Package leaflet: Information for the patient

Levetiracetam Pinewood 100mg/ml concentrate for solution for infusion
Levetiracetam
(referred to as Levetiracetam concentrate for solution for infusion)

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, pharmacist 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 of the side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Levetiracetam concentrate for solution for infusion is and what it is used for

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

Levetiracetam concentrate for solution for infusion 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 and children from 4 years of age with epilepsy
  - 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 concentrate for solution for infusion is an alternative for patients when administration of the antiepileptic oral levetiracetam is temporarily not feasible.

2. What you need to know before you are given Levetiracetam concentrate for solution for infusion

Do not use Levetiracetam concentrate for solution for infusion:
- 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 concentrate for solution for infusion:

- 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 concentrate for solution for infusion 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 treatment or increase of the dose. If you experience any of these new symptoms while taking Levetiracetam, see a doctor as soon as possible

Children and adolescents

- Levetiracetam concentrate for solution for infusion is not indicated in children and adolescents below 16 years on its own (monotherapy).

Other medicines and Levetiracetam concentrate for solution for infusion

Tell your doctor or pharmacist 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 loss of its effect.

Pregnancy and breastfeeding

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 it 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

Levetiracetam concentrate for solution for infusion 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 concentrate for solution for infusion contains sodium

Other ingredients include sodium chloride, sodium acetate trihydrate, acetic acid solution and water for injections.

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

3. How Levetiracetam concentrate for solution for infusion is given

A doctor or a nurse will administer your levetiracetam as an intravenous infusion.
Levetiracetam 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.

Adjunctive therapy and Monotherapy (from 16 years of age).

Adults (≥18 years) and adolescents (12 to 17 years) weighing 50 kg or more:
Recommended dose: between 1000mg and 3000mg each day.
When you will first start taking levetiracetam, your doctor will prescribe you a **lower dose** during 2 weeks before giving you the lowest daily dose.

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

Method and route of administration:
Levetiracetam concentrate for solution for infusion is for intravenous use.
The recommended dose must be diluted in at least 100ml of a compatible diluent and infused over 15 minutes.
For doctors and nurses, more detailed direction for the proper use of levetiracetam 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:
If stopping treatment, as with other antiepileptic medicines, levetiracetam should be discontinued gradually to avoid an increase of seizures. Should your doctor decide to stop your Levetiracetam concentrate for solution for intravenous use treatment, he/she will instruct you about the gradual withdrawal.

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 user 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), blurred vision
- Elevated/abnormal values in a liver function test
- Hair loss, eczema, pruritis
- 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 abnormally (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, hyperkinesias (hyperactivity)

- Change in 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
- 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.

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

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

5. How to store Levetiracetam concentrate for solution for infusion

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date stated on the vial and carton box after EXP.
The expiry date refers to the last day of the month.

Store below 25˚C. Chemical and physical in-use stability has been demonstrated for 7 days at 5°C to 22°C when diluted with 0.9% sodium chloride, 5% dextrose or Hartmann's Solution to 2mg/ml. From a microbiological point of view, in-use storage time and conditions prior to use are the responsibility of the user.

Do not use if the product shows signs of deterioration such as discolouration.
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

- The active substance is levetiracetam. Each ml of concentrate for solution for infusion contains 100 mg of levetiracetam. Each 5ml vial contains 500mg levetiracetam.
- The other ingredients are sodium chloride, sodium acetate trihydrate, acetic acid solution and water for injection.

Levetiracetam Pinewood 100mg/ml concentrate for solution for infusion is a clear, colourless, sterile concentrate. Presented in packs of five or ten, 5ml clear, neutral glass (Type I) vials. The vials are sealed with 13mm grey chlorobutyl PTFE (Teflon) faced rubber closures, secured with magenta aluminium Flip-Off caps.

Marketing Authorisation Holder and Manufacturer
Marketing authorisation holder: Pinewood Laboratories Limited, Ballymacarbry, Clonmel, Co. Tipperary, Ireland
Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF.

This medicine is authorised in the Member States of the European Economic Area under the following names:
Ireland: Levetiracetam Pinewood 100mg/ml concentrate for solution for infusion

This leaflet was last revised in 07/2022

The following information is intended for healthcare professionals only:

Directions for the proper use of Levetiracetam 100mg/ml concentrate for solution for infusion is provided in Section 3.

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

Table 1. Preparation and administration of Levetiracetam 100mg/ml concentrate for solution for infusion

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

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

Chemical and physical in-use stability has been demonstrated for 7 days at 5°C to 22°C when diluted with 0.9% sodium chloride, 5% dextrose or Hartmann's Solution to 2mg/ml. From a microbiological point of view, in-use storage time and conditions prior to use are the responsibility of the user.

Do not use if the product shows signs of deterioration such as discolouration.

Levetiracetam 100mg/ml concentrate for solution for infusion was found to be physically compatible and chemically stable when diluted to 2mg/ml and mixed with the following diluents for seven days when stored in infusion bags and stored at room temperature (5°C – 22°C).

Diluents:

- 0.9% sodium chloride
- 5% dextrose
- Hartmanns Solution to 2mg/ml