

Package leaflet: Information for the user

Xyrem 500 mg/mL oral solution Sodium oxybate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Xyrem is and what it is used for
2. What you need to know before you take Xyrem
3. How to take Xyrem
4. Possible side effects
5. How to store Xyrem
6. Contents of the pack and other information

1. What Xyrem is and what it is used for

Xyrem contains the active substance sodium oxybate. Xyrem works by consolidating night-time sleep, though its exact mechanism of action is unknown.

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

Narcolepsy is a sleep disorder that may include attacks of sleep during normal waking hours, as well as cataplexy, sleep paralysis, hallucinations and poor sleep. Cataplexy is the onset of sudden muscle weakness or paralysis without losing consciousness, in response to a sudden emotional reaction such as anger, fear, joy, laughter or surprise.

2. What you need to know before you take Xyrem

Do not take Xyrem

- if you are allergic to sodium oxybate or any of the other ingredients of this medicine (listed in section 6);
- if you have succinic semialdehyde dehydrogenase deficiency (a rare metabolic disorder);
- if you suffer from major depression;
- if you are being treated with opioid or barbiturate medicines.

Warnings and precautions

Talk to your doctor or pharmacist before taking Xyrem:

- if you have breathing or lung problems (and especially if you are obese), because Xyrem has the potential to cause difficulty in breathing;
- if you have or have previously had depressive illness, suicidal thoughts, anxiety, psychosis (a mental disorder that may involve hallucinations, incoherent speech, or disorganized and agitated behaviour) or bipolar disorder
- if you have heart failure, hypertension (high blood pressure), liver or kidney problems as your dose may need to be adjusted;
- if you have previously abused drugs;

- if you suffer from epilepsy as the use of Xyrem is not recommended in this condition;
- if you have porphyria (an uncommon metabolic disorder).

If any of these apply to you, tell your doctor before you take Xyrem.

While you are taking Xyrem, if you experience bed wetting and incontinence (both urine and faeces), confusion, hallucinations, episodes of sleepwalking or abnormal thinking you should tell your doctor straight away. Whilst these effects are uncommon, if they do occur they are usually mild-to-moderate in nature.

If you are elderly, your doctor will monitor your condition carefully to check whether Xyrem is having the desired effects.

Xyrem has a well-known abuse potential. Cases of dependency have occurred after the illicit use of sodium oxybate.

Your doctor will ask if you have ever abused any drugs before you start taking Xyrem and whilst you are using the medicine.

Children and adolescents

Xyrem can be taken by adolescents and children from 7 years of age when they are over 15 kg in weight.

Xyrem cannot be taken by children below 7 years of age or below 15 kg in weight.

If you are a child or adolescent, your doctor will monitor your body weight regularly.

Whilst the doctor is adjusting the dose which may take a number of weeks, parent/caregivers should carefully monitor the child's breath during the first 2 hours after sodium oxybate intake to assess if there is any abnormality in breathing, for example stoppage of breathing for short periods while sleeping, noisy breathing and bluish colour of the lips and face. If abnormality in breathing is observed medical support should be sought and the doctor should be informed as soon as possible. If any abnormality is noted after the first dose, the second dose should not be administered. If no abnormality is noted the second dose can be administered. The second dose should not be given earlier than 2.5 hours or later than 4 hours after the first dose.

If you have had or are having upsetting feelings particularly if you are feeling very sad or have lost interest in life it is important that you tell the doctor or caregiver.

Other medicines and Xyrem

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular Xyrem should not be taken together with sleep inducing medicines and medicines that reduce central nervous system activity (the central nervous system is the part of the body related to the brain and spinal cord).

Also tell your doctor or pharmacist if you are taking any of the following types of medicines:

- medicines that increase central nervous system activity
- antidepressants
- medicines that may be processed in a similar way by the body (e.g., valproate, phenytoin or ethosuximide which are used for the treatment of fits)
- topiramate (used for treatment of epilepsy)

If you are taking Valproate, your daily dose of Xyrem will need to be adjusted (see section 3) as it may lead to interactions with Valproate

Xyrem with alcohol

You must not drink alcohol while taking Xyrem, as its effects can be increased.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

There have been very few women who have taken Xyrem sometime during their pregnancy and a few of them had spontaneous abortions. The risk of taking Xyrem during pregnancy is unknown, and, therefore, the use of Xyrem in pregnant women or women trying to become pregnant is not recommended.

