

Package Insert

1. Name of the product

Quetra 100 mg/ml oral solution

2. Name and Strength of Active Ingredient

Each ml contains 100 mg levetiracetam.

3. Dosage form

Oral solution.

Clear, colourless liquid with sweet fruity odour and bitter raspberry flavour.

4. Pharmacological Properties

Pharmacodynamics

Pharmacotherapeutic group: Antiepileptics, ATC code: N03AX14

The active substance, levetiracetam, is a pyrrolidone derivative (S-enantiomer of α -ethyl-2-oxo-1-pyrrolidine acetamide), chemically unrelated to existing antiepileptic active substances.

Mechanism of action

The mechanism of action of levetiracetam still remains to be fully elucidated. Levetiracetam does not alter basic cell characteristics and normal neurotransmission.

Levetiracetam affects intraneuronal Ca^{2+} levels by partial inhibition of N-type Ca^{2+} currents and by reducing the release of Ca^{2+} from intraneuronal stores. In addition, it partially reverses the reductions in GABA- and glycine-gated currents induced by zinc and β -carbolines. Furthermore, levetiracetam binds to a specific site in rodent brain tissue. This binding site is the synaptic vesicle protein 2A, believed to be involved in vesicle fusion and neurotransmitter exocytosis. Levetiracetam and related analogues show a rank order of affinity for binding to the synaptic vesicle protein 2A which correlates with the potency of their anti-seizure protection in the mouse audiogenic model of epilepsy. This finding suggests that the interaction between levetiracetam and the synaptic vesicle protein 2A seems to contribute to the antiepileptic mechanism of action of the medicinal product.

Pharmacodynamic effects

Levetiracetam induces seizure protection and primary generalised seizures without having a pro-convulsant effect. The primary metabolite is inactive.

An activity in both partial and generalised epilepsy conditions (epileptiform discharge/photoparoxysmal response) has confirmed the broad spectrum pharmacological profile of levetiracetam.

Pharmacokinetics

Levetiracetam is a highly soluble and permeable compound. The pharmacokinetic profile is linear with low intra- and inter-subject variability. There is no modification of the clearance after repeated administration. There is no evidence for any relevant gender, race or circadian variability. The pharmacokinetic profile is comparable in healthy volunteers and in patients with epilepsy.

Due to its complete and linear absorption, plasma levels can be predicted from the oral dose of levetiracetam expressed as mg/kg bodyweight. Therefore, there is no need for plasma level monitoring of levetiracetam.

A significant correlation between saliva and plasma concentrations has been shown in adults and children (ratio of saliva/plasma concentrations ranged from 1 to 1.7 for oral tablet formulation and after 4 hours post-dose for oral solution formulation).

Adults and adolescents

Absorption

Levetiracetam is rapidly absorbed after oral administration. Oral absolute bioavailability is close to 100 %. Peak plasma concentrations (C_{max}) are achieved at 1.3 hours after dosing. Steady-state is achieved after two days of a twice daily administration schedule.

Peak concentrations (C_{max}) are typically 31 and 43 µg/ml following a single 1,000 mg dose and repeated 1,000 mg twice daily dose, respectively.

The extent of absorption is dose-independent and is not altered by food.

Distribution

No tissue distribution data are available in humans.

Neither levetiracetam nor its primary metabolite are significantly bound to plasma proteins (< 10 %). The volume of distribution of levetiracetam is approximately 0.5 to 0.7 l/kg, a value close to the total body water volume.

Biotransformation

Levetiracetam is not extensively metabolised in humans. The major metabolic pathway (24 % of the dose) is an enzymatic hydrolysis of the acetamide group. Production of the primary metabolite, ucb L057, is not supported by liver cytochrome P450 isoforms. Hydrolysis of the acetamide group was measurable in a large number of tissues including blood cells. The metabolite ucb L057 is pharmacologically inactive.

Two minor metabolites were also identified. One was obtained by hydroxylation of the pyrrolidone ring (1.6 % of the dose) and the other one by opening of the pyrrolidone ring (0.9 % of the dose).

