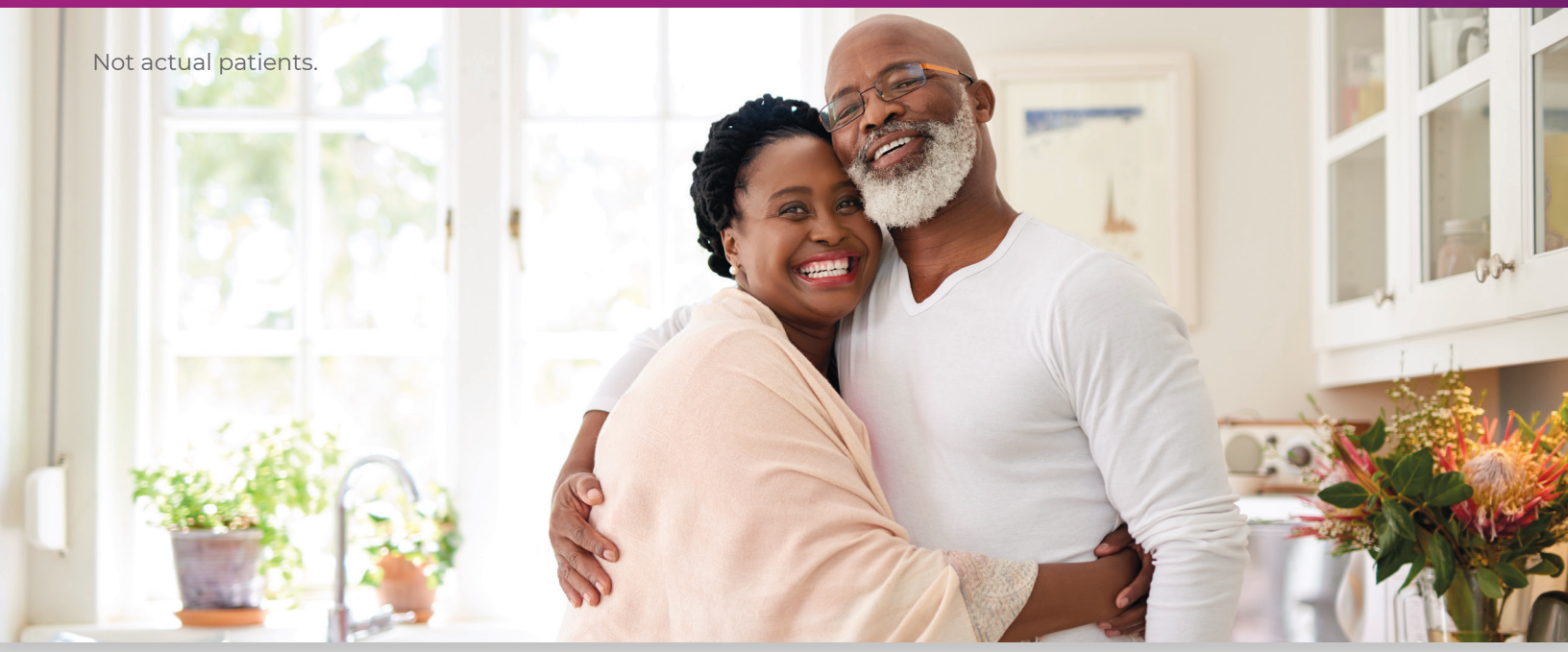


Tegsedi®
(inotersen) injection
284 mg/1.5 mL

Consider home injection with TEGSEDI®

Ask your doctor how a once-weekly self-injection of TEGSEDI can treat the polyneuropathy of hereditary ATTR amyloidosis

Abbreviation: ATTR, transthyretin-mediated amyloidosis.

INDICATION

TEGSEDI is a medicine that treats the polyneuropathy caused by hereditary transthyretin-mediated amyloidosis. TEGSEDI is for use in adults only.

IMPORTANT SAFETY INFORMATION

TEGSEDI can cause serious side effects including:

TEGSEDI may cause low platelet counts and kidney problems. Because of these risks, TEGSEDI is available only through a restricted program called the TEGSEDI Risk Evaluation and Mitigation Strategy (REMS) Program. Talk to your healthcare provider about how to enroll in the TEGSEDI REMS Program.

