Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Iracet 250 Tablet
(Levetiracetam USP 250 mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains Levetiracetam USP 250 mg.

Excipient(s) with known effect: Lactose.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

A pink coloured, caplet-shaped, film-coated tablet having a break-line on one side and plain on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Iracet (Levetiracetam) is indicated as adjunctive therapy for:

- Partial onset seizures
- Myoclonic seizures in patients with Juvenile Myoclonic Epilepsy
- Primary generalised tonic-clonic seizures

4.2 Posology and method of administration

Treatment should be initiated with a daily dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Additional dosing increments may be given (1000 mg/day additional every 2 weeks) to a maximum recommended daily dose of 3000 mg.

Use in paediatric patients

Dosing in paediatric patients should be based on age and body weight as follows:

Age / weight	**Initial dose (daily)**	**Incremental dose (daily)***
1 month to < 6 months	7 mg/kg twice daily	21 mg/kg twice daily
6 months to < 4 years	10 mg/kg twice daily	25 mg/kg twice daily
4 years to < 16 years	10 mg/kg twice daily	30 mg/kg twice daily
Adolescent with 20-40 kg body weight	250 mg twice daily	750 mg twice daily

*The daily dose should be increased every 2 weeks.

Adult patients with impaired renal function

Levetiracetam dosing must be individualised according to the patient's renal function status. The recommended doses and dose adjustment for adult patients with impaired renal function are shown below:

Group	**Creatinine clearance (mL/min)**	**Dosage (mg)**	**Frequency**

Normal	> 80	500 to 1,500	Every 12 h
Mild	50 - 80	500 to 1,000	Every 12 h
Moderate	30 - 50	250 to 750	Every 12 h
Severe	< 30	250 to 500	Every 12 h
Patients using dialysis	—	500 to 1,000	Every 24 h*

*Following dialysis, a 250 to 500 mg supplemental dose is recommended.

Method of administration: For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Patients should be advised to seek prompt medical attention should any of the following occur during treatment: severe allergic reactions; abnormal thoughts; dark urine; decreased coordination; extreme dizziness, drowsiness, tiredness or weakness; fever, chills or persistent sore throat; hallucinations; memory loss; mouth sores; muscle or neck pain; new or worsening mental problems; mood or behaviour changes; suicidal thoughts or attempts; unusual bruising or bleeding; vision changes; or yellowing of the skin or eyes.

4.5 Interaction with other medicinal products and other forms of interaction

No potential drug interaction has been reported.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Pregnancy category C.

Lactation:

No data on the use of Levetiracetam in breast-feeding women are available. Data from animals indicate that Levetiracetam is secreted into milk. Therefore, Levetiracetam is contraindicated during breast-feeding.

4.7 Effects on ability to drive and use machines

Levetiracetam has minor or moderate influence on the ability to drive and use machines. Due to possible 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.

4.8 Undesirable effects

Dizziness, drowsiness, irritability, sore throat, tiredness and weakness are some of the common adverse effects. In rare cases, severe allergic reactions may occur.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms:

Somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma have been 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiepileptics, other antiepileptics.
ATC Code: N03AX14

Mechanism of action

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.
Levetiracetam induces seizure protection in a broad range of animal models of partial and primary generalised seizures without having a pro-convulsant effect. The primary metabolite is inactive. In man, activity in both partial and generalised epilepsy conditions (epileptiform discharge / photo paroxysmal response) has confirmed the broad-spectrum pharmacological profile of levetiracetam.

5.2 Pharmacokinetic properties

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.
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 the oral tablet formulation and after 4 hours post-dose for the oral solution formulation).

Adults and adolescents
Absorption:
Levetiracetam is rapidly absorbed after oral administration. Oral absolute bioavailability is close to 100%. Peak plasma concentrations (Cmax) are achieved at 1.3 hours after dosing. Steady-state is achieved after two days of a twice-daily administration schedule. Peak concentrations (Cmax) 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 obtained by hydroxylation of the pyrrolidone ring (1.6% of the dose) and the other by opening of the pyrrolidone ring (0.9% of the dose). Other unidentified components accounted for only 0.6% of the dose. No enantiomeric interconversion was evidenced in vivo for either levetiracetam or its primary metabolite.
In vitro, levetiracetam and its primary metabolite have been shown not to inhibit the major human liver cytochrome P450 isoforms (CYP3A4, 2A6, 2C9, 2C19, 2D6, 2E1 and 1A2), glucuronyl transferase (UGT1A1 and UGT1A6) and epoxide hydroxylase activities. In addition, levetiracetam does not affect the in vitro glucuronidation of valproic acid. In human hepatocytes in culture, levetiracetam had little or no effect on CYP1A2, SULT1E1 or UGT1A1. Levetiracetam caused mild induction of CYP2B6 and CYP3A4. The in vitro data and in vivo interaction data on oral contraceptives, digoxin and warfarin indicate that no significant enzyme induction is expected in vivo. Therefore, the interaction of levetiracetam with other substances, or vice versa, is unlikely.

Elimination:
The plasma half-life in adults was 7 ± 1 hour 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 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.
Following repeated oral dose administration (20 to 60 mg/kg/day) to epileptic children (4 to 12 years), levetiracetam was rapidly absorbed. Peak plasma concentration was observed 0.5 to 1.0 hour after dosing. Linear and dose proportional increases were observed for peak plasma concentrations and area under the curve. The elimination half-life was approximately 5 hours. The apparent body clearance was 1.1 ml/min/kg.

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).
In the population pharmacokinetic analysis conducted in patients from 1 month to 16 years of age, body weight was significantly correlated to apparent clearance (clearance increased with an increase in body weight) and apparent volume of distribution. Age also had an influence on both parameters; this effect was pronounced for the younger infants, and subsided as age increased, to become negligible around 4 years of age.
In both population pharmacokinetic analyses, there was about a 20% increase of apparent clearance of levetiracetam when it was co-administered with an enzyme-inducing antiepileptic medicinal product.

5.3 Preclinical safety data
Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients
Microcrystalline Cellulose BP (PH 101)
Lactose
Pregelatinised Starch
Povidone
Sodium Starch Glycolate Type A
Isopropyl Alcohol
Colloidal Anhydrous Silica
Magnesium Stearate
Opadry II 85G 54101 Pink

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months (2 years).

6.4 Special precautions for storage
Store below 30°C, protect from light and moisture.

6.5 Nature and contents of container
30 tablets in Alu-PVDC blister pack.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorisation holder
SQUARE Pharmaceuticals Ltd.
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8. Marketing authorisation number
H2025/CTD9261/20039

9. Date of first authorisation/renewal of the authorisation
1st September, 2025

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