Other unidentified components accounted only for 0.6 % of the dose.

No enantiomeric interconversion was evidenced in vivo for either levetiracetam or its primary metabolite.

Elimination

The plasma half-life in adults was 7 ± 1 hours and did not vary either with dose, route of administration or repeated administration. The mean total body clearance was 0.96 ml/min/kg.

The major route of excretion was via urine, accounting for a mean 95 % of the dose (approximately 93 % of the dose was excreted within 48 hours). Excretion via faeces accounted for only 0.3 % of the dose.

The cumulative urinary excretion of levetiracetam and its primary metabolite accounted for 66 % and 24 % of the dose, respectively during the first 48 hours.

The renal clearance of levetiracetam and ucb L057 is 0.6 and 4.2 ml/min/kg respectively indicating that levetiracetam is excreted by glomerular filtration with subsequent tubular reabsorption and that the primary metabolite is also excreted by active tubular secretion in addition to glomerular filtration. Levetiracetam elimination is correlated to creatinine clearance.

Elderly

In the elderly, the half-life is increased by about 40 % (10 to 11 hours). This is related to the decrease in renal function in this population.

Renal impairment

The apparent body clearance of both levetiracetam and of its primary metabolite is correlated to the creatinine clearance. It is therefore recommended to adjust the maintenance daily dose of levetiracetam, based on creatinine clearance in patients with moderate and severe renal impairment.

In anuric end-stage renal disease adult subjects the half-life was approximately 25 and 3.1 hours during interdialytic and intradialytic periods, respectively.

The fractional removal of levetiracetam was 51 % during a typical 4-hour dialysis session.

Hepatic impairment

In subjects with mild and moderate hepatic impairment, there was no relevant modification of the clearance of levetiracetam. In most subjects with severe hepatic impairment, the clearance of levetiracetam was reduced by more than 50 % due to a concomitant renal impairment.

Paediatric population

Children (4 to 12 years)

Following single oral dose administration (20 mg/kg) to epileptic children (6 to 12 years), the half-life of levetiracetam was 6.0 hours. The apparent body weight adjusted clearance was approximately 30 % higher than in epileptic adults.

Infants and children (1 month to 4 years)

Following single dose administration (20 mg/kg) of a 100 mg/ml oral solution to epileptic children (1 month to 4 years), levetiracetam was rapidly absorbed and peak plasma concentrations were observed approximately 1 hour after dosing. The pharmacokinetic results indicated that half-life was shorter (5.3 h) than for adults (7.2 h) and apparent clearance was faster (1.5 ml/min/kg) than for adults (0.96 ml/min/kg).

5. Clinical Particulars

Indications

Quetra is indicated as monotherapy in the treatment of partial onset seizures with or without secondary generalisation patients from 16 years of age with newly diagnosed epilepsy.

Quetra is indicated as adjunctive therapy

- in the treatment of partial onset seizures with or without secondary generalisation in adults and children from 4 years of age with epilepsy.
- in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.
- in the treatment of primary generalised tonic-clonic seizures in adults and children from 12 years of age with Idiopathic Generalised Epilepsy.

Posology and method of administration

Posology

The oral solution may 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. The daily dose is administered in two equally divided doses.

Adults

Monotherapy

Adults and adolescents from 16 years of age

The recommended starting dose is 250 mg twice daily which should be increased to an initial therapeutic dose of 500 mg twice daily after two weeks. The dose can be further increased by 250 mg twice daily every two weeks depending upon the clinical response. The maximum dose is 1500 mg twice daily.

Add-on therapy

Adults (≥ 18 years) and adolescents (12 to 17 years) weighing 50 kg or more

The initial therapeutic dose is 500 mg twice daily. This dose can be started on the first day of treatment.

Depending upon the clinical response and tolerability, the daily dose can be increased up to 1500 mg twice daily. Dose changes can be made in 500 mg twice daily increases or decreases every two to four weeks.

