FACTSHEET

Amyloidosis Research Consortium

Tegsedi™ (Inotersen)

What is Tegsedi?

Tegsedi is a drug that has been licensed for the treatment of patients with nerve damage (polyneuropathy) due to hereditary ATTR (hATTR) amyloidosis. hATTR amyloidosis is a genetic disease which causes the build-up of a protein called transthyretin in the tissues and organs of the body, stopping them from working properly. Transthyretin – or TTR for short – is produced mainly in the liver. Its usual job is to transport the hormone thyroxine and retinol (vitamin A) around the bloodstream.

How does Tegsedi work?

Tegsedi has been designed to reduce the production of TTR protein in the liver. It belongs to a group of drugs called RNA interference (RNAi) drugs. RNAi drugs aim to prevent the production of disease-causing proteins in the body by blocking the instructions of a gene. For this reason they are also referred to as gene silencing drugs.

Genes are made up of DNA and contain the information needed to make proteins. The journey from gene to protein is complex and tightly controlled within the cell. The target for Tegsedi is a molecule called RNA (ribonucleic acid), which is present in almost all living cells. The main role of RNA is to act as a messenger – it carries instructions from a gene's DNA to the cell's machinery responsibe for making proteins. These instructions are then used by the cell to make a protein.

Tegsedi attaches to and blocks RNA in liver cells, meaning the cells do not receive instructions to make more TTR protein. This reduces the amount of TTR protein being made in the liver, entering the bloodstream and depositing in the tissues and organs of the body.

How is Tegsedi taken?

Tegsedi is given by subcutaneous (under the skin) injections in the stomach (abdomen), thigh or upper arm. The recommended dose is 284 mg, which comes in a 1.5 ml syringe, once a week. Treatment carries on for as long as a patient continues to benefit from it. Patients will be supported to self-administer the injections at home rather than having to go into the hospital to be given it.

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Clinical trial evidence for Tegsedi

The Phase III NEURO-TTR trial compared Tegsedi to a placebo (inactive drug) in 172 hATTR amyloidosis patients with stae 1 or 2 polyneuropathy for 15 months. Results from the trial showed that, compared with those on placebo, patients on Tegsedi:

- saw statistically significant improvements in their symptoms of neuropathy
- saw statistically significant improvements in quality of life

Side effects of Tegsedi

Like all drugs, Tegsedi can cause side effects. The most commonly observed side effects of Tegsedi in patients on the Phase III NEURO-TTR trial were reactions at the site of the injections (e.g. pain, swelling, redness), nausea, anemia (which can cause fatigue and breathlessness), headache, fever, vomiting, low platelet counts (also known as thrombocytopenia, which can cause increased bleeding and bruising), and inflammation of the kidney (glomerulonephritis). There are other more rare, but potentially serious, side effects which should be discussed with your doctor.

Patients taking Tegsedi will have routine monitoring of blood and urine samples to evaluate and manage side effects. Patients will have their platelet levels checked every week, markers of kidney function monitored every other week, and markers of liver function monitored every 4 months. Tegsedi can lower the body's levels of vitamin A so patients will be asked by their doctor to take a daily vitamin A supplement during treatment.

Availability of Tegsedi

Tegsedi was approved by the FDA on October 5, 2018 for the treatment of hATTR amyloidosis polyneuropathy in the United States. However, Tegsedi may still not be available while the drug company gets it ready for commercialization. Once ready for market, you or a loved one who has hATTR polyneuropathy will be able to ask your physician to prescribe it.

Insurance coverage of Tegsedi will vary depending on the particular plan. If your insurance does not provide enough coverage, there are additional programs that may be able to help with the cost. These include co-pay assistance and other programs by the pharmaceutical company, Akcea. Learn more about Akcea's assistance programs through the following link: https://akceaconnect.com/

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More information

Tegsedi For more information you can visit us a www.arci.org or Akcea's website www.akceatx.com. If you have further questions you can contact us by phone at 617-467-5170 or by email at arc@arci.org.