Levetiracetam in Sodium Chloride Injection for intravenous use only

Premixed bags are prelabeled and color-coded

Single-use 100-mL bags available in the following dosage forms and strengths:
- Levetiracetam in 0.82% sodium chloride injection (500 mg/100 mL)
- Levetiracetam in 0.75% sodium chloride injection (1000 mg/100 mL)
- Levetiracetam in 0.54% sodium chloride injection (1500 mg/100 mL)

Designed specifically for hospital use

**Preparation**
- Premixed and ready to administer; no dilution required

**Administration**
- Administered as a 15-minute IV infusion

**Access**
- Single-use 100-mL dual port bag

**Storage instructions**
- Store at 20°C to 25°C (68°F to 77°F)
- Physically compatible and chemically stable for at least 24 hours when mixed with lorazepam, diazepam, and valproate sodium and stored at controlled room temperature 15°C to 30°C (59°F to 86°F)*
- Shelf life is 24 months

**Indications and Usage**

Levetiracetam in Sodium Chloride Injection is an antiepileptic drug for intravenous use indicated as adjunctive therapy for adults (16 years and older) with the following seizure types when oral administration is temporarily not feasible: epilepsy with partial onset seizures; myoclonic seizures in patients with juvenile myoclonic epilepsy (JME); primary generalized tonic-clonic seizures with idiopathic generalized epilepsy.

**Important Safety Information**

**Neuropsychiatric Adverse Reactions:** Levetiracetam in Sodium Chloride Injection causes neuropsychiatric reactions including somnolence and fatigue, muscle coordination difficulties and behavioral abnormalities (e.g., psychotic symptoms, suicide ideation, and other abnormalities). Patients treated with any antiepileptic drug (AED) for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

**Withdrawal Seizures:** Antiepileptic drugs, including levetiracetam, should be withdrawn gradually to minimize the risk of increased seizure frequency.

**Hematologic Abnormalities:** Minor, but statistically significant, decreases in total mean red blood cell (RBC) count, mean hemoglobin, and mean hematocrit, and possible significant decreases in white blood cell (WBC) and neutrophil count, were seen in levetiracetam-treated patients. Although there were no obvious hematologic abnormalities observed in patients with JME, the limited number of patients makes any conclusion tentative. The data from the partial seizure patients should be considered to be relevant for JME patients.

**Hepatic Abnormalities:** There were no meaningful changes in mean liver function tests (LFT) in controlled trials in adult patients; lesser LFT abnormalities were similar in drug and placebo treated patients in controlled trials (1.4%).

**Adverse Reactions:** In clinical trials, the most common adverse reactions observed with levetiracetam were somnolence, asthenia, infection and dizziness. Depression, nervousness, anxiety and emotional lability were also observed. In postmarketing experience, the following additional reactions have been reported: abnormal liver function test, hepatic failure, hepatitis, leukopenia, neutropenia, pancreatitis, pancytopenia (including bone marrow suppression), thrombocytopenia, weight loss, alopecia (with recovery after drug discontinuation), and suicidal behavior.

Important Safety Information continued on back.
Dosing instructions

➤ Starting dose: 1000 mg/day, given as 500 mg twice daily
➤ Dose increase: Every 2 weeks by 1000 mg/day as needed and tolerated to the recommended dose of 3000 mg/day
➤ For adult patients with impaired renal function, dosing must be individualized according to patient’s renal function status. Please see enclosed full Prescribing Information for additional information
➤ Patients must be advised to notify their physician if they are pregnant prior to therapy

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For more information or to order products, please contact Mylan Institutional Customer Relations: 800.848.0462

Learn more at mylan.com

Important Safety Information (continued)

The prescriber should be aware that adverse reactions were reported in clinical trials of levetiracetam in addition to concurrent AED therapy, and cannot be used to predict the frequency of adverse experiences in medical practice where patient characteristics and other factors may differ from those prevailing during clinical studies. An inspection of the adverse reactions frequencies provides the prescriber with one basis to estimate the relative contribution of drug and non-drug factors to the adverse reaction incidences in the population studied.

**Pregnancy Category C:** Based on animal data, levetiracetam may cause fetal harm and should be used during pregnancy only after considering the potential benefit-risk ratio.