Children

The physician should prescribe the most appropriate pharmaceutical form, presentation and strength according to age, weight and dose. The tablet formulation is not adapted for use in children under the age of 6 years. Levetiracetam oral solution is the preferred formulation for use in this population. In addition, the available dose strengths of the tablets are not appropriate for initial treatment in children weighing less than 25 kg, for patients unable to swallow tablets or for the administration of doses below 250 mg. In all of the above cases levetiracetam oral solution should be used.

The safety and efficacy of levetiracetam concentrate for solution for infusion in infants and children less than 4 years have not been established.

Monotherapy

The safety and efficacy of levetiracetam in children and adolescents below 16 years as monotherapy treatment have not been established.

There are no data available.

Add-on therapy

Add-on therapy for children (4 to 11 years) and adolescents (12 to 17 years) weighing less than 50 kg

Levetiracetam oral solution is the preferred formulation for use in children under the age of 6 years.

For children 6 years and above, levetiracetam oral solution should be used for doses under 250 mg, for doses not multiple of 250 mg when dosing recommendation is not achievable by taking multiple tablets and for patients unable to swallow tablets.

The initial therapeutic dose is 10 mg/kg twice daily.

Depending upon the clinical response and tolerability, the dose can be increased up to 30 mg/kg twice daily. Dose changes should not exceed increases or decreases of 10 mg/kg twice daily every two weeks.

The lowest effective dose should be used.

Dose in children 50 kg or greater is the same as in adults.

Dose recommendations for children and adolescents:

Weight	Starting dose: 10 mg/kg twice daily	Maximum dose: 30 mg/kg twice daily
10 kg ⁽¹⁾	100 mg (1 ml) twice daily	300 mg (3 ml) 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 twice daily	750 mg twice daily
From 50 kg ⁽²⁾	500 mg twice daily	1,500 mg twice daily

⁽¹⁾Children 25 kg or less should preferably start the treatment with Levetiracetam 100 mg/ml oral solution.

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

Special populations

Elderly

Adjustment of the dose is recommended in elderly patients with compromised renal function.

Renal impairment

The daily dose must be individualised according to renal function (see Section ‘Warnings and precautions’).

For adult patients, refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CL_{Cr}) in ml/min is needed. The CL_{Cr} in ml/min may be estimated from serum creatinine (mg/dl) determination, for adults and adolescents weighing 50 kg or more, the following formula:

$$\text{CL}_{\text{Cr}} (\text{ml/min}) = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}} \quad (\times 0.85 \text{ for women})$$

Then CL_{Cr} is adjusted for body surface area (BSA) as follows:

$$\text{CL}_{\text{Cr}} (\text{ml/min}/1.73 \text{ m}^2) = \frac{\text{CL}_{\text{Cr}} (\text{ml/min})}{\text{BSA subject (m}^2\text{)}} \times 1.73$$

Dosing adjustment for adult and adolescent patients weighing more than 50 kg with impaired renal function:

Group	Creatinine clearance (ml/min/1.73m ²)	Dosage and frequency
Normal	≥ 80	500 to 1500 mg twice daily
Mild	50-79	500 to 1000 mg twice daily
Moderate	30-49	250 to 750 mg twice daily
Severe	< 30	250 to 500 mg twice daily
End-stage renal disease patients undergoing dialysis (1)	-	500 to 1000 mg once daily (2)

(1) A 750 mg loading dose is recommended on the first day of treatment with levetiracetam.

(2) Following dialysis, a 250 to 500 mg supplemental dose is recommended.

For children with renal impairment, levetiracetam dose needs to be adjusted based on the renal function as levetiracetam clearance is related to renal function. This recommendation is based on a study in adult renally impaired patients.

The CLcr in ml/min/1.73 m² may be estimated from serum creatinine (mg/dl) determination, for young adolescents and children using the following formula (Schwartz formula):

$$\text{CLcr (ml/min/1.73 m}^2\text{)} = \frac{\text{Height (cm)} \times \text{ks}}{\text{Serum Creatinine (mg/dl)}}$$

ks= 0.55 in Children to less than 13 years and in adolescent female; ks= 0.7 in adolescent male.

