AMVUTTRA® (vutrisiran)

Just the ticket for ATTR-CM and hATTR-PN

AMVUTTRA was proven to help people living with ATTR-CM and hATTR-PN

Indications

What is AMVUTTRA® (vutrisiran)?

AMVUTTRA is a prescription medicine that treats the:

- cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce heart-related death, hospital stays and urgent visits.
- polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults.

Important Safety Information

What are the most important things I should know about AMVUTTRA?

AMVUTTRA can cause low vitamin A levels

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Low vitamin A levels can affect vision. If you have problems with your vision (e.g., night blindness) while taking AMVUTTRA, talk to your doctor. Your doctor may refer you to an eye specialist.

Please see additional Important Safety Information on page 15, and full Prescribing Information.

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

With ATTR amyloidosis, time is critical

Symptoms get worse over time and can lead to serious health risks

- **Heart failure**
- **Nerve damage**
- **Physical disability**
- **Early death**

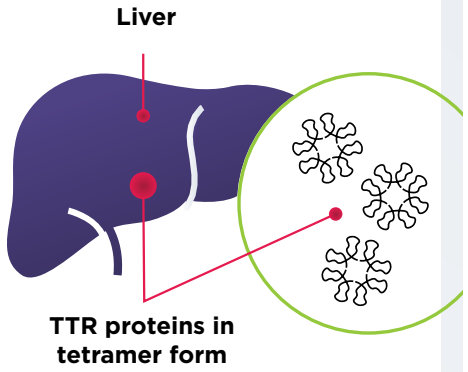
There are 2 types of ATTR

Wild-type ATTR (wtATTR), though the cause is unknown, may be associated with aging and is commonly associated with heart (cardiac) symptoms.

Hereditary ATTR (hATTR) is caused by an inherited gene variant and is commonly associated with both heart (cardiac) and nerve (neuropathy) symptoms.

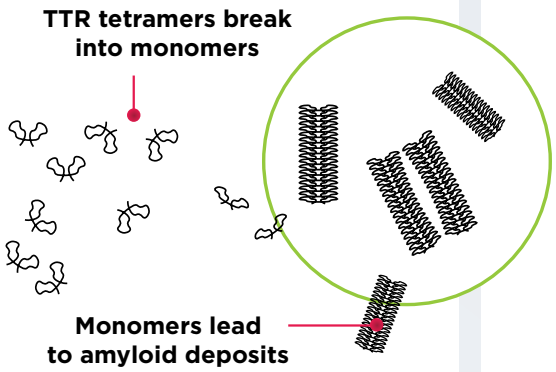
Misfolded TTR proteins build up in the body, causing symptoms

TTR is made mostly in the liver



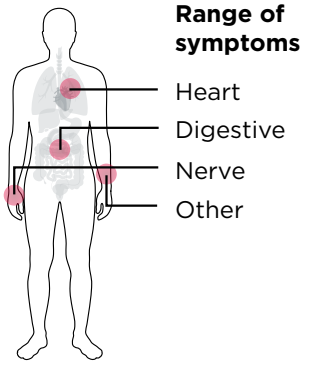
Transthyretin (TTR) is a protein made primarily in the liver and circulated in the blood. It carries vitamin A throughout the body.

TTR misfolds and builds up



When these proteins become unstable, it can lead to amyloid deposits in different parts of the body.

Amyloid deposits cause damage



These amyloid deposits cause damage to the heart, nerves, digestive system and other organs, leading to a range of debilitating symptoms.