Physicians are advised to recommend pregnant patients taking levetiracetam injection enroll in the North American Antiepileptic Drug (NAAED) pregnancy registry. Patients can find registry information at http://www.aedpregnancyregistry.org or by calling 1-888-233-2334.

Levetiracetam is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from levetiracetam, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Safety and effectiveness of levetiracetam injection in patients below the age of 16 years have not been established.

In clinical trials, no overall differences in safety were observed between geriatric subjects (≥ 65 years) and younger subjects. There were insufficient numbers of elderly subjects to adequately assess the effectiveness of levetiracetam in these patients. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Clearance of levetiracetam is decreased in patients with renal impairment and is correlated with creatinine clearance. Caution should be taken in dosing patients with moderate and severe renal impairment and in patients undergoing hemodialysis. The dosage should be reduced in patients with impaired renal function receiving levetiracetam and supplemental doses should be given to patients after dialysis.

To report SUSPECTED ADVERSE REACTIONS, contact Mylan Institutional LLC at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for contraindications, warnings, precautions, adverse events and complete dosing guidelines.

*There are no data to support the physical compatibility of Levetiracetam Injection with antiepileptic drugs that are not listed on the reverse side.

Please refer to the enclosed full Prescribing Information regarding the following:

- 3000 mg/day is the maximum recommended dose for partial onset seizures
- The effectiveness of doses lower than 3000 mg/day has not been studied in treating myoclonic seizures in patients with juvenile myoclonic epilepsy
- The effectiveness of doses lower than 3000 mg/day has not been adequately studied in patients with primary generalized tonic-clonic seizures
Levetiracetam in Sodium Chloride Injection is an antiepileptic drug indicated for the treatment of certain types of seizures. The following sections outline the use and administration of the drug.

**INDICATIONS AND USES**
Levetiracetam in Sodium Chloride Injection is indicated for the treatment of:
- Primary generalized tonic-clonic seizures (1.1)
- Partial onset seizures (1.1)

**DOSAGE FORMS AND STRENGTHS**
- Single-use 100 mL bags

**CONTRAINDICATIONS**
- None (4)

**WARNINGS AND PRECAUTIONS**
- Neurropsychiatric adverse reactions including 1) somnolence and fatigue, 2) coordination difficulties, and 3) behavioral abnormalities (e.g., psychotic symptoms, suicide ideation, and other behaviors). Monitor for these events and discontinue the drug if they persist.
- Withdrawal Seizures: Levetiracetam must be gradually withdrawn (5.2).
- Most common adverse reactions (incidence in children is >50% between levetiracetam-treated patients and placebo-treated patients) include seizure frequency, dizziness, asthenia, and headache. Discontinue the drug if these events are severe.
- Significant behavioral adverse reactions (incidence of levetiracetam-treated patients greater than levetiracetam-treated patients, but <5%) include depression, nervousness, anxiety, and emotional lability (5.1).

**ADVERSE REACTIONS**
In controlled trials of adult patients with epilepsy experiencing partial onset seizures, 3.2% of levetiracetam-treated patients reported somnolence, compared to 0.8% of placebo patients. The events did not lead to discontinuation or dose reduction. The treatment dose was decreased in 0.8% of treated patients and in 0.2% of placebo patients. In 0.2% of patients, the dose was reduced due to coordination difficulties, while one of the treated patients was hospitalized due to worsening of pre-existing ataxia.

**Dosage Forms and Strengths**
Single-use 100 mL bags of Levetiracetam in Sodium Chloride Injection are available.

**Contraindications**
None (4)

**Warnings and Precautions**
- Neurpsychiatric adverse reactions including 1) somnolence and fatigue, 2) coordination difficulties, and 3) behavioral abnormalities (e.g., psychotic symptoms, suicide ideation, and other behaviors). Monitor for these events and discontinue the drug if they persist.
- Withdrawal Seizures: Levetiracetam must be gradually withdrawn (5.2).
- Most common adverse reactions (incidence in children is >50% between levetiracetam-treated patients and placebo-treated patients) include seizure frequency, dizziness, asthenia, and headache. Discontinue the drug if these events are severe.
- Significant behavioral adverse reactions (incidence of levetiracetam-treated patients greater than levetiracetam-treated patients, but <5%) include depression, nervousness, anxiety, and emotional lability (5.1).

