Getting started with your PrTEGSEDI™ treatment

AKCEA™ THERAPEUTICS CANADA

Pr Tegsedi™ (inotersen) injection 284 mg/1.5 mL

Your guide to TEGSEDI™

You have been given this booklet because you have been diagnosed with hereditary transthyretin amyloidosis (hATTR) and prescribed with TEGSEDI™ to treat stage 1 or 2 polyneuropathy. This booklet contains information about your disease condition and TEGSEDI™.

TEGSEDI™ is used for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR.

The information provided in this booklet is not meant to take the place of speaking with your healthcare professional or the advice given to you by your healthcare team. However, this booklet will provide you with resources that can help you access hATTR disease information. If you have questions after reading this booklet, please discuss them with your healthcare professional.

AKCEA CONNECT™
SUPPORT PROGRAM

Akcea Therapeutics Canada is proud to offer its complimentary Akcea Connect™ Patient Support Program, which provides various resources to help assist you during your treatment journey. The goal of the program is to help you feel empowered about your healthcare through education.

You can contact the Akcea Connect™ Patient Support Program at:

1-833-327-0723

support@akceaconnect.ca

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What is hATTR?

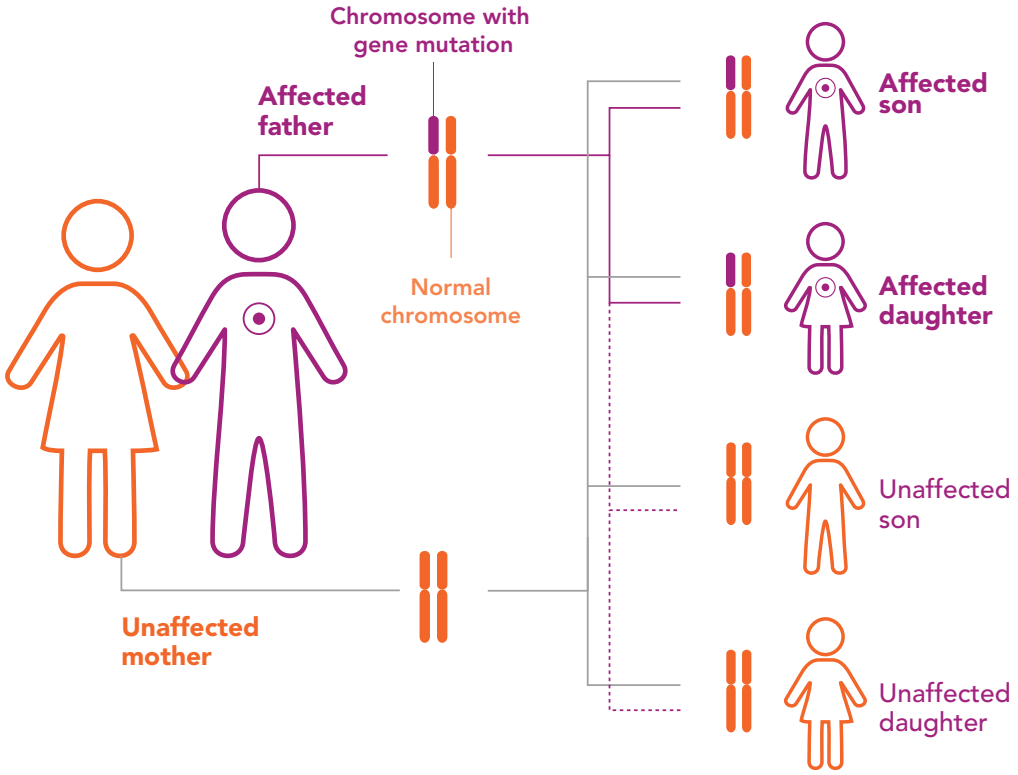
In hATTR, a change or mutation in the gene alters the structure of a protein in your body called TTR. This causes the TTR protein to fold into an unusual shape or clump together and build up in the body. This buildup of TTR protein can stop the organs in your body from working properly.

Why do I have hATTR?

hATTR is inherited in an autosomal dominant pattern.

- One copy of the altered gene in each cell is sufficient to cause the disorder.
- In most cases, an affected person inherits the mutation from one affected parent.