Dosing adjustment for children and adolescents patients weighing less than 50 kg with impaired renal function:

Group	Creatinine clearance (ml/min/1.73m ²)	Dose and frequency (1)
		Children and adolescents weighing less than 50 kg
Normal	≥ 80	10 to 30 mg/kg (0.10 to 0.30 ml/kg) twice daily
Mild	50-79	10 to 20 mg/kg (0.10 to 0.20 ml/kg) twice daily
Moderate	30-49	5 to 15 mg/kg (0.05 to 0.15 ml/kg) twice daily
Severe	< 30	5 to 10 mg/kg (0.05 to 0.10 ml/kg) twice daily
End-stage renal disease patients undergoing dialysis	--	10 to 20 mg/kg (0.10 to 0.20 ml/kg) once daily (2) (3)

(1) Quetra oral solution should be used for doses under 250 mg, for doses not multiple of 250 mg when dosing recommendation is not achievable by taking multiple tablets and for patients unable to swallow tablets.

(2) A 15 mg/kg (0.15 ml/kg) loading dose is recommended on the first day of treatment with levetiracetam.

(3) Following dialysis, a 5 to 10 mg/kg (0.05 to 0.10 ml/kg) supplemental dose is recommended.

Hepatic impairment

No dose adjustment is needed in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the creatinine clearance may underestimate the renal insufficiency. Therefore a 50 % reduction of the daily maintenance dose is recommended when the creatinine clearance is < 60 ml/min/1.73 m².

Method of administration

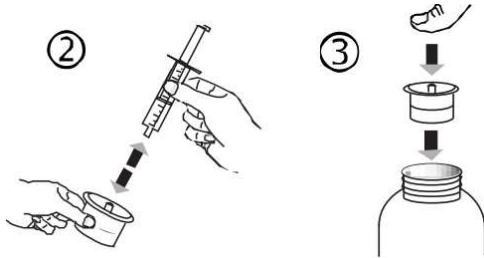
The oral solution may be diluted in a glass of water and may be taken with or without food. After oral administration the bitter taste of levetiracetam may be experienced. The daily dose is administered in two equally divided doses.

Instructions for use:

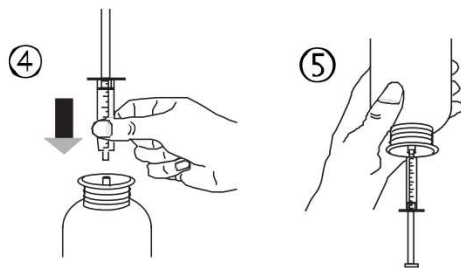
- Open the bottle: press the cap and turn it anticlockwise (figure 1).



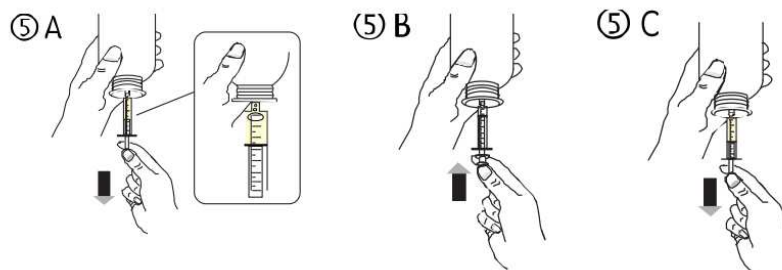
- Separate the adaptor from the syringe (figure 2). Insert the adaptor into the bottle neck (figure 3). Ensure it is well fixed.



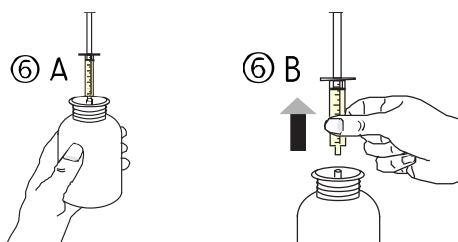
- Take the syringe and put it in the adaptor opening (figure 4). Turn the bottle upside down (figure 5).