Learn more about ATTR
amvuttra.com/disease

Symptoms can make it harder to live your life

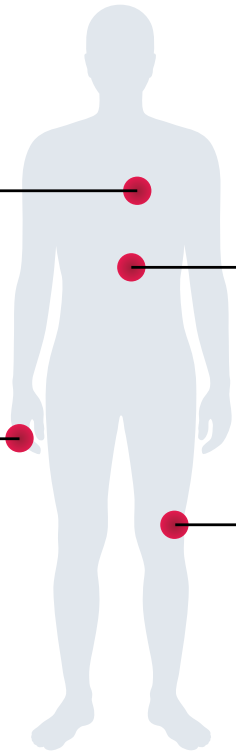
Different types of ATTR can affect different parts of the body

Heart-related symptoms

- Abnormal heart rhythms (arrhythmias)
- Irregular heartbeat
- Shortness of breath
- Fatigue
- Fainting
- Leg swelling (edema)

Bodily function-related symptoms

- Digestive issues (nausea and vomiting, diarrhea, constipation)
- Dizziness upon standing
- Recurrent urinary tract infections (UTIs)
- Abnormal sweating
- Sexual dysfunction
- Unintentional weight loss



Nerve-related symptoms

- Tingling
- Numbness
- Burning pain
- Loss of sensitivity to temperature
- Loss of movement control
- Weakness

Muscles, joints, and tendon-related symptoms

- Carpal tunnel syndrome
- Lumbar spinal stenosis
- Biceps tendon rupture
- Rotator cuff injury
- Osteoarthritis
- Trigger finger

You may not have all of these symptoms at once or experience all of them over time. Each person has a different experience.

AMVUTTRA® (vutrisiran) does not treat all types or symptoms of ATTR. AMVUTTRA is approved to treat ATTR-CM and hATTR-PN in adults.

ATTR impacts daily life

Daily activities become more difficult, such as:

- Walking distances
- Doing things for yourself like daily chores
- Climbing stairs
- Enjoying outings with friends and family

Talk to your doctor about options that may help slow the progression of your disease.

Please see additional Important Safety Information on page 15, and full Prescribing Information.

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AMVUTTRA® (vutrisiran) reduces TTR at the source

How AMVUTTRA works

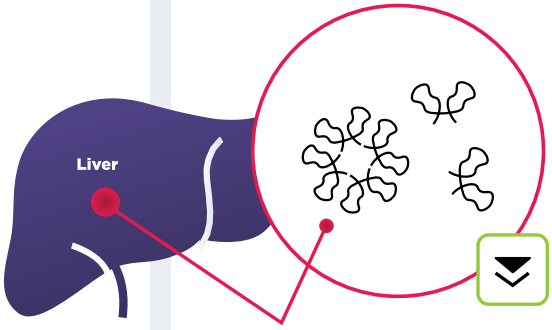
As a silencer, AMVUTTRA suppresses TTR production in the liver—where most of it is made.

Suppresses TTR in the liver

AMVUTTRA

AMVUTTRA works in the liver to reduce the amount of TTR produced and circulated in the blood.

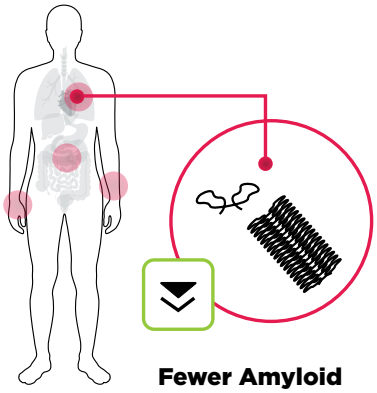
Reduces TTR in the blood



Fewer TTR Proteins

Less TTR in the blood means there's less that can misfold and build up as amyloid deposits in the body.

Leads to fewer amyloid deposits



Fewer Amyloid Deposits

With fewer amyloid deposits building up, the progression of ATTR-CM and hATTR-PN may be slowed.

Important Safety Information

What are the common side effects of AMVUTTRA?

The most common side effects of AMVUTTRA were pain in the arms or legs, pain in the joints, shortness of breath, and low vitamin A levels.

