Package Leaflet: Information for the patient

Keppra 100 mg/ml oral solution
Levetiracetam

Read all of this leaflet carefully before you or your child start taking 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 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 Keppra is and what it is used for

Levetiracetam is an antiepileptic medicine (a medicine used to treat seizures in epilepsy).

Keppra is used:
- on its own in adults and adolescents from 16 years of age with newly diagnosed epilepsy, to treat a certain form of epilepsy. Epilepsy is a condition where the patients have repeated fits (seizures). Levetiracetam is used for the epilepsy form in which the fits initially affect only one side of the brain but could thereafter extend to larger areas on both sides of the brain (partial onset seizure with or without secondary generalisation). Levetiracetam has been given to you by your doctor to reduce the number of fits.
- as an add-on to other antiepileptic medicines to treat:
  - partial onset seizures with or without generalisation in adults, adolescents, children and infants from one month of age
  - myoclonic seizures (short, shock-like jerks of a muscle or group of muscles) in adults and adolescents from 12 years of age with juvenile myoclonic epilepsy
  - primary generalised tonic-clonic seizures (major fits, including loss of consciousness) in adults and adolescents from 12 years of age with idiopathic generalised epilepsy (the type of epilepsy that is thought to have a genetic cause).

2. What you need to know before you take Keppra

Do not take Keppra
- If you are allergic to levetiracetam, pyrrolidone derivatives or any of the other ingredients of this medicine (listed in Section 6).

Warnings and precautions
Talk to your doctor before taking Keppra

- If you suffer from kidney problems, follow your doctor's instructions. He/she may decide if your dose should be adjusted.
- If you notice any slowdown in the growth or unexpected puberty development of your child, please contact your doctor.
- A small number of people being treated with anti-epileptics such as Keppra have had thoughts of harming or killing themselves. If you have any symptoms of depression and/or suicidal ideation, please contact your doctor.
- If you have a family or medical history of irregular heart rhythm (visible on an electrocardiogram), or if you have a disease and/or take a treatment that make(s) you prone to heartbeat irregularities or salt imbalances.

Tell your doctor or pharmacist if any of the following side effects gets serious or last longer than a few days:

- Abnormal thoughts, feeling irritable or reacting more aggressively than usually, or if you or your family and friends notice important changes in mood or behaviour.
- Aggravation of epilepsy:
  Your seizures may rarely become worse or happen more often, mainly during the first month after the start of the treatment or increase of the dose.
  In a very rare form of early-onset epilepsy (epilepsy associated with SCN8A mutations) that causes multiple types of seizures and loss of skills you may notice that the seizures remain present or are becoming worse during your treatment.

If you experience any of these new symptoms while taking Keppra, see a doctor as soon as possible.

Children and adolescents

- Keppra is not indicated in children and adolescents below 16 years on its own (monotherapy)

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

Do not take macrogol (a drug used as laxative) for one hour before and one hour after taking levetiracetam as this may results in a reduction of its effect.

Pregnancy and breast-feeding
If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine. Levetiracetam can be used during pregnancy, only if after careful assessment it is considered necessary by your doctor.
You should not stop your treatment without discussing this with your doctor.
A risk of birth defects for your unborn child cannot be completely excluded.
Breast-feeding is not recommended during treatment.

Driving and using machines
Keppra may impair your ability to drive or operate any tools or machinery, as it may make you feel sleepy. This is more likely at the beginning of treatment or after an increase in the dose. You should not drive or use machines until it is established that your ability to perform such activities is not affected.

Keppra contains methyl parahydroxybenzoate, propyl parahydroxybenzoate and maltitol
Keppra oral solution includes methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) which may cause allergic reactions (possibly delayed).
Keppra oral solution also contains maltitol. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Keppra

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
Keppra must be taken twice a day, once in the morning and once in the evening, at about the same time each day.
Take the oral solution following your doctor's instructions.

Monotherapy (from 16 years of age)

Adults (≥18 years) and adolescents (from 16 years of age):
Measure the appropriate dosage using the 10 ml syringe included in the package for patients 4 years and above.
Recommended dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 5 ml (500mg) and 15 ml (1,500mg).
When you will first start taking Keppra, your doctor will prescribe you a **lower dose** during 2 weeks before giving you the lowest daily dose.

