Not actual patients.

Tegsedi® (inotersen) injection 284 mg/1.5 mL

# Getting started with TEGSEDI®

## How to build a treatment routine

## 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.***

# Welcome to TEGSEDI® (inotersen)

Actual patient.

# Your comprehensive guide to treatment with TEGSEDI

Hereditary transthyretin-mediated amyloidosis (AM-uh-loy-DOH-sis), or hereditary ATTR amyloidosis, with polyneuropathy (POL-ee-nur-OP-uh-thee) can bring many fears and challenges, but you're taking a positive step by preparing for treatment. Use the resources in this guide to incorporate TEGSEDI into your lifestyle.

## Table of contents



## Important contact information

Keep a record of important phone numbers below should any questions or concerns arise.

Nurse Case Manager: _____

Doctor's office: _____

Lab monitoring: _____

Lab technician: _____

Specialty pharmacy: _____

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Not an actual patient.

# About this disease

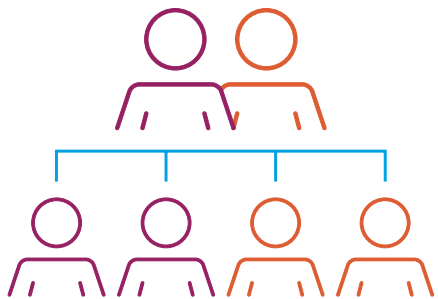
# Hereditary ATTR amyloidosis is a rare genetic disease that worsens over time

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

- This mutation causes TTR proteins to clump together into clusters
- Clusters of TTR proteins are called “amyloid”
- Amyloid builds up in the body and damages tissues and organs

## This disease is passed down through family members

A parent who has hereditary ATTR amyloidosis has a 50% chance of passing the gene mutation on to his or her child. It is important for people with hereditary ATTR amyloidosis to talk openly with their families about it. You may want to speak with a doctor together to learn about your condition and consider genetic testing as a family.



**Key**

Carries the gene mutation for hereditary ATTR amyloidosis

Does not carry the gene mutation for hereditary ATTR amyloidosis

hATTR Compass™
Map Your Genetic Journey

For more information about hereditary ATTR amyloidosis or genetic testing, call **1-800-GENE-MATTERS** (1-800-436-3628) or visit **hattrcompass.com**.

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## Hereditary ATTR amyloidosis may cause polyneuropathy, or multiple types of nerve damage

**This could include**

- Nerve damage such as tingling, numbness, or pain in the hands and feet
- Difficulty walking
- Dizziness from low blood pressure
- Sexual dysfunction

## The disease may also affect other parts of the body

**Eyes**

- Eye floaters
- Glaucoma

**Kidneys**

- Kidney failure

**Wrists**

- Carpal tunnel syndrome

**Heart**

- Heart disease or heart failure
- Irregular heartbeat

**Stomach**

- Vomiting and feeling sick
- Diarrhea or constipation
- Unintended weight loss

**Not all patients with hereditary ATTR amyloidosis will experience all of these symptoms.**

# Polyneuropathy progresses over time

Nerve damage can occur as tingling, numbness, or pain. It can make daily tasks—such as fastening buttons, turning a key in a lock, or walking—more difficult over time.

- In one study of people with hereditary ATTR amyloidosis, those who had polyneuropathy experienced more pain and showed more signs of depression and anxiety than those who did not have polyneuropathy

Nerve damage may worsen over time. These symptoms can advance quickly, but there are treatment choices available.

