PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

KEPPRA 100 mg oral solution

Levetiracetam 100 mg/mL

Contains sugar (as maltitol 300 mg/mL)

Contains sweetener (as acesulfame potassium 4,50 mg/mL)

Read all of this leaflet carefully before you start taking KEPPRA.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- KEPPRA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet:

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

1. What KEPPRA is and what it is used for:

KEPPRA is an anti-epileptic medicine (a medicine used to treat seizures in epilepsy).

KEPPRA is used in patients who are already taking another anti-epileptic medicine, to treat partial seizures in adults and children over 4 years of age with epilepsy.

2. What you need to know before you take KEPPRA:

Do not take KEPPRA:

Before taking this medicine, you should tell your doctor:

- if you are hypersensitive (allergic) to levetiracetam or to any of the other ingredients of KEPPRA (listed in section 6).

Warnings and precautions:

Take special care with KEPPRA:

- If you suffer from kidney problems, follow your doctor's instructions. They may decide that your dose should be adjusted.
- If your treatment has to be stopped, your doctor will tell you how to withdraw it gradually.
- KEPPRA has not been approved for children below the age of 4 years.
- If you notice any slowing down in the growth or unexpected puberty development of your child, please contact your doctor.
- A small number of people being treated with KEPPRA have had thoughts of harming or killing themselves. If you have, or your child has any symptoms of depression and or thoughts of committing suicide, please contact your doctor.
- If you notice any abnormal and aggressive behaviours, or if you or your family and friends notice important changes in mood or behaviour, immediately contact your doctor.
- if you have a family or medical history of heart problems, for example disturbance in heart rhythm (visible on an electrocardiogram) or if you are

taking any other medicine that makes you prone to have disturbance in heart rhythm or unusual amount of salt in the body.

- Your seizures may rarely become worse or happen more often, mainly during the first month after starting the treatment or increase of the dose of KEPPRA. If you notice any of these symptoms while taking KEPPRA, immediately contact your doctor. 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.

Other medicines and KEPPRA:

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of KEPPRA with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.

Don't take macrogol (a medicine used as laxative) for one hour before and one hour after taking KEPPRA as this may results in a loss of its effect.

You will be closely monitored if you are taking KEPPRA with:

- methotrexate (used to treat certain types of cancer).

Some other medicines may affect how KEPPRA works or make it more likely that you'll have side effects. KEPPRA can also affect how some other medicines work. These include:

- probenecid (used to treat gout).

Tell your doctor or pharmacist if you are taking any of these.

KEPPRA with food and drink and alcohol:

You may take KEPPRA with or without food.

Caution is advised if alcohol is taken at the same time as KEPPRA.

Pregnancy and breastfeeding and fertility:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice, before taking KEPPRA.

Driving and using machines:

KEPPRA may make you dizzy or sleepy.

Do not drive, operate any tools or machines until you know how KEPPRA affects you.

KEPPRA contains:

KEPPRA oral solution contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions.

KEPPRA contains glycerol which can cause headache, stomach upset and diarrhoea.

KEPPRA oral solution also contains maltitol. If you have been told that you have an intolerance to some sugars, contact your doctor before you start taking KEPPRA.

Maltitol can also cause diarrhoea.

3. How to take KEPPRA:

Do not share medicines prescribed for you with any other person.

Always take KEPPRA exactly as your doctor has told you.

You should check with your doctor, pharmacist or other healthcare professional if you are unsure.

If you think that the effect of KEPPRA is too strong or too weak, talk to your doctor or pharmacist.

Tablets are also available for adults and adolescents that can swallow tablets.

The oral solution should be diluted in a glass of water and may be taken with or without food. After oral administration the bitter taste of levetiracetam may be experienced. A graduated oral syringe and instructions for use in the patient information leaflet are provided with the oral solution. The daily dose is administered in two equal divided doses.