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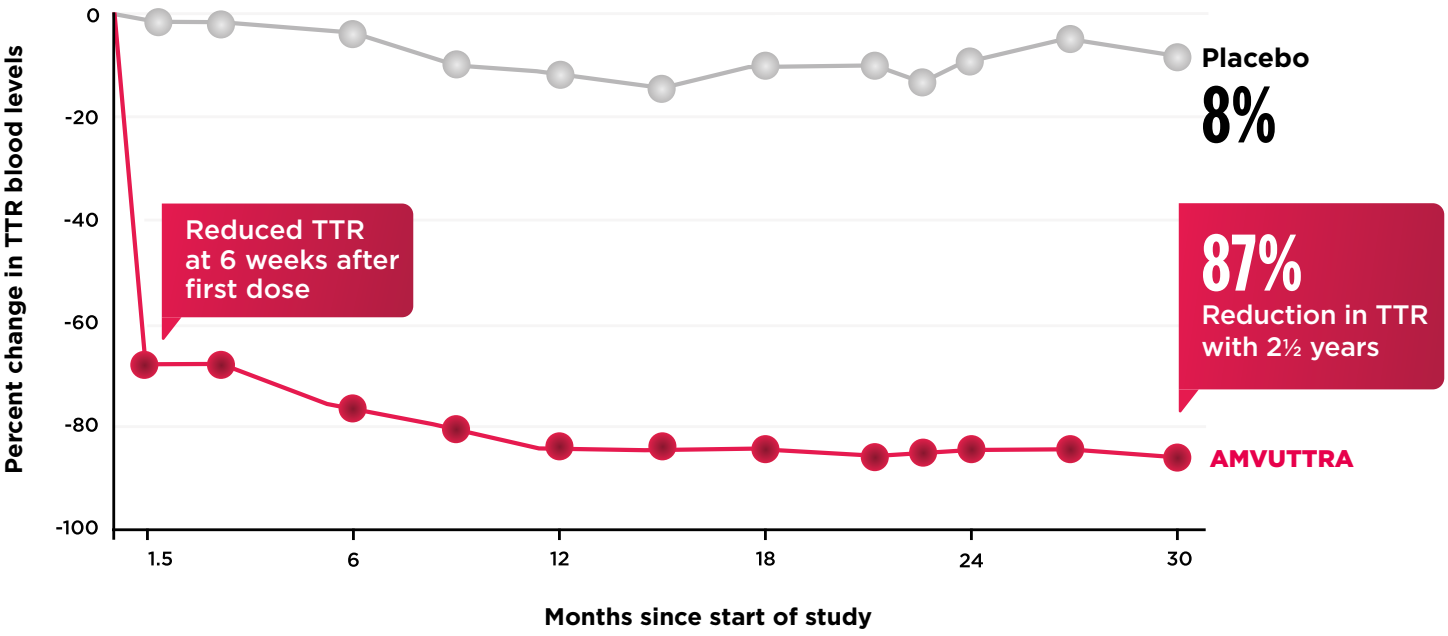
amvuttra® (vutrisiran) injection 25 mg/0.5 mL

The first and only silencer for ATTR-CM and hATTR-PN

Rapidly knocks down TTR

In a clinical study, AMVUTTRA® (vutrisiran) reduced TTR at 6 weeks after the first dose and maintained reductions with continued treatment.



Results shown are from the ATTR-CM study. Similar reductions were seen in the hATTR-PN study (at 3 weeks after the first dose and with 1½ years of treatment). Individual results may vary.

Important Safety Information

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amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Studied in people with ATTR-CM and hATTR-PN