Please see additional Important Safety Information throughout this brochure including WARNINGS about Low Platelet Count and Kidney Inflammation, and see full Prescribing Information, including the Medication Guide, in pocket.

What is hereditary ATTR amyloidosis?

Hereditary ATTR amyloidosis is caused by a change in the gene that makes a specific protein in your body.

There are 2 types of ATTR amyloidosis:

- **Wild-type ATTR amyloidosis** is caused by changes to a specific protein that may occur in some people as they age; it is not caused by a genetic mutation
- **Hereditary ATTR amyloidosis** is caused by a genetic mutation and can be passed down through family members

What happens in people with hereditary ATTR amyloidosis?

Your genes

You have a change or mutation in the gene that makes a protein called transthyretin (trans-THIGH-ree-tin), or TTR

Your liver

TTR is made in the liver. Your gene causes TTR proteins to form in an unusual shape

Protein clusters

The unusual shape causes TTR proteins to clump together in clusters. These clusters are called amyloid fibrils

Amyloid buildup

Amyloid fibrils build up in the body and damage tissues and organs

Did you know? A parent who has hereditary ATTR amyloidosis has a 50% chance of passing the gene mutation on to their child.

IMPORTANT SAFETY INFORMATION (CONT'D)

TEGSEDI can cause serious side effects, including:

Low platelet counts (thrombocytopenia): TEGSEDI may cause the number of platelets in your blood to be reduced. This is a common side effect of TEGSEDI. When your platelet count is too low, your body cannot form clots. You could have serious bleeding that could lead to death. **Call your healthcare provider immediately if you have:**

- Unusual bruising or a rash of tiny reddish-purple spots, often on the lower legs
- Bleeding from skin cuts that does not stop or oozes
- Bleeding from your gums or nose
- Blood in your urine or stools
- Bleeding into the whites of your eyes
- Sudden severe headaches or neck stiffness
- Vomiting or coughing up blood
- Abnormal or heavy periods (menstrual bleeding)

Please see additional Important Safety Information throughout this brochure and see full Prescribing Information, including the Medication Guide, in pocket.

Hereditary ATTR amyloidosis may cause polyneuropathy (the damage of multiple nerves)

The 2 main types of polyneuropathy are peripheral sensorimotor polyneuropathy and autonomic neuropathy.

Peripheral sensorimotor polyneuropathy can cause

- Nerve damage, leading to symptoms such as tingling, numbness, or pain in the hands or feet
- Difficulty walking
- Loss of balance

Autonomic neuropathy can affect other organs of the body and cause

- Nausea and vomiting
- Diarrhea or constipation
- Unintended weight loss
- Irregular heartbeat
- Dizziness from low blood pressure
- Sexual dysfunction

Note: TEGSEDI has not been proven to treat all of these symptoms.

People with the polyneuropathy of hereditary ATTR amyloidosis may not experience all of these symptoms, and having some of these symptoms does not necessarily mean you have the polyneuropathy of hereditary ATTR amyloidosis.

Symptoms of the polyneuropathy of hereditary ATTR amyloidosis worsen over time

With the polyneuropathy of hereditary ATTR amyloidosis, some everyday activities may become more challenging. As your disease progresses, these same simple daily tasks may become more difficult.

Receiving appropriate treatment as soon as possible may help to preserve quality of life.

IMPORTANT SAFETY INFORMATION (CONT'D)

TEGSEDI can cause serious side effects, including:

Kidney inflammation (glomerulonephritis): Your kidneys may stop working properly. Glomerulonephritis can lead to severe kidney damage and kidney failure that need dialysis. **Call your healthcare provider immediately if you have:**

- Puffiness or swelling in your face, feet, or hands
- New onset or worsening shortness of breath and coughing
- Blood in your urine or brown urine
- Foamy urine (proteinuria)
- Passed less urine than usual

Tegsedi® (inotersen) injection 284 mg/1.5 mL

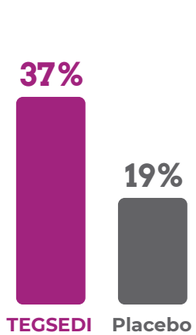
With TEGSEDI®, some people saw improvements in symptoms

Results from the NEURO-TTR clinical study

The safety and effectiveness of TEGSEDI were tested in a pivotal study called NEURO-TTR. NEURO-TTR studied TEGSEDI in measures of both nerve pain (neuropathy) and quality of life.