Autosomal dominant inheritance example

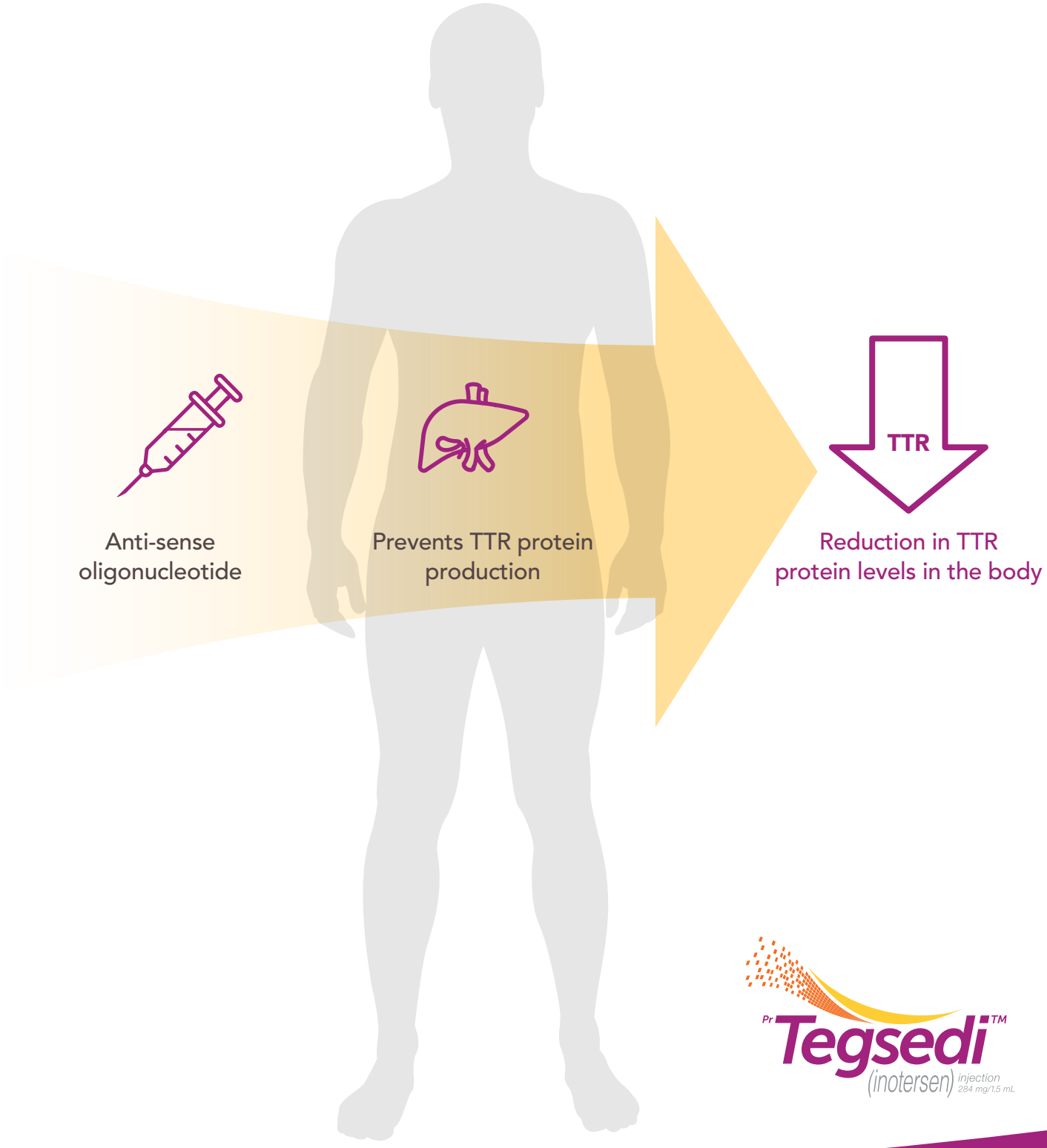


Your doctor may have used genetic testing to confirm your diagnosis. This will also help determine your risk of passing this genetic disorder on to your children.

How TEGSEDI™ works

TEGSEDI™ belongs to a group of medicines called **anti-sense oligonucleotides**.

It helps to reduce the levels of TTR proteins in the body by **preventing TTR production** by the liver.