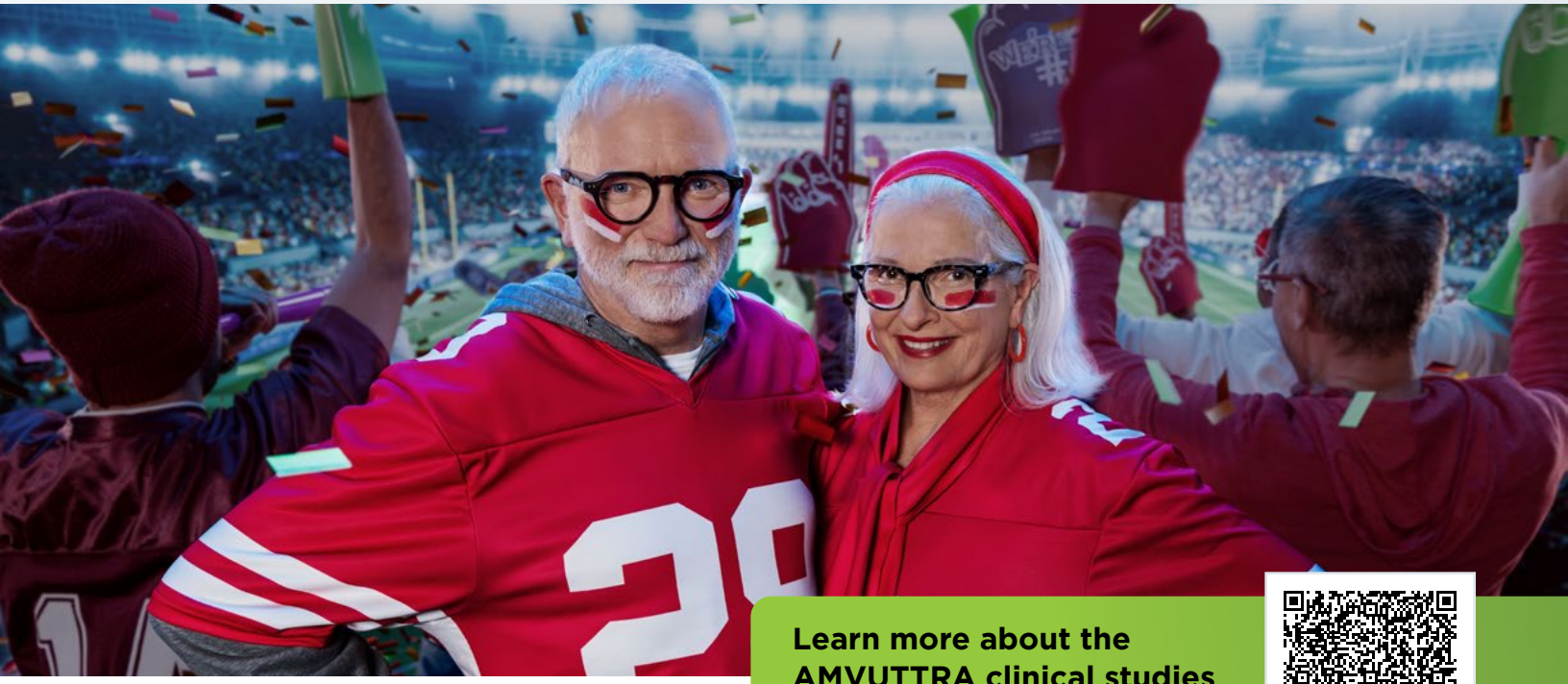
The safety and effectiveness of AMVUTTRA® (vutrisiran) were shown in 2 clinical studies.

The ATTR-CM study

- 654 adults with cardiomyopathy of wild-type or hereditary ATTR
- Up to 3½ years of data

The hATTR-PN study

- 164 adults with polyneuropathy of hereditary ATTR
- 18 months of data



Learn more about the AMVUTTRA clinical studies
amvuttra.com/studies

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Proven to help people with ATTR-CM live longer and have fewer hospital visits

28%

Lower risk of death and heart-related hospital visits

over 3 years with AMVUTTRA* compared to placebo

Effectiveness was determined by comparing the results of people treated with AMVUTTRA® (vutrisiran) to those who received placebo (a treatment without any active medication).

The main measure of effectiveness was the combined risk of death and heart-related hospital stays and urgent visits over 3 years.

*Most deaths were heart-related. Hospital visits included hospital stays and urgent visits.