Add-on therapy

Dose in adults and adolescents (12 to 17 years):
Measure the appropriate dosage using the 10 ml syringe included in the package for patients of 4 years and above.
Recommended dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 5 ml (500mg) and 15 ml (1,500mg).
Dose in children 6 months and older:
Your doctor will prescribe the most appropriate pharmaceutical form of Keppra according to the age, weight and dose.
For children 6 months to 4 years, measure the appropriate dosage using the **3 ml** syringe included in the package.
For children above 4 years, measure the appropriate dosage using the **10 ml** syringe included in the package.
Recommended dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 0.1 ml (10mg) and 0.3 ml (30mg), per kg bodyweight of the child. (see table below for dose examples).

Dose in children 6 months and older:

Weight	Starting dose: 0.1 ml/kg twice daily	Maximum dose: 0.3 ml/kg twice daily
6 kg	0.6 ml twice daily	1.8 ml twice daily
8 kg	0.8 ml twice daily	2.4 ml twice daily
10 kg	1 ml twice daily	3 ml twice daily
15 kg	1.5 ml twice daily	4.5 ml twice daily

20 kg	2 ml twice daily	6 ml twice daily
25 kg	2.5 ml twice daily	7.5 ml twice daily
From 50 kg	5 ml twice daily	15 ml twice daily

Dose in infants (1 month to less than 6 months):
For infants 1 month to less than 6 months, measure the appropriate dosage using the **1 ml** syringe included in the package.
Recommended dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 0.07 ml (7mg) and 0.21 ml (21mg), per kg bodyweight of the infant. (see table below for dose examples).

Dose in infants (1 month to less than 6 months):

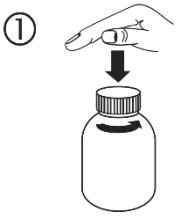
Weight	Starting dose: 0.07 ml/kg twice daily	Maximum dose: 0.21 ml/kg twice daily
4 kg	0.3 ml twice daily	0.85 ml twice daily
5 kg	0.35 ml twice daily	1.05 ml twice daily
6 kg	0.45 ml twice daily	1.25 ml twice daily
7 kg	0.5 ml twice daily	1.5 ml twice daily

Method of administration:

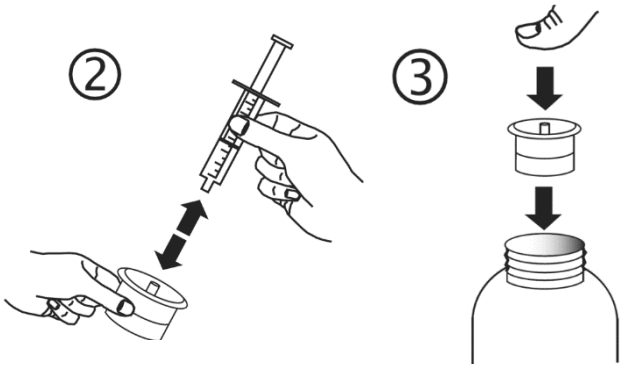
After measuring the correct dosage with an appropriate syringe, Keppra oral solution may be diluted in a glass of water or baby's bottle. You may take Keppra with or without food. After oral administration the bitter taste of levetiracetam may be experienced.

Instructions for use:

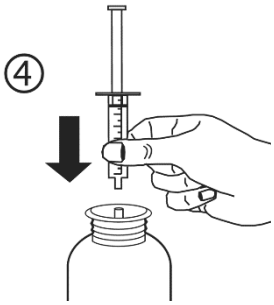
- Open the bottle: press the cap and turn it anticlockwise (figure 1)

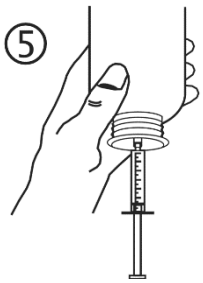


- Separate the adaptor from the syringe (figure 2). Insert the adaptor into the bottle neck (figure 3). Ensure it is well fixed.

