EMA/583034/2023
EMEA/H/C/006084

Skyclarys (*omaveloxolone*)

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

What is Skyclarys and what is it used for?

Skyclarys is a medicine used in patients aged 16 years and older to treat Friedreich's ataxia, an inherited disease that causes damage to the nervous system, resulting in difficulties with coordination, balance and movement, fatigue, difficulty speaking, as well as an increased risk of cardiomyopathy (damage to the heart muscle) and diabetes.

Friedreich's ataxia is rare, and Skyclarys was designated an 'orphan medicine' (a medicine used in rare diseases) on 27 June 2018. Further information on the orphan designation can be found on the EMA website.

Skyclarys contains the active substance omaveloxolone.

How is Skyclarys used?

Skyclarys can only be obtained by 'special' prescription, which means it is used under stricter conditions than normal. The medicine should only be started and supervised by a doctor experienced in the treatment of patients with Friedrich's ataxia.

The medicine is available as capsules to be taken by mouth once daily. The dose may need to be reduced if the patient is taking other medicines called 'CYP3A inhibitors' that could interfere with the way Skyclarys is broken down in the body.

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

How does Skyclarys work?

It is not fully understood how the active substance in Skyclarys, omaveloxolone, works. However, it has been shown to activate the Nrf2 pathway, which helps cells to respond to oxidative stress (a condition that may occur when there are too many free radicals in the body and not enough antioxidants to get rid of them, which can lead to cell and tissue damage). NrF2 levels and activity appear to be reduced in patients with Friedreich's ataxia.

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What benefits of Skyclarys have been shown in studies?

In a main study involving 103 patients with Friedreich's ataxia aged between 16 and 40 years, Skyclarys was more effective than placebo (a dummy treatment) at reducing physical impairment after 48 weeks of treatment.

The modified Friedreich's ataxia rating scale (mFARS), which consists of a series of physical examination assessments, was used to assess the severity of the neurologic (having to do with nerves or the nervous system) symptoms of Friedreich's ataxia. If the mFARS score decreases, it means that there is a reduction in physical impairment.

Pes cavus is a foot deformity often seen as a complication of Friedreich's ataxia. Since there is no standardised method to classify the severity of pes cavus and due to the possible impact of the condition on the mFARS score, patients with pes cavus were not included in the primary analyses.

In 82 patients without pes cavus, those given Skyclarys had a reduction of around 1.6 in their mFARS score compared to an increase of around 0.9 in those who were given placebo.

The study also evaluated the impact of treatment on the patients FA-ADL score, a measure used to assess how well people with Friedrich's ataxia can carry out activities of daily living, such as getting dressed, bathing, and eating, with higher scores indicating greater levels of disability. Of the 82 patients without pes cavus, those given Skyclarys had a reduction of around 0.2 in their FA-ADL score compared to an increase of around 1.1 in those who were given placebo.

What are the risks associated with Skyclarys?

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

The most common side effects with Skyclarys (which may affect more than 1 in 10 people) include increased levels of liver enzymes (known as alanine transaminase and aspartate aminotransferase), headache, decrease in weight, feeling sick, vomiting, diarrhoea, feeling tired, mouth and throat pain, back pain, muscle spasms, flu and decreased appetite.

Why is Skyclarys authorised in the EU?

At the time of approval, there was a significant unmet medical need for patients with Friedreich's ataxia given that there were no other medicines authorised for the treatment of the disease. Skyclarys was shown to benefit patients with Friedreich's ataxia. Although there were uncertainties associated with the main study, such as the small number of patients, the exclusion of patients with severe forms of the disease (those with advanced heart disease and diabetes) and complications such as pes cavus (as defined in the study), the Agency considered that the benefits seen also applied to these patients. Overall, the safety profile of Skyclarys was considered manageable given that the side effects in the main study were generally mild to moderate in severity and mostly resolved within two months.

The European Medicines Agency therefore decided that Skyclarys'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 Skyclarys?

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

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

Other information about Skyclarys

Skyclarys received a marketing authorisation valid throughout the EU on 09 February 2024.

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

This overview was last updated in 02-2024.