Survival was estimated in a separate analysis at 3½ years

80%

Survival rate

for people taking AMVUTTRA over 3½ years compared to **72% for people taking placebo**

Analyses done over 3½ years compared the original AMVUTTRA and placebo groups from the beginning of the study. After 3 years, people taking placebo switched to AMVUTTRA so that everyone still in the study received AMVUTTRA for up to an additional 6 months.

Survival rate was not included in the original study plan, and other factors could have influenced the results. Talk to your doctor about what this might mean for you.

Explore more results from the ATTR-CM study
amvuttra.com/heart

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amvuttra® (vutrisiran) injection 25 mg/0.5 mL

People maintained more of their quality of life at 2½ years

People taking AMVUTTRA® (vutrisiran) reported better health-related quality of life than people on placebo at 2½ years.

Both groups reported lower quality of life than at the start of the study.

Quality of life measures

Heart-related symptoms

like shortness of breath, tiredness, and swollen feet or ankles

Physical activities

like hobbies, chores, and errands

Social relationships

like engaging with friends and family

Important Safety Information

What are the common side effects of AMVUTTRA?

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People retained more of their exercise capacity at 2½ years

People taking AMVUTTRA® (vutrisiran) walked 72 feet farther, on average, than people on placebo at 2½ years.

Both groups walked shorter distances than at the start of the study.

Results are from the 6-MWT that assesses the distance a person can walk in 6 minutes and how well the heart can support physical activity. A larger loss in distance indicates a larger impact from heart failure.

6-MWT=6-minute walk test.

AMVUTTRA slowed disease progression in people with ATTR-CM.

Important Safety Information

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amvuttra (vutrisiran) injection 25 mg/0.5 mL

Explore the full hATTR-PN study results
amvuttra.com/nerve

About the hATTR-PN study

Safety and effectiveness were evaluated by comparing results from people taking AMVUTTRA® (vutrisiran) and people taking placebo in a similar study.

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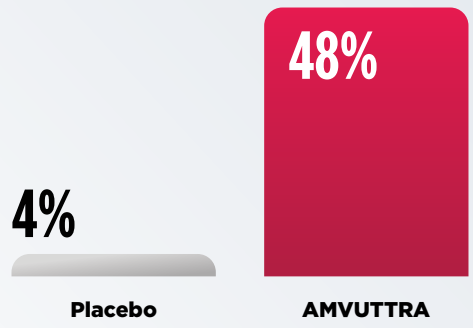
amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Proven to help people with hATTR-PN have better nerve function and quality of life

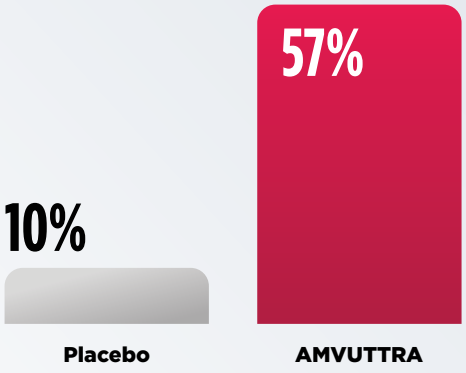
AMVUTTRA® (vutrisiran) significantly improved nerve function and quality of life for people at 9 months, with continued improvement over 18 months, compared to people on placebo.

AMVUTTRA was evaluated in separate analyses

Percentage of people who regained some nerve function at 18 months



Percentage of people who reported better quality of life at 18 months



Those who didn't regain some nerve function saw slower progression of their nerve symptoms compared to placebo.

People saw other positive effects in their daily life

At 18 months, people taking AMVUTTRA did better than those on placebo in the following ways:

- **Maintained better walking speed**
- **Improved nutritional health**
- **Performed daily activities more easily**

Important Safety Information

AMVUTTRA can cause low vitamin A levels (continued)

Low vitamin A levels can affect vision. If you have problems with your vision (e.g., night blindness) while taking AMVUTTRA, talk to your doctor. Your doctor may refer you to an eye specialist.