**Adverse Reactions**
In controlled trials of adult patients with epilepsy experiencing partial onset seizures, 3.2% of levetiracetam-treated patients reported somnolence, compared to 0.8% of placebo patients. The events did not lead to discontinuation or dose reduction. The treatment dose was decreased in 0.8% of treated patients and in 0.2% of placebo patients. In 0.2% of patients, the dose was reduced due to coordination difficulties, while one of the treated patients was hospitalized due to worsening of pre-existing ataxia.
6. ADVERSE REACTIONS

6.1 Clinical Trials Experience

The adverse reactions that are described in this section include all those reported for levetiracetam injection, tablets and oral solution. Equivalent doses of IV and oral levetiracetam result in equivalent Cmax, Cmin, and total systemic exposure to levetiracetam when the IV dose is administered as a 15 minute infusion.

A total of 3.2% of treated and 1.8% of placebo patients had at least one laboratory abnormality (u.01% of patients) and at least one laboratory abnormality (u.01% of patients) was considered to be of significant clinical importance. No patients had at least one laboratory abnormality (u.01% of patients) considered to be of significant clinical importance in the course of usual medical practice where patient characteristics and other factors may differ from those prevailing during clinical studies. Similarly, the adverse reaction pattern for patients with JME is expected to be different from that seen in patients with partial seizures, this is likely due to the smaller sample size.

The overall adverse experience profile of levetiracetam was similar between females and males. There are insufficient data to support a statement regarding the distribution of adverse experience reports by age and race.

6.2 Postmarketing Experience

In vitro and in vivo data on possible interactions indicate that levetiracetam is unlikely to produce, or be subject to, pharmacokinetic interactions. Levetiracetam, and its major metabolite, at concentrations well above Cmax levels achieved during therapeutic use, does not display any pharmacodynamic interaction with substances that are used to measure liver function test, hepatic failure, hepatitis, leukaemia, leuponemia, pancreatitis, paracynopha (for patients with bone marrow suppression identified in some of these cases), thrombocytopenia and weight loss. Alopecia has been associated with levetiracetam use; recovery was observed in majority of cases when levetiracetam was discontinued due to LFT abnormalities of such severity (including completed suicide, suicide attempt and suicidal ideation) with marketed levetiracetam [see Patient Counseling Information (7.1)].

There have been rare reports of bone and joint pain, usually in the lower extremities of patients treated with levetiracetam.

In the placebo-controlled study using levetiracetam tablets in patients with myoclonic seizures, the most frequently reported adverse reactions in patients using levetiracetam in combination with other AEDs, not seen at an equivalent frequency among placebo-treated patients, were somnolence, neck pain, and pharyngitis.

Table 3 lists adverse reactions that occurred in at least 5% of juvenile idiopathic epileptic patients treated with levetiracetam tablets and more commonly in patients treated with placebo. In this study, either levetiracetam or placebo was added to concurrent AED therapy. Adverse reactions were usually mild to moderate in intensity. Table 4 lists adverse reactions that occurred in at least 5% of idiopathic generalized epileptic patients experiencing PGTC seizures treated with levetiracetam tablets and more commonly in patients treated with placebo. In this study, either levetiracetam or placebo was added to concurrent AED therapy. Adverse reactions were usually mild to moderate in intensity. Table 5 shows the most common adverse events that required the lowering of the dose of levetiracetam.

Table 6: Adverse Reactions that Resulted in Discontinuation or Dose Reduction that Occurred More Frequently in Levetiracetam-Treated Patients than in Placebo-Treated Patients

Although the pattern of adverse reactions in this study seems somewhat different from that seen in partial epilepsy patients, this is likely due to the smaller sample size. The data from the partial seizure patients should be considered to be tentative. The data from the partial seizure patients should be considered to be tentative. The data from the partial seizure patients should be considered to be tentative. The data from the partial seizure patients should be considered to be tentative.
3.9 Probenecid
Probenecid, a renal tubular secretion blocking agent, administered at a dose of 500 mg four times a day, did not change the pharmacokinetics of levetiracetam when administered to humans. UCB LS07, which is approximately doubled in the presence of probenecid while the fraction of oral absorption is not significantly altered. The elimination half-life of UCB LS07 in the presence of probenecid decreased 60%, probably related to competitive inhibition of tubular secretion of UCB LS07. The effect of probenecid on probenecid is not known.

8. USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C

In animals, levetiracetam produced evidence of developmental toxicity, including teratogenicity. At doses similar to or greater than human therapeutic doses, levetiracetam should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. As with other antiepileptic drugs, physiological changes during pregnancy may affect levetiracetam concentration during pregnancy. Discontinuation of antiepileptic treatments may result in disease worsening, which can be harmful to the mother and the fetus.

Administration to female rats throughout pregnancy and lactation led to increased incidences of minor fetal skeletal abnormalities and retardation of offspring growth pre- and postnatally at doses ≥350 mg/kg/day (approximately equivalent to the maximum recommended human dose of 1200 mg/kg/day). Maternal toxicity was also observed at a dose of 1800 mg/kg/day (6 times the MRHD on a mg/m² basis). There was no overt maternal toxicity at the doses used in this study.

Treatment of pregnant rabbits during the period of organogenesis resulted in increased incidences of minor fetal skeletal abnormalities and retardation of offspring growth pre- and postnatally at doses ≥3000 mg/kg/day (approximately 4 times MRHD on a mg/m² basis). No obvious maternal toxicity was observed at any dose. Histopathological examinations of maternal tissues did not reveal any toxic effects. Administration of levetiracetam to rats in the presence of probenecid decreased 60%, probably related to an increase in the maternal toxicity at doses ≥3000 mg/kg/day (12 times the MRHD on a mg/m² basis). Maternal toxicity was also observed at a dose of 1800 mg/kg/day.

When pregnant rats were treated during the period of organogenesis, fetal weights were decreased and the incidence of fetal skeletal variations was increased at a dose of 1000 mg/kg/day (3.5 times the MRHD on a mg/m² basis). The development of a dose of 200 mg/kg/day (1.3 times the MRHD on a mg/m² basis). Maternal toxicity was also observed at an dose of 1800 mg/kg/day.

Treatment of rats during the last third of gestation and throughout lactation produced no adverse developmental or maternal effects at doses of up to 1800 mg/kg/day (6 times the MRHD on a mg/m² basis).

North American Antiepileptic Drug Pregnancy Registry
To provide information regarding the effects of in utero exposure to levetiracetam injection, physicians are advised to recommend that pregnant patients taking levetiracetam injection enroll in the North American Antiepileptic Drug Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by the patients themselves. Information on the registry or on how to access it can also be found at the website [http://www.aedpregnancyregistry.org].

3.10 Labor and Delivery
The effect of levetiracetam on labor and delivery in humans is unknown.

3.11 Nursing Mothers
Levetiracetam is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from levetiracetam, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

3.12 Pediatric Use
Safety and effectiveness of levetiracetam injection in patients below the age of 16 years have not been established.

3.13 Geriatric Use
The safety and effectiveness of this drug have not been established in elderly patients; however, clinical experience suggests that it is probably safe to use in patients 65 years or older. Although there is no evidence that age itself affects the pharmacokinetics of levetiracetam, decreased renal function in elderly patients may necessitate reduced dosage in the elderly.

4. OVERDOSE
5.2 Generalized Status Epilepticus
In cases of generalized status epilepticus or life-threatening acute seizures which do not respond to conventional anticonvulsant therapy, levetiracetam 1000 mg intravenous infusion is equivalent to levetiracetam 1500 mg intravenous injection when administered over 20 minutes. For adult patients, the time interval between consecutive doses should be at least 4 hours.

4.5 Administration of Levetiracetam Injection
Clinicians should be aware that levetiracetam is not extensively metabolized in humans. The major metabolic pathways of levetiracetam are not known. The pharmacokinetics of levetiracetam may be altered by other drugs that are extensively metabolized, such as those with a high hepatic extraction ratio.

5.2.1 Administration of Levetiracetam Injection
Levetiracetam injection is an antiepileptic drug available as a clear, colorless, sterile solution for intravenous administration.

The chemical name of levetiracetam, a single anion, is (S)-2-ethyl-2-oxo-pyrrolidin-3-yl acetate trihydrate. It is not liver cytochrome P450 dependent. The metabolites of levetiracetam are not extensively metabolized to produce, or be subject to, pharmacokinetic interactions. Levetiracetam is not a substrate for, human liver cytochrome P450 isoforms, epoxide hydrolase or PAPS-dependent UDP-glucuronidation enzymes. In addition, levetiracetam does not affect the in vitro glucuronidation of valproic acid.