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How to administer TEGSEDI™

Before first using TEGSEDI™, your healthcare provider should show you or your caregiver how to use it the right way. If you or your caregiver have any questions, ask your healthcare provider. Read the instructions for use included in the Patient. Medication Information section of the TEGSEDI™ Product Monograph before you start using your TEGSEDI™ prefilled syringe and each time you get a repeat prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

The TEGSEDI™ syringe

- Each TEGSEDI™ prefilled syringe has a Safety Syringe Device (SSD).
- The prefilled syringe delivers one dose (284 mg inotersen/1.5 mL per syringe) of TEGSEDI™ and is for one-time use only.
- TEGSEDI™ is given as an injection just below the skin once a week on the lower part of the belly area, outer area of the upper arm or front of the thigh. If injected in the upper arm, the injection should be administered by a caregiver. Choose the same day of the week to have your dose. It is important to rotate injection sites. Select a different spot each time you inject TEGSEDI™. Your doctor may change how often you inject your dose depending on the results of your platelet count. Your doctor will recommend taking vitamin A while on TEGSEDI™.

Injecting TEGSEDI™

Please refer to the TEGSEDI™ Step-by-Step Injection Guide and the Patient Medication Information leaflet that came with your medication for detailed instructions on injecting TEGSEDI™.

The Akcea Connect™ Patient Support Program offers injection training and administration support services in your home or through a specialty clinic network. Before using TEGSEDI™, your healthcare provider should show you or your caregiver how to use it the right way.

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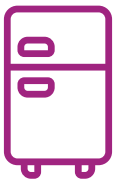
Storing TEGSEDI™

2°C to 30°C

- TEGSEDI™ may be stored unrefrigerated (2°C to 30°C) in the original container for up to 6 weeks.
  - If not used within the 6 weeks, throw TEGSEDI™ away.



- Store TEGSEDI™ in the refrigerator at 2°C to 8°C in the original container and protect from light.

30 minutes

- Let TEGSEDI™ warm up at room temperature (20°C to 25°C) for at least 30 minutes before giving the injection.
  - Other warming methods should **NOT** be used (for example, do not warm in a microwave, or hot water or near other heat sources).

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Proper use of TEGSEDI™

Do not use TEGSEDI™ if:

- You are allergic to inotersen or to any ingredient in the formulation
- Your blood platelet count is below 100 x 10^9/L
- You have a protein to creatinine ratio (UPCR) of equal to or greater than 113 mg/mmol
- Your estimated glomerular filtration rate (eGFR) is less than 45 mL/min/1.73m^2
- You suffer from severe liver disease

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TEGSEDI™. Talk about any health conditions or problems you may have, including if:

- Your blood platelet count is low. Some symptoms of low platelet count are:
  - Easy or unexplained bruising
  - Prolonged bleeding from cuts
  - Blood in urine or stools
  - Bleeding from your gums and nose
  - Bleeding into the skin that appears as a rash of red spots
- You take blood thinners or medications that may lower the platelet count such as acetylsalicylic acid or warfarin
- You had severe bleeding in the past
- You are 65 years or older
- You suffer from kidney damage
- You take any medication that may damage your kidney function, such as some pain killers (opioids)
- You are breast-feeding

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Serious warnings and precautions

TEGSEDI™ can lower the platelet count in your blood. Some patients taking TEGSEDI™ have also developed glomerulonephritis. This is a condition where your kidneys do not work properly. Therefore, before you start TEGSEDI™ and while you are using it, you will need regular blood and urine tests done by a medical lab or field nurse for your doctor to assess the effects of TEGSEDI™ on your platelet counts and kidneys. Please continue reading for more information on decreased platelet count, glomerulonephritis and the frequency of laboratory tests.

Decreased platelet count (thrombocytopenia):

TEGSEDI™ can lower the platelet count in your blood. Your doctor should monitor you every 2 weeks while you are taking TEGSEDI™ and for 8 weeks after you stop taking it. This is especially important if you are elderly (since you may be at a greater risk of bleeding), or taking medicines to prevent the formation of blood clots or platelets or those that lower your platelet count.

If you experience or notice:

- unusual or prolonged bleeding (such as a rash of red spots on your skin, spontaneous bruising or bleeding in your eye)
- stiffness in your neck or
- an unusual severe headache

Call your doctor right away.

Tell your doctor before you take TEGSEDI™ if you take blood thinners or medications that may lower the platelet count such as acetylsalicylic acid and warfarin.

Glomerulonephritis/kidney problems:

It is important to know that treatment with TEGSEDI™ may cause glomerulonephritis (kidney inflammation), which is a condition where your kidneys do not work properly. Your doctor will check how well your kidneys are working before you start TEGSEDI™, regularly while you are taking TEGSEDI™, and for 8 weeks after you stop taking it.

Symptoms of glomerulonephritis are:

- Foaming urine
- Pink or brown coloured urine
- Blood in the urine
- Passing less urine than usual

Some patients taking TEGSEDI™ have also developed a decline in how well their kidneys are working without having had glomerulonephritis.