**It is important to get treatment for nerve damage from hereditary ATTR amyloidosis as soon as possible.**

## IMPORTANT SAFETY INFORMATION

**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)

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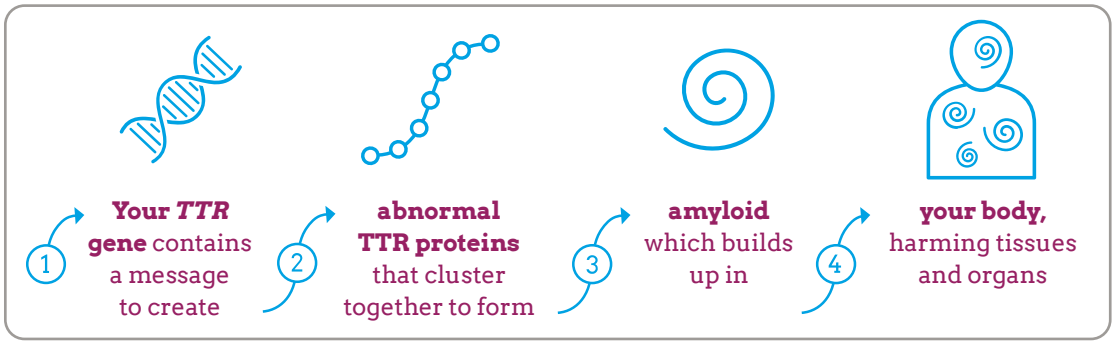
Tegsedi® (inotersen) injection 284 mg/1.5 mL

# How TEGSEDI® (inotersen) works

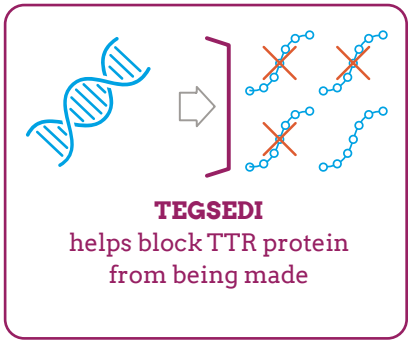
## In patients with nerve damage, TEGSEDI targets the disease at its source

Not actual patients.

## Before TEGSEDI




## With TEGSEDI




Nerve damage from hereditary ATTR amyloidosis results from amyloid buildup damaging organs and tissues. Amyloid is made up of clusters of the TTR protein. TEGSEDI prevents the creation of TTR proteins, reducing the amount of amyloid that builds up.

- In the NEURO-TTR clinical study, people who received TEGSEDI experienced significant reductions in TTR protein levels

**TEGSEDI significantly reduced the production of TTR protein**

**75%-79%** less TTR protein

## 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

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Not actual patients.

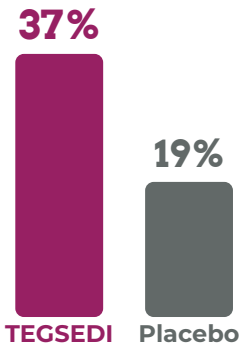
# Results with TEGSEDI® (inotersen)

## In the NEURO-TTR clinical study, some people saw improvements in symptoms

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 adults) or placebo (no treatment [60 adults]) 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

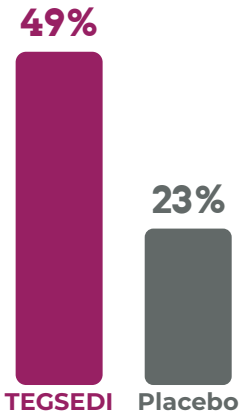
# At 66 weeks, patients treated with TEGSEDI experienced the following benefits vs those treated with placebo




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.

On average, patients receiving TEGSEDI were already showing significant improvements at 8 months compared with patients who did not receive treatment based on 2 instruments that measure how much better or worse your nerve pain and quality of life become. In general, success will mean slowing disease progression.

## 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.**

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Not actual patients.

# Safety and potential side effects

***Please see 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.***

## 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
- Flu-like symptoms were also common and included general flu-like illness and fever in combination with at least 2 of the following: chills, muscle pain, and/or joint pain. These side effects tended to occur after the initial injections and became less frequent over time
- Please speak with your doctor to find out if there are options to alleviate these symptoms. While not everyone will experience these side effects, your doctor can help you create a plan to manage them if they occur

## Your doctor should tell you to take a vitamin A supplement while using TEGSEDI

- TEGSEDI can lower the vitamin A levels in your blood
- Your doctor will tell you how much supplemental vitamin A to take each day; only take the amount they tell you to take
- Call your doctor if you get eye problems, such as difficulty seeing at night or in low-lit areas (night blindness)

## TEGSEDI may cause serious allergic reactions

- 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

Tegsedi® (inotersen) injection 284 mg/1.5 mL

Not an actual patient.

