PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Levetiracetam Hikma 100 mg/ml

concentrate for solution for infusion

levetiracetam

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 nurse.
- 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 nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. WHAT LEVETIRACETAM HIKMA IS AND WHAT IT IS USED FOR

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

Levetiracetam Hikma 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 generalization). 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 and children from 4 years 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).

Levetiracetam Hikma concentrate for solution for infusion is an alternative for patients when administration of the antiepileptic oral levetiracetam medicine is temporarily not feasible.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN LEVETIRACETAM HIKMA

Do not use Levetiracetam Hikma
- 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 you are given Levetiracetam Hikma.
- 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 Levetiracetam Hikma have had thoughts of harming or killing themselves. If you have any symptoms of depression and/or suicidal ideation, please contact your doctor.

Children and adolescents
Levetiracetam Hikma is not indicated in children and adolescents below 16 years on it's own (monotherapy).

Other medicines and Levetiracetam Hikma
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

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 breast-feeding, think you may be pregnant or planning to have a baby, ask your doctor for advice before taking this medicine.
Levetiracetam Hikma should not be used during pregnancy unless clearly necessary. A risk of birth defects for your unborn child cannot be completely excluded. Levetiracetam Hikma has shown unwanted reproductive effects in animal studies at dose levels higher than you would need to control your seizures.
Breast-feeding is not recommended during treatment.

Driving and using machines
Levetiracetam Hikma 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.

Levetiracetam Hikma contains sodium
One maximum single dose of Levetiracetam Hikma concentrate contains 2.5 mmol (or 57 mg) of sodium (0.8 mmol (or 19 mg) of sodium per vial). This should be taken into consideration if you are on a controlled sodium diet.

3. HOW LEVETIRACETAM HIKMA IS GIVEN

A doctor or a nurse will administer you Levetiracetam Hikma as an intravenous infusion. Levetiracetam Hikma must be administered twice a day, once in the morning and once in the evening, at about the same time each day.

The intravenous formulation is an alternative to your oral administration. You can switch from the film-coated tablets or from the oral solution to the intravenous formulation or reverse directly without dose adaptation. Your total daily dose and frequency of administration remain identical.

Monotherapy

Dose in adults and adolescents (from 16 years of age):
General dose: between 1000 mg and 3,000 mg each day.
When you will first start taking Levetiracetam Hikma, your doctor will prescribe you a lower dose during 2 weeks before giving you the lowest general dose.

Add-on therapy

Dose in adults and adolescents (12 to 17 years) weighing 50 kg or more:
General dose: between 1,000 mg and 3,000 mg each day.

Dose in children (4 to 11 years) and adolescents (12 to 17 years) weighing less than 50 kg: General dose: between 20 mg per kg bodyweight and 60 mg per kg bodyweight each day.

Method and route of administration:
Levetiracetam Hikma is for intravenous use.
The recommended dose must be diluted in at least 100 ml of a compatible diluent and infused over 15-minutes.
For doctors and nurses, more detailed direction for the proper use of Levetiracetam Hikma is provided in section 6.

Duration of treatment:
There is no experience with administration of intravenous levetiracetam for a longer period than 4 days.

If you stop using Levetiracetam Hikma:
If stopping treatment, as with other antiepileptic medicines, Levetiracetam Hikma should be discontinued gradually to avoid an increase of seizures. Should your doctor decide to stop your Levetiracetam Hikma treatment, he/she will instruct you about the gradual withdrawal of Levetiracetam Hikma.

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Levetiracetam Hikma 100 mg/ml concentrate for solution for infusion
levetiracetam

The following information is intended for medical or healthcare professionals only:

Directions for the proper use of Levetiracetam Hikma is provided in section 3.

One vial of Levetiracetam Hikma concentrate contains 500 mg levetiracetam (5 ml concentrate of 100 mg/ml). See Table 1 for the recommended preparation and administration of Levetiracetam Hikma concentrate to achieve a total daily dose of 500 mg, 1000 mg, 2000 mg, or 3000 mg in two divided doses.

Table 1 - Preparation and administration of Levetiracetam Hikma concentrate

Dose	Withdrawal Volume	Volume of Diluent	Infusion Time	Frequency of administration	Total Daily Dose
250 mg	2.5 ml (half 5 ml vial)	100 ml	15 minutes	Twice daily	500 mg/day
500 mg	5 ml (one 5 ml vial)	100 ml	15 minutes	Twice daily	1000 mg/day
1000 mg	10 ml (two 5 ml vials)	100 ml	15 minutes	Twice daily	2000 mg/day
1500 mg	15 ml (three 5 ml vials)	100 ml	15 minutes	Twice daily	3000 mg/day

This medicinal product is for single use only, any unused solution should be discarded.

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

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 user in 10 people):
- nasopharyngitis;
- somnolence (sleepiness), headache.

Common (may affect 1 to 10 users in 100 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 1 to 10 users in 1000 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 1 to 10 users in 10,000 people):
- infection;
- decreased number of all blood cell types;
- severe allergic reactions (DRESS, anaphylactic reaction [severe and importante 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);
- uncontrollable muscle spasms affecting the head, torso and limbs, difficulty in controlling movements, hyperkinesia (hyperactivity);
- 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.

Reporting of side effects
If you get any side effects talk to your doctor or nurse. 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. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE LEVETIRACETAM HIKMA

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the vial and carton box after EXP. The expiry date refers to the last day of the month.
This medicine does not require any special storage conditions

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Levetiracetam Hikma contains
- The active substance is levetiracetam.
  Each ml of solution for infusion contains 100 mg of levetiracetam.
- The other ingredients are: sodium acetate, glacial acetic acid, sodium chloride, water for injections.

What Levetiracetam Hikma looks like and contents of the pack
Levetiracetam Hikma concentrate for solution for infusion is a clear, colourless, sterile liquid.
Levetiracetam Hikma concentrate for solution for infusion 5 ml vial is packed in a cardboard box of 10 vials.

Marketing Authorisation Holder and Manufacturer:
Hikma Farmacêutica (Portugal), S.A.
Estrada do Rio da Mó nº8, 8A, 8B, Fervença, 2705-906 Terrugem SNT, Portugal.

Distributed by:
Consilient Health (UK) Ltd.
No. 1 Church Road, Richmond upon Thames, Surrey, TW9 2QE

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	Levetiracetam Hikma 100 mg/ml, Konzentrat zur Herstellung einer Infusionslösung
France:	Lévétiracétam Hikma 100 mg/ml Solution à diluer pour perfusion
Germany:	Levetiracetam Hikma 100 mg/ml, Konzentrat zur Herstellung einer Infusionslösung
Italy:	Levetiracetam Hikma, 100 mg/ml, Concentrato per soluzione per infusione
Portugal:	Levetiracetam Hikma 100 mg/ml, Concentrado para solução para perfusão
Spain:	Levetiracetam Hikma 100 mg/ml Concentrado para solución para perfusión
United Kingdom:	Levetiracetam 100 mg/ml Concentrate for solution for infusion

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Consilient Health P0930 hikma.

In use shelf life: from a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at room temperature (15 - 25ºC), unless dilution has taken place in controlled and validated aseptic conditions.

Levetiracetam Hikma concentrate was found to be physically compatible and chemically stable when mixed with the following diluents for at least 24 hours and stored in PVC bags at controlled room temperature 15-25°C.

Diluents:
- Sodium chloride 9 mg/ml (0.9%) solution for injection
- Lactated Ringer's solution for injection
- Dextrose 50 mg/ml (5%) solution for injection