Levetiracetam Injection is for intravenous use only (2.1).

Levetiracetam may cause behavioral abnormalities and psychotic symptoms. Patients treated with levetiracetam should be monitored.

One vial of Levetiracetam Injection contains 500 mg levetiracetam (500 mg per 5 mL).

DOSAGE AND ADMINISTRATION

Levetiracetam Injection is for intravenous use only (2.1).

Adults 16 Years and Older: 500 mg twice daily; increase by 500 mg twice daily every 2 weeks to recommended dose of 2,000 mg twice daily.

Pediatric Patients: 12 Years and Older: For use in the treatment of primary generalized tonic-clonic seizures in patients ≥6 years of age with idiopathic generalized epilepsy (1.3).

In the clinical trial, the mean daily dose was 44 mg/kg in this age group.

Preparation and Administration Instructions

Switching to Oral Dosage

Levetiracetam Injection: 500 mg per 5 mL Single-Dose Vial (3)

Other Antiepileptic Drugs

Lactated Ringer’s injection

Using the following formula:

Total daily dose (mL/day) = ------------------------------------------------------------

Primary Generalized Tonic-Clonic Seizures

9 to 15 Years: 10 mg/kg twice daily; increase by 10 mg/kg twice daily every 2 weeks to recommended dose of 30 mg/kg twice daily (2.3).

Pediatric Patients: 12 Years and Older: For use in the treatment of primary generalized tonic-clonic seizures in patients ≥6 years of age with idiopathic generalized epilepsy (1.3).

These highlights do not include all the information needed to use Levetiracetam Injection safely and effectively. See 17 for PATIENT COUNSELING INFORMATION Revised: 01/2015
In the controlled clinical study that included patients 4 years of age and older with PGTC seizures, the most common adverse reaction was somnolence, neck stiffness, and dizziness. These were observed in a higher percentage of patients receiving levetiracetam in combination with other AEDs compared to those receiving placebo. In the study using levetiracetam tablets in patients with myoclonic seizures, the most common adverse reactions in patients receiving levetiracetam were somnolence, neck stiffness, and dizziness, occurring more frequently than in placebo-treated patients.

Levetiracetam is a white to off-white crystalline powder with a faint odor and a bitter taste. It is very soluble in water (104.0 g/100 mL). It is rapidly absorbed after oral administration. The absolute bioavailability of levetiracetam is 96.2%. The pharmacokinetics of levetiracetam in pediatric patients was studied in a repeat dose pharmacokinetic study conducted in pediatric patients (age 4 to 12 years) at doses of 20 mg/kg/day, 40 mg/kg/day, and 80 mg/kg/day. The AUC(0-12) at steady-state was equivalent to AUC_{inf} following an equivalent single dose.

The precise mechanism(s) by which levetiracetam exerts its antiepileptic effect is unknown. The antiepileptic activity of levetiracetam is believed to result from the ability of levetiracetam to increase the [Ca^{2+}]-dependent release of neurotransmitter from nerve terminals. This increase in neurotransmitter release is thought to produce a broad anticonvulsant activity that may be effective in a variety of seizure types.

12.1 Mechanism of Action

Levetiracetam increases the calcium-dependent release of neurotransmitter from nerve terminals. The mechanism of action of levetiracetam is not well understood, but it is thought that levetiracetam may act by increasing the release of neurotransmitters at the synaptic cleft. This increase in neurotransmitter release is thought to produce a broad anticonvulsant activity that may be effective in a variety of seizure types.

12.2 Pharmacokinetics

Levetiracetam is rapidly absorbed after oral administration. The absolute bioavailability of levetiracetam is 96.2%. The pharmacokinetics of levetiracetam in pediatric patients was studied in a repeat dose pharmacokinetic study conducted in pediatric patients (age 4 to 12 years) at doses of 20 mg/kg/day, 40 mg/kg/day, and 80 mg/kg/day. The AUC(0-12) at steady-state was equivalent to AUC_{inf} following an equivalent single dose.

13.3. Dosage and Administration

In anuric (end stage renal disease) patients, the total body clearance decreased 70% compared to normal subjects (CLcr >80 mL/min). In patients with impaired renal function, the total body clearance decreased by 40% in the mild group (CLcr = 50 to 80 mL/min), 50% in the moderate group (CLcr = 20 to 49 mL/min), and 60% in the severe group (CLcr <20 mL/min).

14.1 Adverse Reactions

The percentage of patients (y-axis) who achieved ≥50% reduction in weekly seizure rates from baseline in partial onset seizure frequency over 12 weeks is displayed in Figure 3. There was no evidence of significant QTc prolongation in this study.

15.9. Pregnancy

There is no information on the use of levetiracetam in pregnant women. The effects of levetiracetam on reproductive function in pregnant women have not been studied. There is no information on the effects of levetiracetam on the fetus in pregnant women.

15.10. Nursing Mothers

The effects of levetiracetam on the ability of breastfeeding women to nurse their babies have not been studied.

15.11. Pediatric Use

Levetiracetam is not recommended for use in children younger than 2 years of age. The safety and effectiveness of levetiracetam in children younger than 2 years of age have not been established. Levetiracetam is not recommended for use in children younger than 2 years of age due to the lack of safety and efficacy data in this population.

17. CARCINOGENESIS

An analysis of the CBCL/6-18 indicated, on average, a worsening in levetiracetam-treated patients in aggressive behavior, one of the domains measured by the CBCL/6-18. There were no significant differences in the rates of other domains measured by the CBCL/6-18 between levetiracetam-treated and placebo-treated patients.

18.1. Impairment of Fertility

There is no information on the effects of levetiracetam on male fertility. There is no information on the effects of levetiracetam on female fertility.

18.2. Pregnancy

There is no information on the use of levetiracetam in pregnant women. The effects of levetiracetam on reproductive function in pregnant women have not been studied. There is no information on the effects of levetiracetam on the fetus in pregnant women.

18.3. Nursing Mothers

The effects of levetiracetam on the ability of breastfeeding women to nurse their babies have not been studied.

18.4. Pediatric Use

Levetiracetam is not recommended for use in children younger than 2 years of age. The safety and effectiveness of levetiracetam in children younger than 2 years of age have not been established. Levetiracetam is not recommended for use in children younger than 2 years of age due to the lack of safety and efficacy data in this population.

19. ADVERSE REACTIONS

The overall adverse reaction profile of levetiracetam was similar between females and males. There are insufficient data to support a difference in the occurrence of adverse reactions based on gender.

20.1. Drug Interactions

The effects of concomitant AEDs on the pharmacokinetics of levetiracetam and the effects of levetiracetam on the pharmacokinetics of concomitant AEDs have not been studied. The effects of levetiracetam on the pharmacokinetics of other medications that are primarily metabolized by CYP3A4 or CYP2C19 have not been studied.

21.2. Oral Contraceptives

The effects of levetiracetam on the effectiveness of oral contraceptives have not been studied. There is no information on the effects of oral contraceptives on the effectiveness of levetiracetam.

21.3. Estrogens

The effects of levetiracetam on the effectiveness of estrogens have not been studied. There is no information on the effects of estrogens on the effectiveness of levetiracetam.