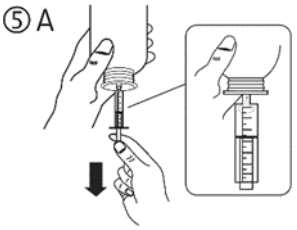


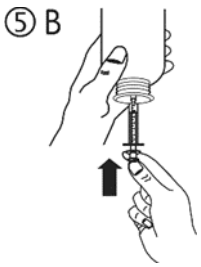
- Take the syringe and put it in the adaptor opening (figure 4). Turn the bottle upside down (figure 5).

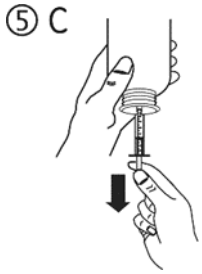




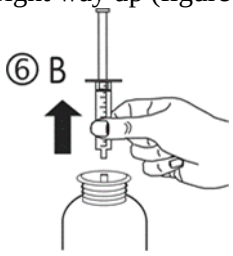
- Fill the syringe with a small amount of solution by pulling the piston down (figure 5A), then push the piston upward in order to remove any possible bubble (figure 5B). Pull the piston down to the graduation mark corresponding to the quantity in milliliters (ml) prescribed by your doctor (figure 5C).





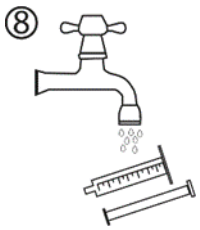


- Turn the bottle the right way up (figure 6A). Remove the syringe from the adaptor (figure 6B).



- Empty the contents of the syringe in a glass of water or baby's bottle by pushing the piston to the bottom of the syringe (figure 7).

- Drink the whole contents of the glass/baby's bottle.
- Close the bottle with the plastic screw cap.



- Wash the syringe with water only (figure 8).

Duration of treatment:
- Keppra is used as a chronic treatment. You should continue Keppra treatment for as long as your doctor has told you.
- Do not stop your treatment without your doctor's advice as this could increase your seizures.

If you take more Keppra than you should
The possible side effects of an overdose of Keppra are sleepiness, agitation, aggression, decrease of alertness, inhibition of breathing and coma.
Contact your doctor if you took more Keppra than you should. Your doctor will establish the best possible treatment of overdose.

If you forget to take Keppra:
Contact your doctor if you have missed one or more doses.
Do not take a double dose to make up for a forgotten dose.

If you stop taking Keppra:
If stopping treatment, Keppra should be discontinued gradually to avoid an increase of seizures. Should your doctor decide to stop your Keppra treatment, he/she will instruct you about the gradual withdrawal of Keppra.

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.

Tell your doctor immediately, or go to your nearest emergency department, if you experience:

- weakness, feel light-headed or dizzy or have difficulty breathing, as these may be signs of a serious allergic (anaphylactic) reaction
- swelling of the face, lips, tongue and throat (Quincke's oedema)
- flu-like symptoms and a rash on the face followed by an extended rash with a high temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes (Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]),.
- symptoms such as low urine volume, tiredness, nausea, vomiting, confusion and swelling in the legs, ankles or feet, as this may be a sign of sudden decrease of kidney function
- a skin rash which may form blisters and look like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) (*erythema multiforme*)
- a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (*Stevens-Johnson syndrome*)
- a more severe form of rash causing skin peeling in more than 30% of the body surface (*toxic epidermal necrolysis*)
- signs of serious mental changes or if someone around you notices signs of confusion, somnolence (sleepiness), amnesia (loss of memory), memory impairment (forgetfulness), abnormal behaviour or

other neurological signs including involuntary or uncontrolled movements. These could be symptoms of an encephalopathy.

The most frequently reported adverse reactions were nasopharyngitis, somnolence (sleepiness), headache, fatigue and dizziness. At the beginning of the treatment or at dose increase side effects like sleepiness, tiredness and dizziness may be more common. These effects should however decrease over time.

Very common: may affect more than 1 in 10 people
- nasopharyngitis;
- somnolence (sleepiness), headache.

