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Xyrem (*sodium oxybate*)

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

What is Xyrem and what is it used for?

Xyrem is used to treat narcolepsy with cataplexy in adults, adolescents and children from 7 years of age.

Narcolepsy is a sleep disorder that causes excessive daytime sleepiness. Cataplexy is a symptom of narcolepsy involving sudden muscle weakness in response to an emotional reaction such as anger, fear, joy, laughter or surprise. Cataplexy can sometimes cause a patient to collapse.

Xyrem contains the active substance sodium oxybate.

How is Xyrem used?

Xyrem is an oral solution which is diluted in water to make up a drink. The patient should take a dose at bedtime, at least two to three hours after food, and a second dose 2.5 to 4 hours later. Both doses should be prepared at the same time before the patient goes to bed. Xyrem is supplied with a measuring syringe and a cup to make it up with.

Adults should usually take 4.5 to 9 g per day in two equally divided doses, while the amount children and adolescents take depends on their weight. Patients start on a low dose and build up gradually.

The medicine can only be obtained with a 'special' prescription. This means that because the medicine can be misused, it is used under stricter conditions than normal. Xyrem treatment should be started and given under the guidance of a doctor who has experience in the treatment of narcolepsy. For more information about using Xyrem, see the package leaflet or contact your doctor or pharmacist.

How does Xyrem work?

The active substance in Xyrem, sodium oxybate, is a central nervous system depressant. The precise way in which it works is not known, but it is thought to attach to receptor molecules on the surface of some cells in the brain. This leads to changes in the activity of the brain, bringing about 'delta' (slow) brain waves and night-time sleep. When taken at bedtime, Xyrem increases deep sleep and increases the amount of time spent asleep at night, whilst reducing the number of daytime sleeping periods and cataplexy attacks. This improves the symptoms of narcolepsy.

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What benefits of Xyrem have been shown in studies?

Four studies in 707 adults have shown that Xyrem was more effective than placebo (a dummy treatment) in reducing symptoms. In the first study, a daily dose of 9 g reduced the number of cataplexy attacks by 16.1 (from 23.5 to 7.4) per week, compared with a fall of 4.3 per week in the patients taking placebo.

The second study showed that Xyrem continued to prevent cataplexy attacks after long-term treatment: there was no change over two weeks in the number of attacks in the patients continuing to take Xyrem, compared to an increase of 21.0 attacks in those switching to placebo.

Two other studies showed that Xyrem also reduced excessive daytime sleepiness in adults who continued to take modafinil (another medicine), as well as in those who took Xyrem alone.

Another study showed that children aged from 7 years to 17 who kept taking Xyrem had less symptoms of narcolepsy with cataplexy than those who started taking placebo after a period of taking Xyrem.

What are the risks associated with Xyrem?

The most common side effects with Xyrem in adults (seen in more than 1 patient in 10) are dizziness, headache and nausea (feeling sick). Nausea is more common in women than in men. The most serious side effects seen with Xyrem are attempted suicide, psychosis (abnormal thinking), respiratory depression (inhibition of breathing) and convulsions (fits). Overall side effects in children are similar to those in adults: the most common side effects (seen in more than 1 in 20) are wetting the bed, nausea (feeling sick) and vomiting, weight loss, loss of appetite, headache and dizziness. For the full list of all side effects reported with Xyrem, see the package leaflet.

Xyrem should not be used in people who may be hypersensitive (allergic) to sodium oxybate or any of the other ingredients. It must also not be used in patients with major depression, in patients with 'succinic semialdehyde dehydrogenase deficiency' (a rare metabolic disease), or in patients being treated with opioids (such as some painkillers) or barbiturates (such as some anaesthetics and medicines used to prevent seizures).

Because sodium oxybate can be abused, doctors must carefully monitor patients using Xyrem. Patients are also advised against taking alcohol while on treatment with Xyrem. For the full list of restrictions, see the package leaflet.

Why is Xyrem authorised in the EU?

The European Medicines Agency decided that Xyrem's benefits are greater than its risks. In adults, although the 9-g dose was the most effective, it was linked to high levels of side effects, so the Committee recommended a starting dose of 4.5 g per day. (In children the starting dose is based on body weight.) Since the effective dose is close to the dose at which side effects become serious, increases in dose must be carried out strictly and under the supervision of a doctor specialised in the treatment of sleep disorders. The Agency recommended that Xyrem be given marketing authorisation.

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

The company that markets Xyrem will provide doctors with educational materials, which will contain information about respiratory depression (inhibition of breathing) and possibility of people misusing the medicine. The material will also include instructions for patients and a patient alert card.

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

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

Other information about Xyrem

Xyrem received a marketing authorisation valid throughout the EU on 13 October 2005.

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

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