Adults (> 18 years) and adolescents (12 to 17 years):

As adjunctive therapy, the initial therapeutic dose is 500 mg twice daily. Depending upon the clinical response and tolerance, the daily dose can be increased up to 1 500 mg twice daily. Dose changes can be made in 500 mg twice daily increments or decrements every two to four weeks. The maximum daily dose is 3 000 mg.

Recommended dosage for children and adolescents with normal renal function.

Weight	**Starting dose** **10 mg/kg twice daily**	**Maximum dose** **30 mg/kg twice daily**
15 kg (1)	150 mg (1,5 mL) twice daily	450 mg (4,5 mL) twice daily
20 kg (1)	200 mg (2 mL) twice daily	600 mg (6 mL) twice daily
25 kg	250 mg (2,5 mL) twice daily	750 mg (7,5 mL) twice daily
From 50 kg (2)	500 mg twice daily	1 500 mg twice daily

(1) Children 20 kg or less should preferably start treatment with KEPPRA 100 mg/mL oral solution.

(2) Dosage in children and adolescents 50 kg or more is the same as in adults.

The graduated syringe contains up to 1 000 mg levetiracetam (corresponding to 10 mL) with a graduation every 25 mg (corresponding to 0,25 mL).

***Elderly (65 years and older)*:**

Adjustment of the dose is recommended in elderly patients with compromised renal function (see 'Patients with renal impairment' below).

Children aged 4 to 11 years:

The initial dose is 10 mg/kg twice daily.

Depending upon the clinical response as determined by your doctor, and how well you

tolerate KEPPRA, the daily dose can be increased up to 30 mg/kg twice daily. Dose changes can be made in 10 mg/kg twice daily increments or decrements every two weeks. Dosage in children 50 kg or greater is the same as in adults.

Your doctor, pharmacist or other healthcare professional may start you on a lower dose of KEPPRA and increase it as your body gets used to the medicine. You should follow their instructions carefully.

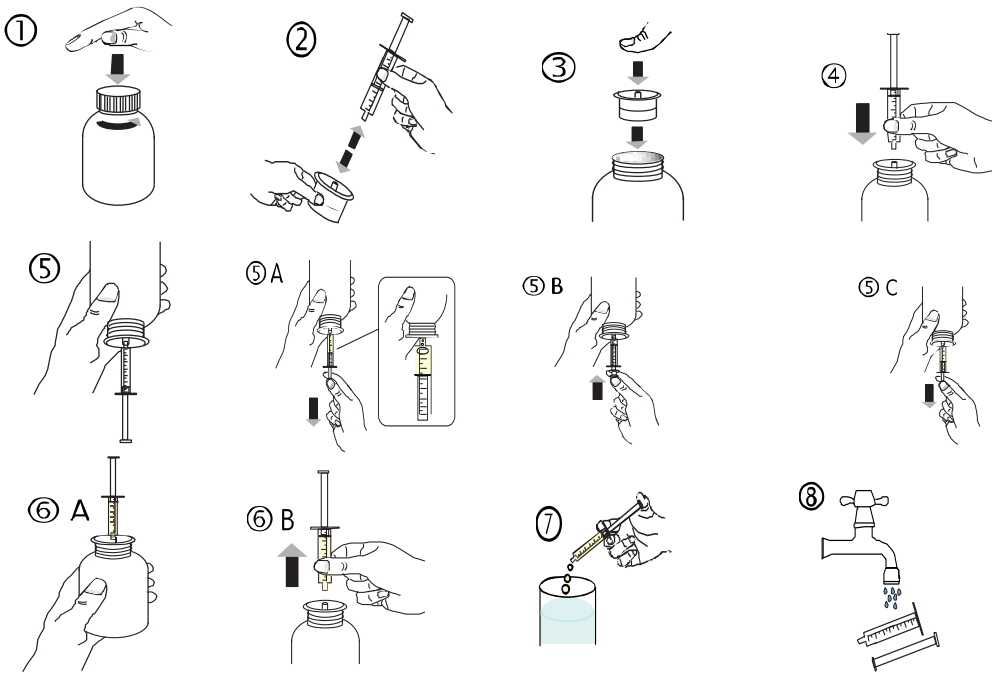
Tell your doctor, pharmacist or other healthcare professional if your seizures get worse or if you have any new types of seizures.