- One hundred seventy-three adults were randomly assigned to receive either treatment with TEGSEDI (113 people) or placebo (no treatment [60 people]) for 15 months
- Nerve pain was evaluated using a tool called the modified Neuropathy Impairment Score +7 (mNIS+7)
- Quality of life was measured with the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) questionnaire, a 35-item questionnaire used to assess the impact of neuropathy on a patient, such as impaired walking, abnormal sensations in limbs, and difficulty bathing and dressing oneself

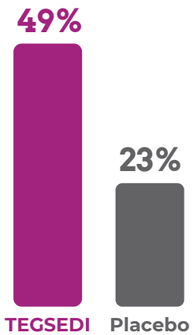
At 66 weeks, patients treated with TEGSEDI experienced the following benefits vs those treated with placebo



Based on mNIS+7

Improvement in symptoms of nerve damage

37% of people treated with TEGSEDI reported improvements in nerve function compared with **19%** of people receiving placebo.



Based on Norfolk QoL-DN

Improved quality of life

49% of people treated with TEGSEDI said their quality of life had improved compared with **23%** of people receiving placebo.

Significant results with TEGSEDI were seen as early as 35 weeks.

IMPORTANT SAFETY INFORMATION (CONT'D)

Because of the risk of serious bleeding caused by low platelet counts and because of the risk of kidney problems, TEGSEDI is available only through a restricted program called the TEGSEDI Risk Evaluation and Mitigation Strategy (REMS) Program. Talk to your healthcare provider about how to enroll in the TEGSEDI REMS Program.

Do not use TEGSEDI if you have:

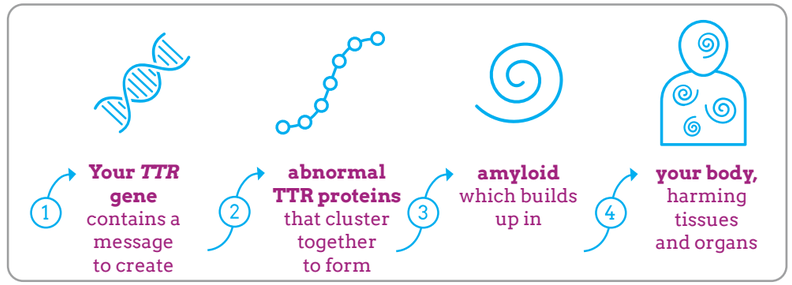
- A platelet count that is low
- Had kidney inflammation (glomerulonephritis) caused by TEGSEDI
- Had an allergic reaction to inotersen or any of the ingredients in TEGSEDI. See the end of the Medication Guide for a complete list of ingredients in TEGSEDI

Please see additional Important Safety Information throughout this brochure and see full Prescribing Information, including the Medication Guide, in pocket.

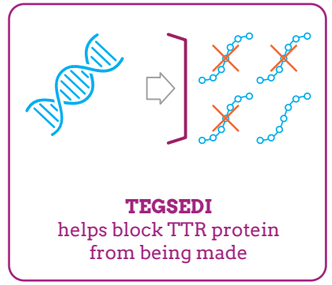
In patients with nerve damage, TEGSEDI targets the disease at its source

