvuttra is a clear, colourless-to-yellow solution that is free of particulate matter and that is intended for subcutaneous (SC) injection.

Each pack contains one 0.5 ml pre-filled syringe equipped with a passive needle safety system intended for single use.

Registration holder's name and address:
Medison Pharma Ltd.
10 Hashiloach St., P.O.B. 7090, Petach Tikva

Manufacturer's name and address:
Alnylam Netherlands B.V.
Antonio Vivaldistraat 150
1083 HP Amsterdam
Netherlands

Revised in January 2026.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 176-25-37761-99

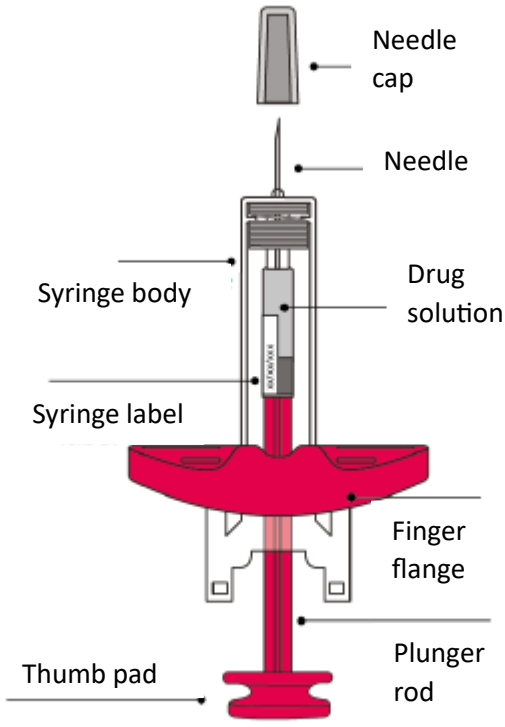
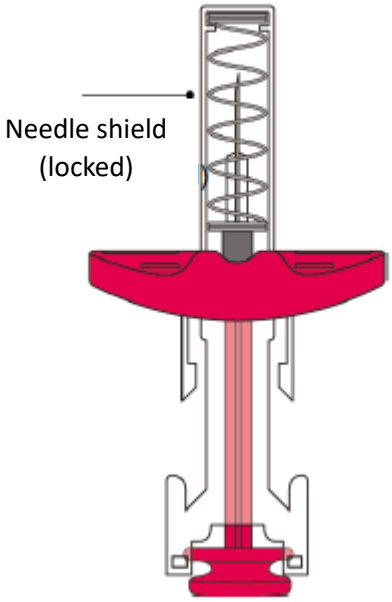
Information for healthcare providers only (see section 3 'How to use this medicine?')

Amvuttra is intended for subcutaneous (SC) injection only by a healthcare professional.

If the medicine was stored cold, leave it in the carton at room temperature for about 30 minutes prior to injection.

- The subcutaneous injection should be administered into one of the following injection sites: the abdomen, thighs, upper arms. Do not inject into an area with scar tissue or areas where the skin is reddened, inflamed, or swollen.
- If injecting into the abdomen, the area around the navel should be avoided.
- Each dose of 25 mg is administered with a pre-filled syringe. Each pre-filled syringe is intended for single use.

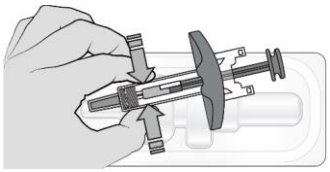
How the syringe looks before and after use:

Before Use	After Use
	

1. Preparing the syringe

If the syringe was stored cold, allow it to warm to room temperature for at least 30 minutes before 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, free of particulate matter.
Visually inspect the solution. **Do not** use the medicine if it contains particulate matter or if it is cloudy or discoloured.
Check:

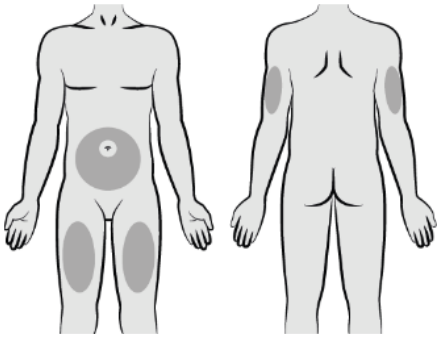
- No signs of damage on the syringe, such as a crack or leak.
- Needle cap is attached to the syringe.
- Expiry date on syringe label is correct.

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

2. Choosing the injection site

Choose one of the following injection sites: abdomen, thighs, or upper arms.
Refrain from injecting into the following areas:

- Area around the navel.
- An area with scar tissue or areas where the skin is reddened, inflamed, or swollen.



Disinfect the chosen injection site.

3. Preparing for injection

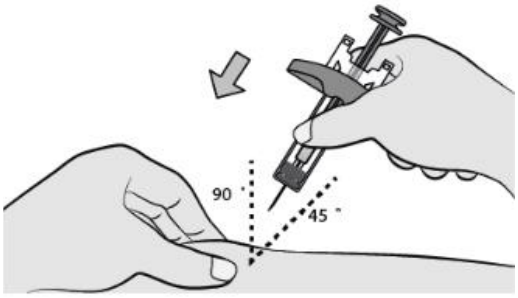
Hold the syringe body with one hand. Pull the needle cap straight off with the other hand and dispose of needle cap immediately into a sharps container.

It is normal to see a drop liquid at the tip of the needle.

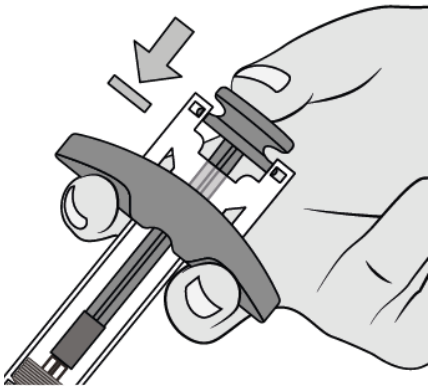
Do not touch the needle or let the needle touch any surface.
Do not recap the syringe.
Do not use the syringe if it is dropped.

4. Performing the injection

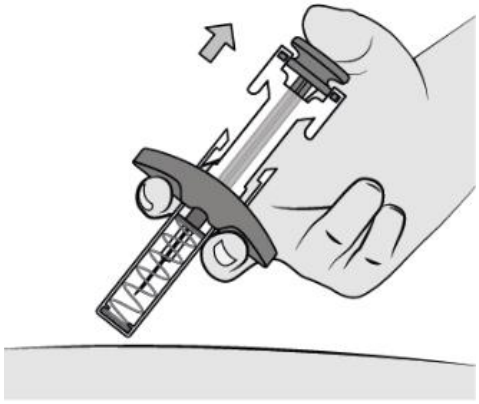
Pinch the skin in the area that was disinfected.
Fully insert the needle into the pinched skin at a 45-90° angle.



Inject all of the medicine.
Push the plunger rod as far as it will go to inject the full 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. Disposing of the syringe

Immediately dispose of the used syringe into a sharps container.
Medicines should be destroyed in accordance with local regulations.