Tell your doctor if you are taking any medicines that damage the kidneys or affect kidney function, for example sulfonamides, aldosterone antagonists and some types of painkillers.

TEGSEDI™ and laboratory monitoring

Before you start TEGSEDI™ and while you are using it, your doctor will perform laboratory tests to assess the effects of TEGSEDI™ on your platelet count, kidneys and liver (see below).

How often do I need to do my laboratory monitoring?

Please use this summary table to understand the recommended laboratory monitoring during TEGSEDI™ treatment.

		Prior to starting treatment	During treatment
	**Blood tests to check platelet count**	✓	**Every 2 weeks** **or more often if needed,** and continue for 8 weeks after stopping TEGSEDI™
	**Blood and urine tests to check kidneys**	✓	**Every 3 months** **or more often if needed** as clinically indicated, based on a history of kidney disease and/or renal amyloidosis, and for 8 weeks after stopping TEGSEDI™
	**Blood tests to check liver**	✓	**4 months after treatment** and once per year thereafter

Patients with protein to creatinine ratio (UPCR) ≥ twice the upper limit of normal, or estimated glomerular filtration rate (eGFR) < 60 ml/min, which is confirmed on repeat testing and in the absence of an alternative explanation should be monitored every 4 weeks or more often.

Make your lab appointments one of your priorities. Regular lab monitoring is an important part of your TEGSEDI™ treatment.

Your Akcea Connect™ Patient Support Program offers blood draw and urine testing services in your home or through a specialty clinic network. The results are directly communicated to your doctor.

TEGSEDI™ may lower the level of vitamin A in your body

If you experience symptoms of low vitamin A before starting TEGSEDI™, your doctor will recommend you take a vitamin A supplement. Once your symptoms are gone, your doctor will start you on TEGSEDI™.

TEGSEDI™ may decrease the levels of vitamin A in your body and you may need to take a vitamin A supplement while on it. Your doctor will tell you the correct dose of vitamin A for you.

Look out for the symptoms of low vitamin A, which include:

- Dry eyes
- Decreased night vision
- Poor vision
- Hazy or cloudy vision

Talk to your doctor right away if you are pregnant, think you may be pregnant or are planning to become pregnant. TEGSEDI™ may affect your levels of vitamin A and low or high levels of vitamin A can harm the baby. If you are of child-bearing age, you should use a contraceptive method while on this treatment.

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Possible side effects of TEGSEDI™

These are not all the possible side effects you may feel when taking TEGSEDI™. If you experience any side effects not listed here, contact your healthcare professional. Be sure to plan with your doctor on suggestions on how to manage the side effects, before you start your treatment with TEGSEDI™. For a complete list of side effects, please consult the Patient Medication Information section of the TEGSEDI™ Product Monograph.

Very common side effects include the following:

- Thrombocytopenia (low levels of platelets which are blood cells that help your body form clots to stop bleeding)
- Anaemia (reduction in red blood cells which can make the skin pale and cause weakness or breathlessness)
- Vomiting or nausea
- Diarrhoea
- Constipation
- Injection site erythema (redness around the injection site), injection site pruritus (injection site itching) or injection site pain
- Fatigue
- Oedema peripheral (swelling of the ankles, feet or fingers)
- Pyrexia (increase in body temperature)
- Chills (feeling cold)
- Myalgia (muscle aches/pain) or arthralgia (joint pain)
- Headache

Common side effects include the following:

- Eosinophilia (an increase in the number of white blood cells called eosinophils in your blood which help fight infection)
- Chest pain or heart disorders, such as atrial fibrillation (an irregular heart beat that may increase your risk of stroke, or heart-related complications) or congestive cardiac failure (a condition in which the heart does not pump blood as effectively as it should, often associated with shortness of breath, weakness and swelling of the legs and ankles)
- Balance disorder, or vertigo (feelings of spinning or being off balance or unsteady)
- Hypothyroidism (low level of thyroid hormone which can cause fatigue, feeling cold, weight gain and poor memory and concentration)
- Eye disorders, such as cataracts (clouding of the eye lens which can lead to decreased vision), ocular hyperaemia (white part of the eye is bloodshot) or vitreous floaters (visual spots that resemble grey or black specks and can drift across the eyes)
- Dry mouth
- Abdominal distension (swelling or bloating of the belly)
- Gastroesophageal reflux disease (this occurs when acid in the stomach flows back into the food pipe causing heartburn)
- Flu like symptoms such as high temperature, aches and chills
- Peripheral swelling (swelling of the lower legs or hands)
- Injection site reaction (inflammation or damage to the tissue around the injection site), injection site bruising, swelling, discolouration, rash, haemorrhage (excessive bleeding from the injection site) haematoma (a solid swelling of clotted blood at the injection site) or induration (hardening of the area around the injection site)
- Upper respiratory tract infection (infection in the mouth, nose, throat or voice box)
- Asymptomatic bacteriuria (the presence of bacteria in the urine that does not cause symptoms)