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The safety of AMVUTTRA® (vutrisiran)

The most common side effects in clinical studies of AMVUTTRA

Side effects in the hATTR-PN study	AMVUTTRA 122 people
Pain in the arms or legs	**15%**
Pain in the joints	**11%**
Shortness of breath	**7%**
Low vitamin A levels	**7%**

Side effects in the ATTR-CM study	AMVUTTRA 326 people	Placebo 328 people
Pain in the arms or legs	**9%**	**10%**
Pain in the joints	**11%**	**13%**
Shortness of breath	**15%**	**17%**

Talk to your doctor about side effects that you experience.

Since AMVUTTRA lowers TTR, which transports vitamin A, supplementation at the recommended daily allowance (RDA) is advised because low vitamin A levels can impact vision. The RDA of vitamin A is contained in many multivitamins and in stand-alone supplements.

Ask your doctor if AMVUTTRA is right for your treatment journey.

Please see additional Important Safety Information on page 15, and full Prescribing Information.

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Stay on course with just 4 doses a year

Given by a healthcare provider

AMVUTTRA® (vutrisiran) injections are given by a healthcare provider so you can feel confident you're getting the full dose on schedule.

Once every 3 months

AMVUTTRA is given once every 3 months, letting you focus on your life and not your treatment plan.

Injected under the skin

AMVUTTRA is given with a small needle in a prefilled syringe in the upper arm, thigh, or abdomen. AMVUTTRA may cause reactions at the injection site such as bruising, redness, pain, itching, and warmth.

Convenient treatment center options

You can work with your doctor to choose where you get treatment—whether at your doctor's office, a treatment center, or even at home, depending on your insurance.

Find nearby treatment centers amvuttra.com/centers

Watch a video on how AMVUTTRA is given
amvuttra.com/treatment

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Support throughout your journey with Alnylam Assist®

Alnylam Assist® offers support with insurance coverage, financial assistance, disease and treatment education, and starting AMVUTTRA® (vutrisiran).

Alnylam Patient Education Liaisons (PELs) provide disease and AMVUTTRA education to patients, their families, and caregivers.

- **Request to connect with a PEL at amvuttra.com/educator**
- Alnylam PELs do not offer medical advice. All diagnosis and treatment decisions should be made by you and your doctor

One-on-one support in understanding insurance coverage and starting treatment through Alnylam Case Managers.

Alnylam offers multiple financial assistance programs* that can help with your medication cost:

- Alnylam Assist® Copay Program† covers certain out-of-pocket costs for eligible patients with commercial insurance
- Alnylam Assist® Patient Assistance Program (PAP) provides AMVUTTRA at no cost to eligible patients, primarily the uninsured, who meet specified eligibility criteria
- Additional programs may be able to help if you have a delay or change in insurance coverage

Alnylam ASSIST®

Visit **AlnylamAssist.com** to learn more.
Call **1-833-256-2748**, Monday–Friday, 8AM–6PM.

*Patients must meet specified eligibility criteria to qualify for assistance. Alnylam reserves the right to make eligibility determinations and to modify or discontinue any program at any time.

†Patients with Medicare, Medicaid, or other government-sponsored insurance are not eligible for the Alnylam Assist® Copay Program. Out-of-pocket costs for the administration of AMVUTTRA will not be covered for patients residing where it is prohibited by law or where otherwise restricted.

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Indications and Important Safety Information

Indications

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Take the first step—talk to your doctor about AMVUTTRA® (vutrisiran)

The first and only silencer for ATTR-CM and hATTR-PN

People with ATTR-CM lived longer and had fewer heart-related hospital visits*

People with hATTR-PN had better nerve function and quality of life

4X

Just 4 injections a year given by a healthcare provider

*Most deaths were heart-related. Hospital visits included hospital stays and urgent visits.

Connect with an Alnylam Patient Educator to learn more about AMVUTTRA
amvuttra.com/educator

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