# How to use TEGSEDI® (inotersen)

**You choose when and where to take your weekly TEGSEDI injection—decide for yourself how TEGSEDI will become part of your routine**

## TEGSEDI is an injection you have the independence to administer 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
- You have the choice of injecting yourself or having a caregiver or doctor help you
- You do not need to take TEGSEDI in a hospital or a doctor's office—you can take the injection anywhere
- TEGSEDI should be refrigerated, but can be stored for up to 6 weeks at room temperature

## You can decide how TEGSEDI fits into your routine and your lifestyle

- Take your TEGSEDI injection at the same time every week
- Receive lab monitoring every week, or as your doctor has instructed
- Consider choosing an event that usually happens at the same time every week to help you remember when to take your injection and when to receive blood and urine tests (such as a family dinner, religious service, or weekly appointment)

## IMPORTANT SAFETY INFORMATION (CONT'D)

**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

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Tegsedi® (inotersen) injection 284 mg/1.5 mL

Actual patient.

# Your guide to lab monitoring

## Regular monitoring can help protect your health

### Blood tests

You will need to take a blood test once every 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.

The guide on the next page will help you navigate the lab monitoring process.

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

# How lab monitoring works and why it's necessary

## How do the tests work?

Before starting treatment, you will be asked to provide blood and urine samples to assess and monitor your platelet count and liver and kidney function. You will also need to provide these samples at regular intervals while you are on treatment.

## Where do I go to get tested?

The AKCEA® CONNECT team is committed to helping you design a testing routine that works for your schedule and lifestyle. The AKCEA CONNECT Lab Monitoring Program, in partnership with Quest Diagnostics, can schedule your tests at one of more than 2200 Quest locations nationwide. Your tests can also be scheduled at a location more convenient to you, such as your home or office, with the option of mobile phlebotomy.

## How do I get started?

Your AKCEA CONNECT Nurse Case Manager will work with Quest to enroll you in the system and ensure a smooth start to testing.

## Do I have to pay for my tests?

Once you are enrolled in AKCEA CONNECT and the Quest system, your testing will be free of charge. Your insurance will not be billed if your doctor orders your test through Quest as part of your treatment monitoring program.

## How do I find out the results of my tests?

Your doctor will receive the results of your lab tests. If an abnormal value is found, your doctor will be notified immediately. You can also access your own test results by enrolling in the secure Quest website (myquest.com) or via the MyQuest mobile app. By signing up online, you will have access to your test results 24 hours a day, 7 days a week.

AKCEA® CONNECT



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Tegsedi® (inotersen) injection 284 mg/1.5 mL

# Build your TEGSEDI® (inotersen) routine

## Take an active role in your care with TEGSEDI

You play an important role in your own healthcare—you can help ensure your treatment is managed.

**Know what to expect:** Your doctor 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. Monitoring will include tests 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).

**Know what to do:** Because monitoring is essential, make a plan to receive regular lab monitoring. Track your treatment over time to give your doctors information about your progress with TEGSEDI.

## Here is a list of things you need to do to prepare for your treatment

1. **Enroll in AKCEA CONNECT and learn about TEGSEDI**
   Once you're enrolled, your AKCEA CONNECT Nurse Case Manager will contact you within 24 hours. She/he will explain the AKCEA CONNECT programs and services that are available to you. After that, review all the materials in this Welcome to TEGSEDI kit. Reach out to your doctor or Nurse Case Manager with any questions.
2. **Have your platelet count and kidney and liver function checked**
   Before your first injection with TEGSEDI, your Nurse Case Manager will coordinate your first blood draw and urine test to check your platelet count and kidney and liver function.
3. **Receive your medicine in the mail**
   Once your insurance has been confirmed, which may take a few weeks, the specialty pharmacy provider will send your first shipment of TEGSEDI.

**4** **Receive injection training and practice proper technique**

TEGSEDI is a once weekly injection that you can administer yourself, giving you the flexibility to incorporate treatment into your lifestyle. Your Nurse Case Manager will contact you to schedule in-person injection training and support for you and your caregiver. This personalized training will help you learn how to properly inject TEGSEDI.

**5** **Work with your doctor to plan for and manage side effects**

After starting TEGSEDI, you may experience injection site reactions and flu-like symptoms. These side effects tended to occur after the initial injection and became less frequent over time. Your doctor can help you create a plan to manage these symptoms if they occur. Some patients in clinical trials experienced low platelet counts (thrombocytopenia) or kidney inflammation (glomerulonephritis). In these cases, additional monitoring, a pause in treatment, or stopping treatment altogether may be needed.