Administration:

KEPPRA oral solution has to be diluted in a glass of water.

Instruction for use:

- Open the bottle: press the cap and turn it anticlockwise (figure 1).
- Insert the syringe 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 liquid by pulling the piston down (figure 5A), then push the piston upward in order to remove any possible bubble (figure 5B), finally pull the piston down to the graduation mark corresponding to the quantity in milligrams (mg) 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 by pushing the piston to the bottom (figure 7).
- Drink the whole contents of the glass.
- Wash the syringe in water (figure 8).
- Close the bottle with the plastic screw cap.



Duration of treatment:

KEPPRA is used as a chronic treatment. You should continue KEPPRA treatment for as long as your doctor has told you.

If you take more KEPPRA than you should:

Talk to your doctor or pharmacist immediately. If neither is available, seek help at the nearest hospital or poison control centre.

Signs of taking too much KEPPRA are increased sleepiness, anxiety, decreased consciousness and difficulty breathing.

If you forget to take KEPPRA:

Do not take a double dose to make up for forgotten dose.

Speak to your doctor, pharmacist or other healthcare professional about what to do if you miss a dose.

If you stop taking KEPPRA:

Do not stop treatment without your doctor's advice as this could increase your seizures. Should your doctor decide to discontinue your KEPPRA treatment, they will instruct you about the gradual withdrawal of KEPPRA.

4. Possible side effects:

KEPPRA can have side effects.

Not all side effects reported for KEPPRA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking KEPPRA, please consult your doctor, pharmacist or other healthcare professional for advice.

Conditions you need to look out for:

If any of the following happens, tell your doctor immediately or go to the casualty department at your nearest hospital:

- **Severe allergic reactions.** Signs include:
  - raised and itchy rash (hives), swelling, sometimes of the face or mouth (angioedema), causing difficulty in breathing, collapse or loss of consciousness
- **Serious skin reactions.** Signs include:
  - skin rash, which may blister, 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)
  - extensive peeling of the skin on much of the body surface (toxic epidermal necrolysis).
- **Drug reaction with eosinophilia and systemic symptoms (DRESS)**. Signs include:
  - flu-like symptoms and a rash on the face followed by an extended rash with a high temperature

- enlarged lymph nodes
- increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia).

- **Sudden decrease of kidney function.** Signs include:
  - low urine volume
  - tiredness, nausea, vomiting
  - confusion
  - swelling in the legs, ankles or feet.
- **Encephalopathy** (degenerative disease of the brain). This generally occurs at the beginning of the treatment (few days to a few months) Signs include:
  - serious mental changes or signs of confusion
  - feeling drowsy (somnolence)
  - loss of memory (amnesia), memory impairment (forgetfulness)
  - abnormal behaviour
  - other neurological signs including involuntary or uncontrolled movements.

These are all very serious side effects. If you have had them, you may have had a serious reaction to KEPPRA. You may need urgent medical attention or hospitalisation.

Tell your doctor, pharmacist or other healthcare professional if you have any of the following side effects.

Frequent side effects include:

- inflammation of the nasopharynx (nasopharyngitis)
- feeling drowsy (somnolence), headache
- loss of appetite (anorexia) - especially if you take another medicine called topiramate
- depression, hostility or aggression, anxiety, difficulty in sleeping,
- nervousness or irritability

- fits (seizures), balance disorder, dizziness, abnormal drowsiness (lethargy), tremor
- spinning sensation (vertigo)
- cough
- stomach pain, diarrhoea, indigestion, vomiting, feeling sick (nausea)
- rash
- feeling weak or lack of energy.