Patients taking Xyrem should not breast feed since it is known that Xyrem passes into breast milk. Changes in sleep patterns have been observed in breastfed infants from exposed mothers.

Driving and using machines

Xyrem will affect you if you drive or operate tools or machines. Do not drive a car, operate heavy machinery, or perform any activity that is dangerous or that requires mental alertness for at least 6 hours after taking Xyrem. When you first start taking Xyrem, until you know whether it makes you sleepy the next day, use extreme care while driving a car, operating heavy machinery or doing anything else that could be dangerous or needs you to be fully mentally alert.

For paediatric patients, physicians, parents or caregivers are advised that the waiting time for performing activities that require mental alertness, motor co-ordination or any activities that may have a physical risk may have to be longer than 6 hours, depending on individual sensitivity.

Xyrem contains sodium

This medicine contains 182.24 mg sodium (main component of cooking/table salt) in each gram. This is equivalent to 9.11% of the recommended maximum daily dietary intake of sodium for an adult. Talk to your doctor or pharmacist if you need 2 g of sodium oxybate (Xyrem) or more daily for a prolonged period, especially if you have been advised to follow a low salt (sodium) diet.

3. How to take Xyrem

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

It is important that you only use the syringe provided in the box when preparing doses of Xyrem. The Xyrem syringe has two different measurement scales, one scale may be more helpful for you than the other depending on which dose your doctor has prescribed. By looking at each scale you will see which one provides the exact mark for your dose.

Adults – taking Xyrem on its own

- For adults the recommended starting dose is 4.5 g each day, given as two separate doses of 2.25 g.
- Your doctor may gradually increase your dose up to a maximum of 9 g each day given as two separate doses of 4.5 g.
- Take Xyrem orally two times each night:
 - Take the first dose upon getting into bed and the second dose 2½ to 4 hours later. You may need to set an alarm clock to make sure you wake up to take the second dose.
 - Food decreases the amount of Xyrem that is absorbed by your body. Therefore, it is best to take Xyrem at set times 2 to 3 hours after a meal.
 - Prepare both doses before bedtime.
 - Take doses within 24 hours after preparation.

Adolescents and children aged 7 years and over who weigh 15 kg or more - taking Xyrem on its own

For those aged 7 years and over who weigh 15 kg or more, a doctor will work out the right dose based on your body weight.

Your doctor will work out the right dose for you. Do not exceed the dose prescribed for you.

Adults - taking Xyrem with Valproate

If you are taking valproate together with Xyrem, the dose of Xyrem will be adapted by your doctor.

- For adults the recommended starting dose for Xyrem, when used together with Valproate, is 3.6 g each day, given as two separate doses of 1.8 g.
- Take the first dose when getting into bed and the second dose 2½ to 4 hours later.

Adolescents and children aged 7 years and older who weigh 15 kg or more - taking Xyrem with Valproate

If you are taking Valproate together with Xyrem, the dose of Xyrem will be adapted by your doctor.

Kidney or liver problems

- If you have kidney problems, you should consider a dietary recommendation to reduce sodium (salt) intake. If you have liver problems, the starting dose should be halved. Your doctor may gradually increase your dose.

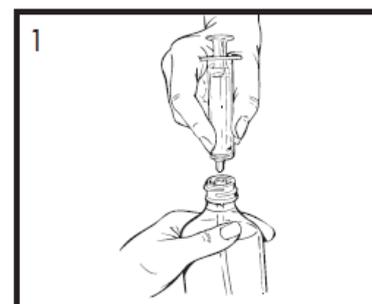
Instructions on how to dilute Xyrem

The following instructions explain how to prepare Xyrem. Please read the instructions carefully and follow them step by step. Do not allow children to prepare Xyrem.

To help you, the Xyrem carton contains 1 bottle of medicine, a measuring syringe (with two different measurement scales) and two dosing cups with child-resistant caps.

