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Epidyolex (*cannabidiol*)

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

What is Epidyolex and what is it used for?

Epidyolex is a medicine used in addition to clobazam, to treat patients from two years of age with Lennox-Gastaut syndrome or Dravet syndrome. It is also used to treat tuberous sclerosis complex (TSC) with other epilepsy treatments in patients also aged two and above. These are rare types of epilepsy that begin in childhood and can continue into adulthood. Symptoms of these conditions include multiple types of seizure (fits), abnormal electrical activity in the brain, learning disability and behavioural problems.

The conditions are rare, and Epidyolex was designated an 'orphan medicine' (a medicine used in rare diseases). Further information on the orphan designations can be found on the European Medicines Agency's website: ([Dravet syndrome](#): 15 October 2014; [Lennox-Gastaut syndrome](#): 20 March 2017; [tuberous sclerosis](#): 17 January 2018).

Epidyolex contains the active substance cannabidiol.

How is Epidyolex used?

Epidyolex can only be obtained with a prescription and treatment should be started and supervised by a doctor experienced in the treatment of epilepsy.

Epidyolex is available as a liquid containing 100 mg cannabidiol per ml. It should be taken consistently either with or without food. The recommended starting dose is 2.5 mg per kilogram body weight given twice a day. Doses are measured and given by mouth with a syringe supplied with the medicine. After one week, the dose should be increased to 5 mg/kg twice a day. Depending on the individual response and how well the medicine is tolerated, the doctor may increase the dose gradually up to a maximum of 10 mg/kg twice a day for Dravet and Lennox-Gastaut syndromes and 12.5 mg/kg twice a day for TSC. For more information about using Epidyolex, see the package leaflet or contact your doctor or pharmacist.

How does Epidyolex work?

Although the way it works is not clearly understood, the active substance in Epidyolex, cannabidiol, is thought to act on targets that play a role in the movement of calcium in the cells. As this is important for the transmission of electrical signals in some nerve cells, and seizures are caused by excessive

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electrical activity in the brain, altering the movement of calcium is expected to reduce or prevent the seizures in patients with Lennox-Gastaut syndrome, Dravet syndrome or TSC. Cannabidiol is also thought to act on adenosine, a chemical messenger in the brain that plays an important role in suppressing seizures.

What benefits of Epidyolex have been shown in studies?

Five studies in over 900 patients with Lennox-Gastaut syndrome, Dravet syndrome or TSC showed that Epidyolex lowered the number of seizures when added to treatment with other epilepsy medicines after 14 to 16 weeks of treatment.

In the first two studies, patients with Lennox-Gastaut syndrome taking Epidyolex in combination with clobazam had a reduction of up to 64% in the number of drop seizures (brief loss of muscle tone and reduced consciousness, causing abrupt falls), compared with a reduction of up to 31% for patients given placebo (a dummy treatment) with clobazam.

In another two studies in patients with Dravet syndrome, the reduction in the number of convulsive seizures (major fits with loss of consciousness) was up to 61% for patients taking Epidyolex and clobazam, and up to 38% for patients on placebo and clobazam.

In a fifth study, patients with TSC taking Epidyolex at maximum dose of 25/mg/kg/day had a reduction of 49% in the number of seizures compared with 27% in patients receiving a placebo.

What are the risks associated with Epidyolex?

The most common side effects with Epidyolex (which may affect more than 1 in 10 people) are somnolence (sleepiness), decreased appetite, diarrhoea, fever, tiredness and vomiting. The most common reason for stopping treatment was increased blood levels of liver enzymes (a sign of liver problems). For the full list of side effects of Epidyolex, see the package leaflet.

Epidyolex must not be used in patients whose blood levels of liver enzymes are more than three times the normal limit and who also have levels of bilirubin (another marker of liver problems) more than twice the normal limit. For the full list of restrictions, see the package leaflet.

Why is Epidyolex authorised in the EU?

The main studies showed that Epidyolex is effective at lowering the number of seizures in patients with Lennox-Gastaut syndrome, Dravet syndrome or TSC who are taking another epilepsy medicine. Regarding safety, treatment with Epidyolex is associated with an increased risk of liver problems. This risk can be managed with restrictions and regular liver monitoring and is considered acceptable given the seriousness of the conditions and the lack of treatments. The European Medicines Agency therefore decided that Epidyolex'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 Epidyolex?

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

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

Other information about Epidyolex

Epidyolex received a marketing authorisation valid throughout the EU on 19 September 2019.

Further information on Epidyolex can be found on the Agency's website:

ema.europa.eu/medicines/human/EPAR/epidyolex.

This overview was last updated in 03-2021.