Common: may affect up to 1 in 10 people
- anorexia (loss of appetite);
- depression, hostility or aggression, anxiety, insomnia, nervousness or irritability;
- convulsion, balance disorder (equilibrium disorder), dizziness (sensation of unsteadiness), lethargy (lack of energy and enthusiasm), tremor (involuntary trembling);
- vertigo (sensation of rotation);
- cough;
- abdominal pain, diarrhoea, dyspepsia (indigestion), vomiting, nausea;
- rash;
- asthenia/fatigue (tiredness).

Uncommon: may affect up to 1 in 100 people
- decreased number of blood platelets, decreased number of white blood cells;
- weight decrease, weight increase;
- suicide attempt and suicidal ideation, mental disorder, abnormal behaviour, hallucination, anger, confusion, panic attack, emotional instability/mood swings, agitation;
- amnesia (loss of memory), memory impairment (forgetfulness), abnormal coordination/ataxia (impaired coordinated movements), paraesthesia (tingling), disturbance in attention (loss of concentration);
- diplopia (double vision), vision blurred;
- elevated/abnormal values in a liver function test;
- hair loss, eczema, pruritus;
- muscle weakness, myalgia (muscle pain);
- injury.

Rare: may affect up to 1 in 1,000 people
- infection;
- decreased number of all blood cell types;
- severe allergic reactions (DRESS, anaphylactic reaction [severe and important allergic reaction], Quincke's oedema [swelling of the face, lips, tongue and throat]);
- decreased blood sodium concentration;
- suicide, personality disorders (behavioural problems), thinking abnormal (slow thinking, unable to concentrate);
- delirium;
- encephalopathy (see sub-section "Tell your doctor immediately" for a detailed description of symptoms);
- seizures may become worse or happen more often;

- uncontrollable muscle spasms affecting the head, torso and limbs, difficulty in controlling movements, hyperkinesia (hyperactivity);
- change of the heart rhythm (Electrocardiogram);
- pancreatitis;
- liver failure, hepatitis;
- sudden decrease in kidney function;
- skin rash, which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) (*erythema multiforme*), a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (*Stevens-Johnson syndrome*), and a more severe form causing skin peeling in more than 30% of the body surface (*toxic epidermal necrolysis*);
- rhabdomyolysis (breakdown of muscle tissue) and associated blood creatine phosphokinase increase. Prevalence is significantly higher in Japanese patients when compared to non-Japanese patients.
- limp or difficulty walking.

Evidence also suggests a possible predisposition of the Japanese population to neuroleptic malignant syndrome (NMS).

Very rare: may affect up to 1 in 10000 people
- repeated unwanted thoughts or sensations or the urge to do something over and over again (Obsessive Compulsive Disorder).

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 Keppra

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

Do not use this medicine after the expiry date stated on the cardboard box and bottle after EXP:
The expiry date refers to the last day of the month.
Do not use after 7 months of first opening the bottle.

Store in the original bottle, in order to protect from light.

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

6. Contents of the pack and other information

What Keppra contains
The active substance is called levetiracetam. Each ml contains 100 mg of levetiracetam.

The other ingredients are: sodium citrate, citric acid monohydrate, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), ammonium glycyrrhizate, glycerol (E422), maltitol liquid (E965), acesulfame potassium (E950), grape flavour, purified water.

What Keppra looks like and contents of the pack
Keppra 100 mg/ml oral solution is a clear liquid.
The 300 ml glass bottle of Keppra (for children aged 4 years and above, adolescents and adults) is packed in a cardboard box containing a 10 ml oral syringe (graduated every 0.25 ml) and an adaptor for the syringe.
The 150 ml glass bottle of Keppra (for infants and young children aged from 6 months to less than 4 years) is packed in a cardboard box containing a 3 ml oral syringe (graduated every 0.1 ml) and an adaptor for the syringe.
The 150 ml glass bottle of Keppra (for infants aged 1 month to less than 6 months) is packed in a cardboard box containing a 1 ml oral syringe (graduated every 0.05 ml) and an adaptor for the syringe.

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