5.2.2 Administration of Levetiracetam Injection
Levetiracetam injection is an antiepileptic drug available as a clear, colorless, sterile solution for intravenous administration.

The precise mechanism(s) by which levetiracetam exerts its antiepileptic effect is unknown. The antiepileptic activity of levetiracetam was assessed in a number of animal models for specific types of human epilepsy is uncertain.

Levetiracetam in Sodium Chloride Injection is a clear, colorless, sterile solution for intravenous administration.

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13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Rats were dosed with levetiracetam in the diet for 104 weeks at doses of 50, 300, and 1800 mg/kg/day. The highest dose corresponds to 6 times the maximum recommended daily human dose (MRHD) of 3000 mg on a mg/m² basis and it also provided systemic exposure (AUC) approximately 6 times that achieved in humans receiving the MRHD. There was no evidence of carcinogenicity. A study was conducted in which mice received levetiracetam in the diet for 80 weeks at doses of 60, 240, and 960 mg/kg/day (high dose is equivalent to 2 times the MRHD on a mg/m² or exposure basis). Although no evidence for carcinogenicity was seen, the potential for a carcinogenic response has not been fully evaluated in that species because adequate doses have not been studied.

Mutagenesis

Levetiracetam was not mutagenic in the Ames test or in mammalian cells in vitro in the Chinese hamster ovary/HGPRT locus assay; it was not clastogenic in an in vitro analysis of metaphase chromosomes obtained from Chinese hamster ovary cells or in an in vivo mouse micronucleus assay. The product formulation and major human metabolite of levetiracetam (ucb L057) was not mutagenic in the Ames test or in the vitro mouse lymphoma assay.

Impairment of Fertility

No adverse effects on male or female fertility or reproductive performance were observed in rats at doses up to 1800 mg/kg/day (approximately 6 times the maximum recommended human dose on a mg/m² or exposure basis).

14. CLINICAL STUDIES

All efficacy trials utilized oral formulations. The recommendation for the parenteral formulation is based upon these studies as well as the demonstration of comparable bioavailability of the oral and the parenteral formulation [see Pharmacokinetics (12.3)].

In the following studies, statistical significance versus placebo indicates a p value <0.05.

14.1 Partial Onset Seizures

Effectiveness in Partial Onset Seizures in Adults with Epilepsy

The effectiveness of levetiracetam as adjunctive therapy in adults was established in three multicenter, randomized, double-blind, placebo-controlled clinical trials in patients who had refractory partial onset seizures with or without secondary generalization. The tablet formulation was used in all these studies. In Study 1, 904 patients were randomized to placebo, 1000 mg, 2000 mg, or 3000 mg/day. Patients enrolled in Study 1 or Study 2 had refractory partial onset seizures for at least two years and had taken two or more antiepileptic drugs (AEDs). In Study 3, 92 patients were randomized to one and could take a maximum of two AEDs. During the baseline period, patients had to have experienced at least two partial onset seizures during each 4-week period. The criteria for statistical significance in all studies was a p<0.05.

Study 1

Study 1 was a double-blind, placebo-controlled, parallel-group study conducted at 41 sites in the United States comparing levetiracetam 1000 mg/day (N=97), levetiracetam 2000 mg/day (N=101), and placebo (N=95) given in equally divided doses twice daily. After a prospective baseline period of 12 weeks, patients were randomized to one of the three treatment groups described above. The 18-week treatment period consisted of a 6-week titration period, followed by a 12-week fixed-dose evaluation period, during which concomitant AEDs were held constant. The primary measure of effectiveness was a between group comparison of the percent reduction in weekly seizure frequency relative to placebo over the entire randomized treatment period (titration + evaluation period) within the three treatment groups (x-axis) is presented in Figure 2.

The percentage of patients (y-axis) who achieved ≥50% reduction in weekly seizure rates from baseline in partial onset seizure frequency over the entire randomized treatment period (titration + evaluation period) within the three treatment groups (x-axis) is presented in Table 7. The responder rate (incidence of patients with ≥50% reduction from baseline in partial onset seizure frequency) displayed in Table 7 shows the results of the analysis of Study 3.