**6** **Perform your first injection**

With confidence from your injection training, you are now ready to perform your first injection of TEGSEDI.

**7** **Create your schedule for regular injections and lab monitoring**

Work with your doctor and Nurse Case Manager to design a TEGSEDI treatment and lab monitoring routine that works for your schedule and lifestyle.



## 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

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Tegsedi® (inotersen) injection 284 mg/1.5 mL

# Support from AKCEA CONNECT

Not actual patients.

# The AKCEA CONNECT patient support program can help empower you to keep living life on your own terms

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 help you feel empowered in your healthcare.

## KNOWLEDGE

We share disease and treatment knowledge with you, your caregiver, and your family.

## ACCESS

We provide assistance with insurance coverage assessment and funding questions.

## EMPOWERMENT

We can connect you with resources and patient support groups to help you manage your disease while continuing to live a meaningful life.

AKCEA® CONNECT

**Get support from AKCEA CONNECT at akceaconnect.com or 1-866-AKCEATX (1-866-252-3289).**



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Tegsedi® (inotersen) injection 284 mg/1.5 mL

# Speak with a peer mentor

## Caring mentors living with the polyneuropathy of hereditary ATTR amyloidosis are ready to help

Mentors who've had similar experiences living with polyneuropathy of hereditary ATTR amyloidosis and taking TEGSEDI® are ready to share their experiences, what they've learned, and how TEGSEDI fits into their lifestyle.

AKCEA® CONNECT

**To participate, please contact your AKCEA CONNECT Nurse Case Manager (NCM) at 1-866-AKCEATX.**

### Mentors are available to discuss topics such as

- Emotions and experiences with starting TEGSEDI
- Personal experiences living with the polyneuropathy of hereditary ATTR amyloidosis
- Lifestyle tips
- Finding support and available resources

### Mentors cannot discuss topics such as

- Treatment with other therapies
- Effect of treatment with TEGSEDI
- Medical advice

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## How it works

1. Contact your AKCEA CONNECT Nurse Case Manager and let them know you're interested in speaking with a mentor living with polyneuropathy of hereditary ATTR amyloidosis and taking TEGSEDI.
2. Your Nurse Case Manager will transfer you to a Team TEGSEDI representative where you will be able to register for the program.
3. During the registration process, you will be matched with a mentor who is the best fit for you, and your first call with your mentor will be scheduled by your Nurse Case Manager.
4. After registering, you will receive a confirmation email with all of the details for your first mentor call.
5. One to two days prior to your scheduled call, you will receive a reminder via phone and email.
6. After your first call, your Nurse Case Manager can help schedule up to 2 additional calls with your mentor.

### AKCEA CONNECT is here to help

Our support program is staffed by a team of dedicated Nurse Case Managers who are here to assist you and your family or caregiver. AKCEA CONNECT can help with many aspects of managing your disease and treatment with TEGSEDI. Whether you are looking for educational materials or are struggling with your routine, need help navigating insurance and funding, or want to make connections in the hereditary ATTR amyloidosis community, we are here to help every step of the way. Learn more at **AkceaConnect.com** or call **1-866-AKCEATX** (1-866-252-3289).

## 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.

**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.

**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 effects 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 and WARNINGS about Low Platelet Counts and Kidney Inflammation, in pocket.***

Actual patient
and his caregiver.

# TEGSEDI® (inotersen): A treatment for the polyneuropathy of hereditary ATTR amyloidosis in adults that may fit your lifestyle

- With TEGSEDI, some people saw improvements in symptoms
- TEGSEDI is a once-weekly injection you have the independence to administer yourself
- Confidently monitor your health with regular blood and urine tests—this can help detect serious side effects
- With TEGSEDI as a part of your routine, you can get back to focusing on what matters most to you

**"You've given me my quality of life back—you've given my family their father, their brother, their grandpa back, and in a good mood. That wouldn't happen without TEGSEDI."**

**Chuck,** living with the polyneuropathy of hereditary ATTR amyloidosis and taking TEGSEDI

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AKCEA THERAPEUTICS



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