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Common side effects (continued)

- Skin infection, abrasion or lesion (scrape, graze, abnormal lump, or sore on the skin)
- Localized infection (an infection that affects a specific part of the body or organ)
- Gastroenteritis viral (infection in the stomach and intestines caused by a virus. Symptoms may include diarrhea, cramps and vomiting)
- Contusion (bruise)
- Limb injury
- Platelet count decreased (decrease in platelets which are blood cells that help your body form clots to stop bleeding)
- Changes to your blood and urine tests (this may indicate infection or liver or kidney damage)

These are not all the common side effects of TEGSEDI™. Please consult the Patient Medication Information leaflet that came with your medication for more information.

Serious allergic reaction (symptoms such as swelling of the face, lip or throat, rash, itchiness, hives, difficulty breathing or wheezing) can occur (frequency unknown). Stop taking TEGSEDI™ and seek immediate medical help if you experience these symptoms.

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AKCEA CONNECT™ * SUPPORT PROGRAM

Our ongoing commitment to Canadians on TEGSEDI™

The Akcea Connect™ Patient Support Program is a complimentary support program offered by Akcea Therapeutics Canada to assist patients on TEGSEDI™. Akcea Connect™ is committed to helping support patients, their families, and their healthcare team.

A dedicated Nurse Case Manager who has extensive clinical knowledge and funding expertise is available in Canada to provide ongoing support to patients, caregivers and healthcare providers.

* The Akcea Connect™ Patient Support Program is sponsored by Akcea Therapeutics Canada and administered through its third-party provider, Innomar Strategies™. The program administrator is required to collect, use and store your personal information in accordance with applicable privacy laws.

Akcea Connect™ is here to help

As part of ongoing commitment, Akcea Connect™ is proud to offer the following personalized resources to help assist you on your treatment journey.

Education

Offering comprehensive education, resources and navigation support services specific to hATTR and TEGSEDI™.

Injection training & administration support

Offering injection training and administration support services in your home or through a specialty clinic network. Before using TEGSEDI™, your healthcare provider should show you or your caregiver how to use it the right way. If you or your caregiver have any questions, ask your healthcare provider.

Blood draw & urine testing services

Offered in your home or through a specialty clinic network.

- Results are communicated directly to your healthcare provider.

Pharmacy services

Coordinating the dispense and delivery of TEGSEDI™ through a dedicated pharmacy network or your preferred pharmacy.

Patient support calls

If you request it, you will receive regular support calls to answer your questions and to remind you to continue taking TEGSEDI™ as prescribed.

Reimbursement navigation

Assessing your coverage options and facilitating payer coverage requirements.

Financial assistance

Investigating reimbursement options and eligibility for financial assistance for you.

While hATTR is a rare disease, you are not alone. Our program is meant for anyone with hATTR that is taking TEGSEDI™ and is enrolled in the Akcea Connect™ Patient Support Program.

How to contact Akcea Connect™ Patient Support Program

AKCEA CONNECT™
SUPPORT PROGRAM

Bilingual support is available

Monday-Friday 8am-8pm EST, excluding holidays.

Translation services in over 200 languages are available upon request.

1-833-327-0723

support@akceaconnect.ca

Available resources for Canadians with hATTR

The Canadian Amyloidosis Support Network
www.thecasn.org

Canadian Organization for Rare Disorders
www.raredisorders.ca

Orphanet (Canada Page)
www.orpha.net/national/CA-EN/index/homepage/

Regroupement québécois des maladies orphelines (RQMO)
https://rqmo.org

Please consult the Patient Medication Information leaflet that came with your medication for more information on TEGSEDI™. This leaflet is only a summary and will not tell you everything about this drug. Talk to your healthcare providers about your medical condition and treatment and ask if there is any new information about TEGSEDI™.

Also, this booklet is not meant to replace the advice of your doctor. For any additional information regarding your treatment or condition, speak with your healthcare providers.

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