Study 2

Study 2 was a double-blind, placebo-controlled, crossover study conducted at 62 centers in Europe comparing levetiracetam 1000 mg/day (N=186), levetiracetam 2000 mg/day (N=105), and placebo (N=111) given in equally divided doses twice daily. The first period of the study (Period A) was designed to be analyzed as a parallel-group study. After a prospective baseline period of up to 12 weeks, patients were randomized to one of the three treatment groups described above. The 16-week treatment period consisted of the 4-week titration period followed by a 12-week fixed-dose evaluation period, during which concomitant AED regimens were held constant. The primary measure of effectiveness was a between group comparison of the percent reduction in weekly partial onset seizure frequency relative to placebo over the entire randomized treatment period (titration + evaluation period). Secondary outcome variables included the responder rate (incidence of patients with ≥50% reduction from baseline in partial onset seizure frequency). The results of the analysis of Period A are displayed in Table 8.

The comparison of levetiracetam 2000 mg/day to levetiracetam 1000 mg/day for responder rate was statistically significant (P<0.002). Analysis of the trial as a cross-over yielded similar results.

The percentage of patients (y-axis) who achieved ≥50% reduction in weekly seizure rates from baseline in partial onset seizure frequency over the entire randomized treatment period (titration + evaluation period) within the two treatment groups (x-axis) is presented in Figure 2.

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The percentage of patients (y-axis) who achieved ≥50% reduction in weekly seizure rates from baseline in partial onset seizure frequency over the entire randomized treatment period (titration + evaluation period) within the two treatment groups (x-axis) is presented in Figure 2.

14.2 Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy

Effectiveness in Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy (JME)

The effectiveness of levetiracetam as adjunctive therapy (added to other antiepileptic drugs) in patients with idiopathic generalized epilepsy experiencing primary generalized tonic-clonic (PGTC) seizures was established in one multicenter, randomized, double-blind, placebo-controlled study, conducted at 50 sites in 8 countries. Eligible patients on a stable dose of 1 or 2 antiepileptic drugs (AEDs) experiencing at least 3 PGTC seizures during the 2-month combination period (titration + evaluation period) within the 4 weeks prior to the prospective baseline period and at least one PGTC seizure during the 4-week prospective baseline period were randomized to either levetiracetam or placebo. The 8-week combined baseline period is referred to as “baseline” in the remainder of this section. The population included 164 patients (levetiracetam N=80, placebo N=84) with idiopathic generalized epilepsy (predominately juvenile myoclonic epilepsy, juvenile absence epilepsy, absence epilepsy with myoclonic seizures, or myoclonus with Grand Mal seizures on awakening) experiencing primary generalized tonic-clonic seizures. Each of these syndromes of idiopathic generalized epilepsy was well represented in this patient population. Patients were titrated over 4 weeks to a target dose of 3000 mg/day for adults or a pediatric target dose of 60 mg/kg/day and treated at a stable dose of 3000 mg/day or 60 mg/kg/day for children over 25 weeks (evaluation period). Study drug was given in 2 equally divided doses per day.

The primary measure of effectiveness was the percent reduction in baseline weekly PGTC seizure frequency for levetiracetam and placebo treatment groups over the treatment period (titration + evaluation period). There was a statistically significant decrease from baseline in PGTC frequency in the levetiracetam-treated patients compared to the placebo-treated patients.

15. HOW SUPPLIED/STORAGE AND HANDLING

New Supplied

Levetiracetam in Sodium Chloride Injection is a clear, colorless, sterile solution that is available in a single-use 100 mL dual port bag with an aluminum over wrap. The container closure is not made with natural rubber latex. It is available in the following presentations:

16. PATIENT COUNSELING INFORMATION

Patients should be advised to notify their physician if they are pregnant prior to therapy.

Patients should be advised that levetiracetam may cause dizziness and somnolence and to be cautious when performing activities requiring alertness and/or sustained attention such as driving and operating potentially hazardous machinery or engage in other hazardous activities until they have gained sufficient experience on levetiracetam to gauge whether it adversely affects their ability to perform these activities.

Patients should be advised that levetiracetam may cause changes in behavior (e.g., aggression, agitation, anger, anxiety, apathy, depression, and increased irritability) and in rare cases patients may experience psychotic symptoms.

Patients should be advised to immediately report any symptoms of depression and/or suicidal ideation to their prescribing physician as suicide is a common complication and suicide ideation have been reported in patients treated withlevetiracetam.

Manufactured for:

Mylan Institutional LLC
P.O. Box 267
Canonsburg, PA 15317
Made in Switzerland

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