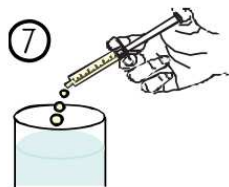
- Fill the syringe with a small amount of solution by pulling the piston down (figure 5A), then push the piston upward in order to remove any possible bubble (figure 5B). Pull the piston down to the graduation mark corresponding to the quantity in milliliters (ml) prescribed by your doctor (figure 5C).



- 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 by pushing the piston to the bottom of the syringe (figure 7).



Drink the whole contents of the glass:

- Close the bottle with the plastic screw cap.
- Wash the syringe with water (figure 8).



Contraindications

Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients.

Warnings and Precautions

Renal impairment

The administration of levetiracetam to patients with renal impairment may require dose adjustment. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection (see section 'Posology and method of administration').

Acute kidney injury

The use of levetiracetam has been rarely associated with acute kidney injury with a time to onset ranging from a few days to several months.

Blood cell counts

Rare cases of decreased blood cell counts (neutropenia, agranulocytosis, leucopenia, thrombocytopenia and pancytopenia) have been described in association with levetiracetam administration, generally at the beginning of the treatment. Complete blood cell counts are advised in patients experiencing important weakness, pyrexia, recurrent infections or coagulation disorders (see section 'Side Effects').

Suicide

Suicide, suicide attempt, suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents (including levetiracetam). Anti-epileptic medicinal products has shown a small increased risk of suicidal thoughts and behaviour. The mechanism of this risk is not known.

There is potential for an increase in risk of suicidal thoughts or behaviours. Therefore patients should be monitored for signs of depression and/or suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of depression and/or suicidal ideation or behaviour emerge.

Abnormal and aggressive behaviours

Levetiracetam may cause psychotic symptoms and behavioural abnormalities including irritability and aggressiveness. Patients treated with levetiracetam should be monitored for developing psychiatric signs suggesting important mood and/or personality changes. If such behaviours are noticed, treatment adaptation or gradual discontinuation should be considered. If discontinuation is considered, it is recommended to withdraw it gradually (e.g. in adults and adolescents weighing more than 50 kg: 500 mg decreases twice daily every two to four weeks; in children and adolescents weighing more than 50 kg: dose decrease should not exceed 10 mg/kg twice daily every two weeks).

Worsening of seizures

As with other types of antiepileptic drugs, levetiracetam may rarely exacerbate seizure frequency or severity. This paradoxical effect was mostly reported within the first month after levetiracetam initiation or increase of the dose, and was reversible upon drug discontinuation or dose decrease. Patients should be advised to consult their physician immediately in case of aggravation of epilepsy.

Electrocardiogram QT interval prolongation

Rare cases of ECG QT interval prolongation have been observed during the post-marketing surveillance. Levetiracetam should be used with caution in patients with QTc-interval prolongation, in patients concomitantly treated with drugs affecting the QTc-interval, or in patients with relevant pre-existing cardiac disease or electrolyte disturbances.

Paediatric population

Available data in children did not suggest impact on growth and puberty. However, long term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children remain unknown.

Excipients

Quetra 100 mg/ml oral solution contains methyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed).

Quetra 100 mg/ml oral solution contains liquid maltitol (E965). Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Interaction with other medicaments

Antiepileptic medicinal products

Levetiracetam did not influence the serum concentrations of existing antiepileptic medicinal products (phenytoin, carbamazepine, valproic acid, phenobarbital, lamotrigine, gabapentin and primidone) and that these antiepileptic medicinal products did not influence the pharmacokinetics of levetiracetam.

Probenecid

Probenecid (500 mg four times daily), a renal tubular secretion blocking agent, has been shown to inhibit the renal clearance of the primary metabolite, but not of levetiracetam. Nevertheless, the concentration of this metabolite remains low.