TEGSEDI prevents the creation of proteins that become amyloid

Before TEGSEDI

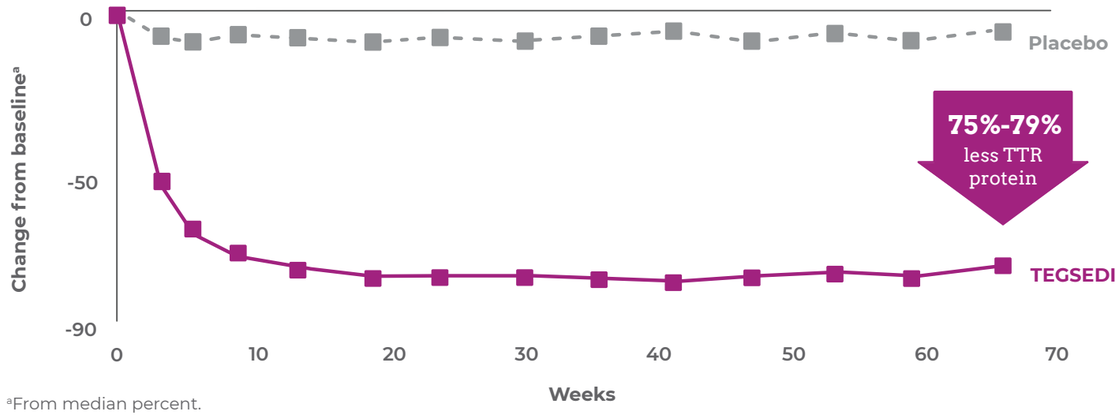


With TEGSEDI



In the pivotal study (NEURO-TTR), TEGSEDI powerfully reduced TTR protein

- Similar TTR reductions were observed regardless of *TTR* mutation, sex, age, or race



[a]From median percent.

In NEURO-TTR, TEGSEDI reduced TTR protein by 75%-79%.

IMPORTANT SAFETY INFORMATION (CONT'D)

Before you start TEGSEDI, tell your healthcare provider about all of your health issues, including if you:

- Have or had bleeding problems
- Have or had kidney problems
- Have received a liver transplant
- Are pregnant or plan to become pregnant. It is not known if TEGSEDI can harm your unborn baby
- Are breastfeeding or plan to breastfeed. It is not known if TEGSEDI can pass into your breast milk or harm your baby. Talk with your healthcare provider about the best way to feed your baby while you are taking TEGSEDI

Tegsedi® (inotersen) injection 284 mg/1.5 mL

TEGSEDI® has a manageable safety profile

Because TEGSEDI can cause serious side effects, including low platelet count (thrombocytopenia) and kidney inflammation (glomerulonephritis), it is available only through the TEGSEDI REMS Program

- Other serious side effects include stroke, inflammatory and immune system problems, liver effects, allergic reactions, and eye problems (low vitamin A levels)
- The most common side effects were injection site reactions (such as redness or pain at the injection site), nausea, headache, tiredness, low platelet count (thrombocytopenia), and fever
- Talk to your doctor about possible side effects with TEGSEDI

While you are receiving TEGSEDI, you will be monitored closely

Your doctor is required to regularly test your blood and urine to measure how well your liver and kidneys are working and the amount of platelets in your blood. Platelets help with normal blood clotting (for example, they help your body stop bleeding if you get a cut). If your doctor asks you to stop taking TEGSEDI, you will need to continue to get your blood and urine tested for 8 more weeks after stopping treatment.

Blood tests

- You will need to get a blood test once a week or more, depending on what your doctor recommends
- Your doctor should do laboratory tests to check your liver function before you start TEGSEDI and every 4 months while you are using it[a]

Urine tests

- You will need to take a urine test once every 2 weeks

Your dosage of TEGSEDI may need to be adjusted or stopped based on your monitoring results.

[a]People who have a history of liver transplant should refer to the Medication Guide for additional monitoring information.

97% of people who finished the NEURO-TTR study chose to take TEGSEDI in an extension study.

IMPORTANT SAFETY INFORMATION (CONT'D)

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you take vitamin A or beta-carotene supplements, blood thinners (anticoagulants), or drugs that affect blood clotting.

Required monitoring. Your healthcare provider will test your blood and urine to check your platelet counts and kidney and liver function before you start TEGSEDI. While you are receiving TEGSEDI, you will be monitored closely for symptoms, which includes checking your platelet counts every week (or more frequently as needed), kidney function every 2 weeks, and liver function every 4 months. If your healthcare provider has you stop taking TEGSEDI, you will need to continue to get your blood and urine tested for 8 more weeks after treatment.

Please see additional Important Safety Information throughout this brochure and see full Prescribing Information, including the Medication Guide, in pocket.

