EMA/381704/2018
EMEA/H/C/004782

Tegsedi (*inotersen*)

An overview of Tegsedi and why it is authorised in the EU

What is Tegsedi and what is it used for?

Tegsedi is a medicine used to treat nerve damage caused by hereditary transthyretin amyloidosis (hATTR), a disease in which proteins called amyloids build up in tissues around the body including around the nerves.

Tegsedi is used in adult patients in the first two stages of the nerve damage (stage 1, when the patient is able to walk unaided, and stage 2, when the patient can still walk but needs help).

hATTR is rare, and Tegsedi was designated an 'orphan medicine' (a medicine used in rare diseases) on 26 March 2014. Further information on the orphan designation can be found here: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

How is Tegsedi used?

Tegsedi can only be obtained with a prescription and treatment should be started and supervised by a doctor experienced in the treatment of patients with hATTR.

The medicine is available as a solution for injection under the skin in pre-filled syringes (284 mg). The recommended dose is one injection once a week, given under the skin in the belly, upper thigh or upper arm. The first injection should be given under the supervision of a qualified healthcare professional, and patients or carers can give the subsequent injections after receiving appropriate training.

As Tegsedi can cause a reduction in the number of platelets in the blood (posing a risk of bleeding), blood platelet counts need to be monitored during treatment with Tegsedi, and the dose of the medicine and how often it is given adjusted accordingly.

For more information about using Tegsedi, see the package leaflet or contact your doctor or pharmacist.

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How does Tegsedi work?

In patients with hATTR, a protein called transthyretin which circulates in the blood is defective and breaks easily. The broken protein forms amyloid deposits in tissues and organs around the body, including around nerves, where it interferes with their normal functions.

The active substance in Tegsedi, inotersen, is an 'antisense oligonucleotide', a very short piece of synthetic genetic material that has been designed to attach to and block the genetic material of the cell responsible for producing transthyretin. This reduces production of transthyretin, thereby reducing the formation of amyloids and relieving the symptoms of hATTR amyloidosis.

What benefits of Tegsedi have been shown in studies?

In one main study involving 173 hATTR patients with stage 1 or 2 nerve damage, Tegsedi was shown to be more effective than placebo (a dummy treatment) at slowing down the nerve damage caused by the disease. The main measures of effectiveness were the changes in the patients' nerve damage and quality of life, as measured using standard scales called 'mNIS+7' and 'Norfolk QoL-DN' respectively. After 15 months of treatment, the mNIS+7 score, used for assessing nerve damage, worsened by a lesser extent with Tegsedi (around 11 points) than with placebo (around 25 points). Quality of life, measured by the Norfolk QoL-DN score, worsened by around 4 points in patients treated with Tegsedi, compared with around 13 points in those on placebo.

What are the risks associated with Tegsedi?

The most common side effects with Tegsedi (which may affect more than 1 in 10 people) are reactions at the site of injection, nausea (feeling sick), low level of red blood cells, headache, fever, peripheral oedema (swelling, especially of the ankles and feet), chills, vomiting and low blood platelet counts which can lead to bleeding and bruising. For the full list of side effects of Tegsedi, see the package leaflet.

Tegsedi must not be used by patients with low platelet counts (less than $100x10^9$/l), and by patients with severe kidney or liver problems. For the full list of restrictions, see the package leaflet.

Why is Tegsedi authorised in the EU?

Tegsedi was shown to be effective in the treatment of stage 1 or stage 2 nerve damage in patients with hATTR; available data were not sufficient to assume a beneficial effect in stage 3 patients (those confined to a wheelchair). In light of the unmet medical need, the safety profile of Tegsedi was considered acceptable and the risks to be manageable with specific monitoring, dose reduction and stopping rules.

The European Medicines Agency therefore decided that Tegsedi's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Tegsedi?

The company that markets Tegsedi will provide an alert card for patients with information about the safety of the medicine and how to manage side effects.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Tegsedi have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Tegsedi are continuously monitored. Side effects reported with Tegsedi are carefully evaluated and any necessary action taken to protect patients.

Other information about Tegsedi

Tegsedi received a marketing authorisation valid throughout the EU on 06 July 2018.

Further information on Tegsedi can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

This overview was last updated in 07-2018.