Methotrexate

Concomitant administration of levetiracetam and methotrexate has been reported to decrease methotrexate clearance, resulting in increased/prolonged blood methotrexate concentration to potentially toxic levels. Blood methotrexate and levetiracetam levels should be carefully monitored in patients treated concomitantly with the two drugs.

Oral contraceptives and other pharmacokinetic interactions

Levetiracetam 1,000 mg daily did not influence the pharmacokinetics of oral contraceptives (ethinyl-estradiol and levonorgestrel); endocrine parameters (luteinizing hormone and progesterone) were not modified. Levetiracetam 2,000 mg daily did not influence the pharmacokinetics of digoxin and warfarin; prothrombin times were not modified. Co-administration with digoxin, oral contraceptives and warfarin did not influence the pharmacokinetics of levetiracetam.

Laxatives

Decreased levetiracetam efficacy when the osmotic laxative macrogol has been concomitantly administered with oral levetiracetam. Therefore, macrogol should not be taken orally for one hour before and for one hour after taking levetiracetam.

Food and alcohol

The extent of absorption of levetiracetam was not altered by food, but the rate of absorption was slightly reduced.

No data on the interaction of levetiracetam with alcohol are available.

Pregnancy and Lactation

Women of child bearing potential

Specialist advice should be given to women who are of childbearing potential. Treatment with levetiracetam should be reviewed when a woman is planning to become pregnant. As with all antiepileptic medicines, sudden discontinuation of levetiracetam should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the unborn child. Monotherapy should be preferred whenever possible because therapy with multiple antiepileptic medicines AEDs could be associated with a higher risk of congenital malformations than monotherapy, depending on the associated antiepileptics.

Pregnancy

Levetiracetam can be used during pregnancy, if after careful assessment it is considered clinically needed. In such case, the lowest effective dose is recommended.

Physiological changes during pregnancy may affect levetiracetam concentration. Decrease in levetiracetam plasma concentrations has been observed during pregnancy. This decrease is more pronounced during the third trimester (up to 60% of baseline concentration before pregnancy). Appropriate clinical management of pregnant women treated with levetiracetam should be ensured.

Breast-feeding

Levetiracetam is excreted in human breast milk. Therefore, breast-feeding is not recommended. However, if levetiracetam treatment is needed during breastfeeding, the benefit/risk of the treatment should be weighed considering the importance of breastfeeding.

Driving and using machines

Levetiracetam has minor or moderate influence on the ability to drive and use machines. Due to possible different individual sensitivity, some patients might experience somnolence or other central nervous system related symptoms, especially at the beginning of treatment or following a dose increase. Therefore, caution is recommended in those patients when performing skilled tasks, e.g. driving vehicles or operating machinery. Patients are advised not to drive or use machines until it is established that their ability to perform such activities is not affected.

Side effects

Summary of the safety profile

The most frequently reported adverse reactions were nasopharyngitis, somnolence, headache, fatigue and dizziness. The safety profile of levetiracetam is generally similar

across age groups (adult and paediatric patients) and across the approved epilepsy indications.

Tabulated list of adverse reactions

<u>MedDRA SOC</u>	<u>Frequency category</u>			
	<u>Very common</u>	<u>Common</u>	<u>Uncommon</u>	<u>Rare</u>
<u>Infections and infestations</u>	Nasopharyngitis			Infection
<u>Blood and lymphatic system disorders</u>			Thrombocytopenia, leukopenia	Pancytopenia, neutropenia, agranulocytosis
<u>Immune system disorders</u>				Drug reaction with eosinophilia and systemic symptoms (DRESS) , Hypersensitivity (including angioedema and anaphylaxis)
<u>Metabolism and nutrition disorders</u>		Anorexia	Weight decreased , weight increase	Hyponatraemia
<u>Psychiatric disorders</u>		Depression , hostility/ aggression, anxiety, insomnia, nervousness /irritability	Suicide attempt, suicidal ideation, psychotic disorder, abnormal behaviour, hallucination, anger, confusional state, panic attack affect lability/mood swings, agitation	Completed suicide, personality disorder, thinking abnormal, delirium
<u>Nervous system disorders</u>	Somnolence, headache	Convulsion, balance	Amnesia, memory	Choreoathetosis , dyskinesia,