Support from AKCEA® CONNECT

You're not alone in managing this disease

Count on AKCEA CONNECT to be your partner and help support you during your treatment with TEGSEDI. With AKCEA CONNECT, you will be assigned a dedicated Nurse Case Manager who can help you learn more about your disease, access your treatment with TEGSEDI, and be empowered in your healthcare.

Disease and treatment education to help you learn more about hereditary ATTR amyloidosis and TEGSEDI

Personalized injection training from your dedicated Nurse Case Manager

Financial assistance and help with reimbursement, whether you have commercial insurance, Medicare/Medicaid, or no insurance

No-cost mobile lab monitoring and more than 2200 sites for no-cost lab monitoring

Direct coordination between you, your doctor, and the specialty pharmacy

A commitment to your safety and assistance with scheduling, reminders, and follow-ups

Want to speak with someone living with the polyneuropathy of hereditary ATTR amyloidosis?

Team TEGSEDI Mentors are available to provide education and support at every step of your journey. To participate, please contact AKCEA CONNECT at 1-866-AKCEATX.

"We've been where you are, and we're here to help."

– Chuck H., Team TEGSEDI Mentor

AKCEA® CONNECT

To find out more about how AKCEA CONNECT is here to support you, visit akceaconnect.com or call 1-866-AKCEATX.

IMPORTANT SAFETY INFORMATION (CONT'D)

TEGSEDI may cause serious side effects, including:

Stroke. TEGSEDI may cause a stroke. One person taking TEGSEDI had a stroke, which occurred within 2 days after the first dose. Get emergency help immediately if you have symptoms of stroke, including sudden numbness or weakness, especially on one side of the body; severe headache or neck pain; confusion; problems with vision, speech, or balance; droopy eyelids.

Inflammatory and immune system problems. Some people taking TEGSEDI had serious inflammatory and immune system problems. Symptoms of inflammatory and immune system problems included unexpected change in walking, weakness and spasms in legs, back pain, weight loss, headache, vomiting, and problems with speech.

Tegsedi® (inotersen) injection 284 mg/1.5 mL

TEGSEDI® is the first and only self-administered injection for the polyneuropathy of hereditary ATTR amyloidosis in adults

Ask your doctor if TEGSEDI is right for you today

- You choose when and where to take TEGSEDI—decide for yourself how TEGSEDI will become part of your routine
- TEGSEDI is an injection you have the independence to give yourself once per week
- Before your first injection, you will be trained on how to inject TEGSEDI
- TEGSEDI arrives ready to inject, already filled in the syringe
- TEGSEDI should be refrigerated, but can be stored for up to 6 weeks at room temperature so it can travel with you

Learn more at TEGSEDI.com

IMPORTANT SAFETY INFORMATION (CONT'D)

TEGSEDI may cause serious side effects, including (cont'd):

Liver Effects. TEGSEDI may cause liver problems. Your healthcare provider should do laboratory tests to check your liver before you start TEGSEDI and every 4 months while you are using it. Tell your healthcare provider if you have symptoms that your liver may not be working right, which could include unexpected nausea and vomiting, stomach pain, being not hungry, yellowing of the skin, or having dark urine.

Allergic reactions. TEGSEDI may cause serious allergic reactions. These allergic reactions often occur within 2 hours after injecting TEGSEDI. Get emergency help immediately if you have any symptoms of a serious allergic reaction, including joint pain, chills, redness on palms of hands, muscle pain, chest pain, flushing, tremor or jerking movements, flu-like symptoms, high blood pressure, or difficulty swallowing.

Eye problems (low vitamin A levels). Treatment with TEGSEDI will lower the vitamin A levels in your blood. Your healthcare provider will tell you how much supplemental vitamin A to take every day; only take the amount they tell you to take. Call your healthcare provider if you get eye problems, such as having difficulty seeing at night or in low-lit areas (night blindness).

The most common side effects of TEGSEDI include injection site reactions (such as redness or pain at the injection site), nausea, headache, tiredness, low platelet counts (thrombocytopenia), and fever. These are not all of the possible side effects of TEGSEDI. Talk to your healthcare provider about any side affects you may be experiencing.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information, including the Medication Guide, in pocket.

AKCEA® THERAPEUTICS

Tegsedi® (inotersen) injection 284 mg/1.5 mL