EPITAM®

Levetiracetam

ACTION

Antiepileptic.

INDICATIONS

Epitam is indicated as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalization in patients with epilepsy.

DOSAGE AND ADMINISTRATION

Epitam tablets must be taken orally, swallowed with a sufficient quantity of liquid and may be taken with or without food. The daily dose is administered in two equally divided doses.

Adults and adolescents older than 16 years:

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 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.

Special consideration:

• Elderly (from 65 years old):

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

• Children

There are insufficient data to recommend the use of levetiracetam in children and adolescents under 16 years of age.

• Patients with renal impairment:

The daily dose must be individualized according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in ml/min is needed. The CLcr in ml/min may be estimated from serum creatinine (mg/dl) determination using the following formula:

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

Dosing adjustment for patients with impaired renal function

Group	Creatinine clearance (ml/min)	Dosage and frequency
Normal	> 80	500 to 1,500 mg twice daily
Mild	50 - 79	500 to 1,000 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 1,000 mg once daily (2)

(1) A 750 mg loading dose is recommended on the first day of treatment with Epitam.
(2) Following dialysis, a 250 to 500 mg supplemental dose is recommended.

• Patients with 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 < 70 ml/min.

CONTRAINDICATIONS

Hypersensitivity to levetiracetam or other pyrrolidone derivatives or any of the excipients.

WARNINGS AND PRECAUTIONS

In accordance with current clinical practice, if levetiracetam has to be discontinued, it is recommended to withdraw it gradually (e.g. 500 mg twice daily decrements every two to four weeks). There are insufficient data for the withdrawal of concomitant antiepileptic medicinal products, once seizure control with Epitam in the add-on situation has been reached, in order to reach monotherapy on Epitam.

The administration of levetiracetam to patients with renal impairment may require dose adaptation. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection.

Drug Interactions

Data indicate that 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 (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. It is expected that other drugs excreted by active tubular secretion could also reduce the renal clearance of the metabolite. The effect of levetiracetam on probenecid was not studied and the effect of levetiracetam on other actively secreted drugs, e.g. NSAIDs, sulphonamides and methotrexate is unknown.

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.

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

Levetiracetam should not be used during pregnancy unless clearly necessary.

Breast-feeding is not recommended during treatment.

Effects on ability to drive and use machines

Due to possible different individual sensitivity, some patients might experience, at the beginning of treatment or following a dose increase, somnolence or other central nervous system related symptoms. Therefore, caution is recommended in those patients when performing skilled tasks, e.g. driving vehicles or operating machinery.

SIDE EFFECTS

The most frequent undesirable effects reported with levetiracetam are somnolence and asthenia.

The other undesirable effects reported with levetiracetam are

- **Nervous system disorders:** dizziness, vertigo, convulsion, depression, emotional instability, hostility, insomnia, nervousness, ataxia, tremor, amnesia
- **General disorders:** headache, accidental injury
- **Digestive disorders:** nausea, dyspepsia, diarrhea, anorexia
- **Skin disorders:** rash
- **Eye disorders:** diplopia

Some of the undesirable effects like somnolence, asthenia and dizziness may be more common at the beginning of the treatment or at dosage increase.

OVERDOSE

• Symptoms

There is no experience with doses greater than 5,000 mg/day.

No serious adverse events were reported by healthy volunteers after single doses of up to and including 5,000 mg.

• 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 hemodialysis. The dialyzer extraction efficiency is 60% for levetiracetam and 74% for the primary metabolite.

STORAGE

Store below 25°C.

PRESENTATIONS

Tablets

EPITAM 250:	Levetiracetam 250 mg/tablet
EPITAM 500:	Levetiracetam 500 mg/tablet
EPITAM 750:	Levetiracetam 750 mg/tablet

Excipients: Povidone, Maize Starch, Croscarmellose sodium, Magnesium-stearate, Opadry II White, Opadry II Yellow, Opadry II pink.

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by:
HIKMA Pharmaceuticals, Amman-Jordan

Keep medicament out of the reach of children

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