Step 1

- Remove the bottle cap by pushing down while turning the cap anticlockwise (to the left).
- After removing the cap, set the bottle upright on a table-top.
- There is a plastic covered foil seal on the top of the bottle, which must be removed before using the bottle for the first time.
- While holding the bottle in its upright position, insert the press-in-bottle-adaptor into the neck of the bottle. This needs only to be done the first time that the bottle is opened. The adaptor can then be left in the bottle for all subsequent uses



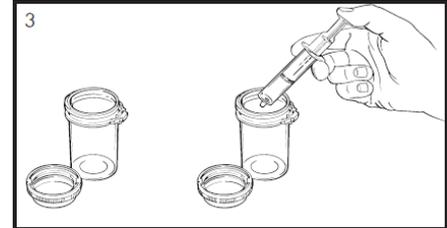
Step 2

- Next, insert the tip of the measuring syringe into the centre opening of the bottle and press down firmly
- While holding the bottle and syringe with one hand, draw up the prescribed dose with the other hand by pulling on the plunger. NOTE: Medicine will not flow into the syringe unless you keep the bottle in its upright position



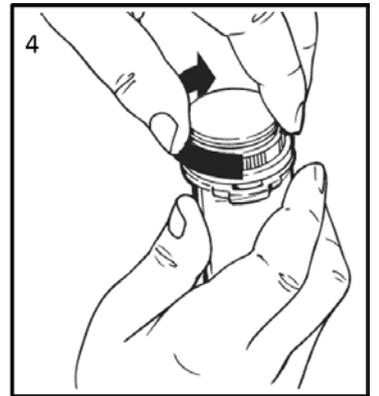
Step 3

- Remove the syringe from the centre opening of the bottle.
- Empty the medicine from the syringe into one of the dosing cups provided by pushing on the plunger Repeat this step for the second dosing cup.
- Then add about 60 ml of water to each dosing cup (60 mL is about 4 tablespoons).



Step 4

- Place the caps provided on the dosing cups and turn each cap clockwise (to the right) until it clicks and locks into its child-resistant position (Caution: as the dosing cup cap is reversible, only after the clicking noise is heard it is ensured that the cap is closed in the child-resistant manner).
- Rinse out the syringe with water.



- Just before going to sleep:
 - Adult patients should place the second dose near their bed .
 - The parent or caregiver of adolescents and children aged 7 years and over should not leave the second dose near the child's bed or within easy reach of the child.
 - You may need to set an alarm so you wake up to take your second dose no earlier than 2½ hours and no later than 4 hours after your first dose.

Then:

- Remove the cap from the first dosing cup by pressing down on the child-resistant locking tab and turning the cap anticlockwise (to the left).
- Drink all of the first dose while sitting in bed, recap the cup, and then lie down right away. For children who sleep longer than 8 hours but less than 12 hours, the first dose may be given after the child has been sleeping for 1 to 2 hours.
-

- When you wake up or wake up the child 2 ½ to 4 hours later, remove the cap from the second dosing cup. While sitting in bed, drink all of the second dose right before lying down to continue sleeping. Recap the second cup.

If you have the impression that the effect of Xyrem is too strong or too weak, talk to your doctor or pharmacist.

If you take more Xyrem than you should

Symptoms of Xyrem overdose may include agitation, confusion, impaired movement, impaired breathing, blurred vision, profuse sweating, headache, vomiting, decreased consciousness leading to coma and seizures, excessive thirst, muscle cramps and weakness. If you take more Xyrem than you were told to take, or take it by accident, get emergency medical help right away. You should take the labelled medicine bottle with you, even if it is empty.

If you forget to take Xyrem

If you forget to take the first dose, take it as soon as you remember and then continue as before. If you miss the second dose, skip that dose and do not take Xyrem again until the next night. Do not take a double dose to make up for a forgotten dose.

If unsure if you took Xyrem

If in doubt about administration of a dose, do not re-administer the dose to reduce the risk of overdose

If you stop taking Xyrem

You should continue to take Xyrem for as long as instructed by your doctor. You may find that your cataplexy attacks return if your medicine is stopped and you may experience insomnia, headache, anxiety, dizziness, sleeping problems, sleepiness, hallucination and abnormal thinking.

If you stop taking Xyrem for more than 14 consecutive days, you should consult your doctor as you should restart taking Xyrem at a reduced dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. These are usually mild to moderate..