		disorder, dizziness, lethargy, tremor	impairment, coordination abnormal/ataxia, paraesthesia, disturbance in attention	hyperkinesia, gait disturbance, encephalopathy, seizures aggravated
<u>Eye disorders</u>			Diplopia, vision blurred	
<u>Ear and labyrinth disorders</u>		Vertigo		
<u>Cardiac disorders</u>				Electrocardio- gram QT prolonged
<u>Respiratory, thoracic and mediastinal disorders</u>		Cough		
<u>Gastrointestinal disorders</u>		Abdominal pain, diarrhoea, dyspepsia, vomiting, nausea		Pancreatitis
<u>Hepatobiliary disorders</u>			Liver function test abnormal	Hepatic failure, hepatitis
<u>Skin and subcutaneous tissue disorders</u>		Rash	Alopecia, eczema, pruritus,	Toxic epidermal necrolysis, Stevens- Johnson syndrome, erythema multiforme
<u>Musculoskeletal and connective tissue disorders</u>			Muscular weakness, myalgia	Rhabdomyoly- sis and blood creatinine phosphokinase increased *
<u>Renal and urinary disorders</u>				Acute kidney injury

<u>General disorders and administration site conditions</u>		Asthenia/fatigue		
<u>Injury, poisoning and procedural complications</u>			Injury	

* Prevalence is significantly higher in Japanese patients when compared to non-Japanese patients.

The risk of anorexia is higher when levetiracetam is coadministered with topiramate.

In several cases of alopecia, recovery was observed when levetiracetam was discontinued.

Bone marrow suppression was identified in some of the cases of pancytopenia.

Cases of encephalopathy have rarely been observed after levetiracetam administration. These undesirable effects generally occurred at the beginning of the treatment (few days to a few months) and were reversible after treatment discontinuation.

Paediatric population

The adverse event profile of levetiracetam is generally similar across age groups and across the approved epilepsy indications. In children and adolescents aged 4 to 16 years, vomiting (very common), agitation (common), mood swings (common), affect lability (common), aggression (common), abnormal behaviour (common), and lethargy (common) were reported more frequently than in other age ranges or in the overall safety profile. In infants and children aged 1 month to less than 4 years, irritability (very common) and coordination abnormal (common) were reported more frequently than in other age groups or in the overall safety profile.

Symptoms and Treatment of Overdose

Symptoms

Somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed with levetiracetam overdoses.

Management of overdose

After an acute overdose, the stomach may be emptied by gastric lavage or by induction of emesis. There is no specific antidote for levetiracetam. Treatment of an overdose will be symptomatic and may include haemodialysis. The dialyser extraction efficiency is 60 % for levetiracetam and 74 % for the primary metabolite.

6. Pharmaceutical Particulars

Storage conditions

Store below 30 °C, in the original container to protect from light.

Shelf-life

3 years

Pack size available

Amber glass bottles with child resistant closure. Pack sizes of:

- 300 ml Quetra oral solution, with an oral syringe of 10 ml (graduated every 0.25 ml) and an adaptor for the syringe.
- 150 ml Quetra oral solution, with an oral syringe of 3 ml (graduated every 0.1 ml) and an adaptor for the syringe.
- 150 ml Quetra oral solution, with an oral syringe of 1 ml (graduated every 0.05 ml) and an adaptor for the syringe.

Not all pack sizes may be marketed.

7. Manufacturer

Remedica Ltd.

Aharnon Street, Limassol Industrial Estate, 3056 Limassol, Cyprus

8. Product registration holder

Eucogen Sdn. Bhd.,

No. 6A, Jalan Sungai Burung U 32/U, Bukit Rimau Seksyen 32, 40460 Shah Alam
Selangor, Malaysia.

9. Date of revision of the text

01/07/2022

For internal use only: my-pi-quetra-oral-sol-a12Font size: 7, as measured in Times New Roman