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Qalsody (*tofersen*)

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

What is Qalsody and what is it used for?

Qalsody is a medicine for treating adults with a type of amyotrophic lateral sclerosis (ALS) caused by a mutation (defect) in the gene responsible for producing an enzyme called superoxide dismutase 1 (SOD1). ALS is a progressive disease of the nervous system where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis.

ALS is rare, and Qalsody was designated an 'orphan medicine' (a medicine used in rare diseases) on 29 August 2016. ALS caused by a mutation in the *SOD1* gene represents about 2% of patients with ALS. Further information on the orphan designation can be found on the EMA website.

Qalsody contains the active substance tofersen.

How is Qalsody used?

Qalsody can only be obtained with a prescription. Treatment should only be started by a doctor with experience in the management of ALS.

Qalsody is delivered into the cerebrospinal fluid (fluid that surrounds the spinal cord and the brain) through an injection between the spinal bones in the lower back (intrathecal injection).

The treatment starts with 3 doses given 2 weeks apart, followed by one dose every 4 weeks. The doctor will regularly review the need to continue treatment with Qalsody, based on the patients' symptoms and the response to the treatment.

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

How does Qalsody work?

In some patients with ALS, their condition is caused by a mutation in the gene responsible for producing the protein SOD1. Because of this mutation, the abnormal SOD1 protein in these patients is toxic to nerve cells, eventually causing the cells to die. Qalsody is made of a small strand of genetic material (called antisense oligonucleotide) made in a laboratory that binds to the SOD1 genetic material in the nerve cell and blocks the production of defective SOD1. By reducing the amount of

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defective SOD1, this medicine is expected to improve the symptoms of ALS caused by a mutation in the *SOD1* gene.

What benefits of Qalsody have been shown in studies?

In a main study involving patients with ALS associated with a mutation in the *SOD1* gene, 72 patients received Qalsody and 36 received placebo (a dummy treatment) for 28 weeks. The main measure of effectiveness was the rate at which a patient's disease symptoms worsened during the study. This was assessed using a standard rating scale known as 'ALS functional rating scale revised' (ALSFRS-R), which measures aspects of a patient's physical functioning, such as difficulty talking, breathing, eating and performing other normal daily activities. The total score ranges from 0 (no function) to 48 (normal function).

After 28 weeks, the ALSFRS-R score decreased by 4.5 points in patients who received Qalsody compared with 5.8 in patients who received placebo; however, this difference was not statistically significant, meaning that it could be due to chance.

Other measurements, in particular long-term data, indicated that Qalsody may slow down the course of the disease. In addition, results showed reductions in the levels of the SOD1 protein in patients who received Qalsody compared with those who received placebo, confirming the way the medicine is expected to work. There were also reductions in the levels of a protein called neurofilament light chain (NfL, an indicator of nerve damage), suggesting reduced nerve damage.

What are the risks associated with Qalsody?

For the full list of side effects and restrictions with Qalsody, see the package leaflet.

The most common side effects with Qalsody (which may affect more than 1 in 10 people) include pain in the back, arms, legs, muscles or joints, tiredness, increased levels of protein and/or white blood cells in the cerebrospinal fluid, and fever.

The most common serious side effects with Qalsody include myelitis (inflammation of the spinal cord), increased pressure around the brain, papilloedema (swelling of the nerve that connects the eyes with the brain), radiculitis (irritation and injury of nerve roots) and aseptic meningitis (inflammation of the lining around the brain and spinal cord).

Why is Qalsody authorised in the EU?

At the time of the authorisation of Qalsody, there were very limited treatment options for patients with ALS. Although the main results from a study in patients with ALS associated with a mutation in the *SOD1* gene failed to show an effect of the medicine after 28 weeks of treatment, other measurements confirmed the way the medicine is expected to work and indicated that Qalsody may slow down the course of the disease.

In terms of safety, Qalsody can have serious side effects involving the nervous system, such as inflammation of the spinal cord; however, these can be managed with appropriate treatment.

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

Qalsody has been authorised under 'exceptional circumstances'. This is because it has not been possible to obtain complete information about the medicine due to the rarity of the disease, and the form of ALS associated with a mutation in the SOD1 gene in particular, as this is only found in 2% of all patients with ALS.

The company marketing Qalsody must provide further data on the long-term safety and effectiveness of the medicine in patients with ALS associated with a mutation in the *SOD1* gene. It also has to investigate the effect of the medicine in patients who do not yet have symptoms. Patients treated with Qalsody must be followed in a registry and the company must provide data from this registry on a yearly basis.

Every year, the Agency will review any new information that becomes available on Qalsody.

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

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

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

Other information about Qalsody

Qalsody received a marketing authorisation under exceptional circumstances valid throughout the EU on 29 May 2024.

Further information on Qalsody can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/qalsody.

This overview was last updated in 05-2024.