Adults - most common side effects observed in clinical studies (occurring in 10% to 20% of patients):

- dizziness
- nausea
- headache.

If you experience any of these side effects, **tell your doctor straight away.**

Children and adolescents - most common side effects observed in a clinical study:

- bed wetting (18.3%)
- nausea (12.5%)
- vomiting (8.7%)
- weight decrease (8.7%)
- decreased appetite (6.7%)
- headache (5.8%)
- dizziness (5.8%)
- suicidal thoughts (1%)
- feeling mentally unwell (loss of contact with reality) (1%)

If you experience any of these side effects, **tell your doctor straight away**

The side effects in adults and children are the same. If you experience any of the side effects listed below, tell your doctor straight away:

Very common (may affect more than 1 in 10 people):

- nausea
- dizziness
- headache

Common (may affect up to 1 in 10 people):

- sleeping problems including insomnia, abnormal dreams, sleep paralysis, sleepiness, nightmares, sleep walking, bed wetting, excessive daytime sleepiness, difficulty in falling asleep in the middle of the night
- feeling drunk, trembling, confusion/ disorientation, blurred vision, balance disorder, fall, feeling of “spinning” (vertigo),
- feeling the heart beat, increased blood pressure, shortness of breath
- vomiting, stomach pains, diarrhoea
- anorexia, decreased appetite, weight loss
- weakness, tiredness, sedation
- sweating
- depression
- muscle cramps, swelling
- joint pain, back pain
- disturbance in attention, disturbed sensitivity particularly to touch, abnormal touch sensation, abnormal taste
- anxiety, nervousness
- urinary incontinence
- snoring, congestion of the nose
- rash

inflammation of the sinuses, inflammation of nose and throat

Uncommon (may affect up to 1 in 100 people):

- psychosis (a mental disorder that may involve hallucinations, incoherent speech, or disorganized and agitated behaviour)
 - paranoia, abnormal thinking, hallucination, agitation, suicide attempt
 - difficulty in falling asleep, restless legs
 - forgetfulness
 - myoclonus (involuntary contractions of muscles)
 - involuntary passage of faeces
- hypersensitivity

Not known (cannot be estimated from the available data):

- convulsion
- decreased breathing depth or rate, short cessation of breathing during sleep
- hives
- suicidal thoughts, delusion, thoughts of committing violent acts (including harming others)
- irritability, aggression
- euphoric mood
- panic attack
- mania / bipolar disorder
- dry mouth, dehydration
- swelling face (angioedema)
- bruxism (teeth grinding and jaw clenching)
- pollakiuria / micturition urgency (increase need to urinate)
- tinnitus (noise in the ears such as ringing or buzzing)
- sleep-related eating disorder
- increased appetite
- loss of consciousness
- dyskinesia (e.g. abnormal, uncontrolled movements of the limbs)
- dandruff

- increased sexual desire
- nocturia (excessive urination at night)
- choking sensation

If you experience any of the side effects listed above, **tell your doctor straight away.**

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Xyrem

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date stated on the bottle after (EXP). The expiry date refers to the last day of that month.

After dilution in the dosing cups, the preparation should be used within 24 hours.

Once you open a bottle of Xyrem, any contents that you have not used with 90 days of opening should be disposed of.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Xyrem contains

- The active substance is sodium oxybate. Each mL contains 500 mg of sodium oxybate.
- The other ingredients are purified water, malic acid and sodium hydroxyde.

What Xyrem looks like and contents of the pack

Xyrem is supplied in a 240 mL amber plastic bottle containing 180 mL of oral solution and closed with a child-resistant cap. When the bottle is delivered, there is a plastic covered foil seal which is on the top of the bottle, underneath the cap. Each pack contains one bottle, a press-in-bottle-adaptor (PIBA), a plastic measuring syringe and two dosing cups with child-resistant caps.

Xyrem is a clear to slightly opalescent solution.

Marketing Authorisation Holder

UCB Pharma Limited, 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.

Manufacturer

UCB Pharma S.A., Chemin du Foriest, B-1420 Braine l'Alleud, Belgium

You should have received a Xyrem Information Pack from your physician, which includes a booklet on how to take the medicine, a Frequently Asked Questions patient information sheet and a patient alert card.

This leaflet was last revised in February 2022.