Less frequent side effects include:

- decreased or increased weight
- suicide attempt and suicidal ideation, mental disorder, abnormal behaviour, seeing or hearing things that are not really there (hallucination), anger, confusion, panic attack, emotional instability/mood swings, agitation
- loss of memory, memory impairment (forgetfulness), abnormal coordination or loss of coordinated bodily movements, tingling or numbness of the hands or feet, disturbance in attention (loss of concentration)
- double vision, blurred vision
- unusual hair loss or thinning, eczema, itching
- muscle weakness, muscle pain, injury
- other side effects that may show up in blood tests:
  - decrease in number of blood platelets - cells that help blood to clot (thrombocytopenia)
  - decrease in the number of white blood cells (leukopenia)
  - elevated/abnormal values in a liver function test
- infection
- allergic reactions (see ‘subsection conditions to look out for ‘Severe allergic reactions’)

- drug-induced hypersensitivity reaction that includes fever, rash, and blood abnormalities (see subsection conditions to look out for ‘Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS’))
- suicide, personality disorders (behavioural problems), abnormal thinking, severe confusion (delirium)
- uncontrollable muscle spasms affecting the eyes, head, neck and body, uncontrollable movements, hyperactivity (unusually overactive)
- encephalopathy (degenerative disease of the brain) (see ’Encephalopathy’ under subsection “Conditions to look out for”)
- seizures may become worse or happen more often
- disturbance in heart rhythm (electrocardiogram)
- inflammation of the pancreas
- liver failure, inflammation of the liver
- erythema multiforme, Stevens Johnson Syndrome, toxic epidermal necrolysis (see ‘Serious skin reactions’)
- acute kidney injury (see subsection conditions to look out for ‘Sudden decrease of kidney function’)
- 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.
- combination of fever, muscle stiffness, unstable blood pressure and heart rate, confusion, low level of consciousness (may be signs of a disorder called neuroleptic malignant syndrome). Prevalence is significantly higher in Japanese patients when compared to non-Japanese patients.
- repeated unwanted thoughts or sensations or the urge to do something over and over again (Obsessive Compulsive Disorder).

Other side effects that may show up in blood tests:

- decrease in number of all types of blood cells
- decrease in sodium in the blood.

Tell your doctor or pharmacist if any of the side effects listed becomes **severe or troublesome**, or if you notice any side effects not listed in this leaflet.

Some of the side effects like sleepiness, tiredness and dizziness may be common at the beginning of treatment or at dosage increase.

If any of these side effects get serious, please tell your doctor or pharmacist immediately.

Not all side effects reported for KEPPRA are included in this leaflet.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of KEPPRA.

5. How to store KEPPRA:

Keep all medicines out of the reach and sight of children.

Due to sensitivity to light, store in the original container.

Store at or below 30 °C.

Do not use after the expiry date stated on the label.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information:

What KEPPRA contains:

The active substance is called levetiracetam.

Each mL of oral solution contains 100 mg levetiracetam.

Preservatives: methyl parahydroxybenzoate 0,27 % *m/v* and propyl parahydroxybenzoate 0,03 % *m/v.*

Contains sugar (as maltitol liquid 300 mg/mL).

Contains sweetener (as acesulfame potassium 4,50 mg/mL)

The other ingredients are sodium citrate, citric acid monohydrate, ammonium glycyrrhizate, glycerol, grape flavour and purified water.

What KEPPRA looks like and contents of the pack:

A clear and colourless solution.

KEPPRA 100 mg/mL oral solution is supplied in a 300 mL amber glass bottle with a white plastic child-resistant cap. It is packed in a cardboard box and may or may not contain a 10 mL graduated syringe and an adaptor for the syringe.

Holder of certificate of registration:

GlaxoSmithKline South Africa (Pty) Ltd

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Epping Industria 1, 7460

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