HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use LEVETIRACETAM TABLETS USP safely and effectively. See full prescribing information for LEVETIRACETAM TABLETS USP.

LEVETIRACETAM tablets USP, for oral use Initial U.S. Approval: 1999

3/2024 INDICATIONS AND USAGE Levetracetam tablets USP are indicated for the treatment of partial-onset seizures in patients 1 month of age and older (1.1) EVEN are indicated for adjunctive therapy for treatment of Partial onset seizures in patients one month of age and older with hiplicpy (1.1) Myochonic seizures in patients 12 years of age and older with juvenile myochonic epilepsy (1.2) Primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy (1.3)

DOSAGE AND ADMINISTRATION
 Use the oral solution for pediatric patients with body weight ± 20 kg (2.1).
 For pediatric patients, use weight-based dosing for the oral solution with a calibrated measuring device
 (not a householt teaspoon or tablespoon) (2.1)

- Partial Onset Seizures (monotherapy or adjunctive therapy)

 1 Month to < 6 Months: 7 mg/kg twice daily; increase by 7 mg/kg twice daily every 2 weeks to recommended dose of 21 mg/kg twice daily; corease by 10 mg/kg twice daily; or easily control to < 4 Years; 10 mg/kg twice daily; C2)</td>

 6 Months to < 4 Years; 10 mg/kg twice daily; C2)</td>
- recommended dose of 2.5 mg/kg twice daily. (*i*,*c*) 4 Years to -1 for 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. (*i*,*c*) Adults 16 Years and Older: 500 mg twice daily. (*i*, crease by 500 mg twice daily every 2 weeks to a recommended dose of 1500 mg twice daily (2.2)
- Myoclonic Seizures in Adults and Pediatric Patients 12 Years and Older 500 mg twice daily; increase by 500 mg twice daily every 2 weeks to recommended dose of 1500 mg twice daily (2.3)

- Primary Centralized Totics-Crinic Selecters 6 Years 10 8 Years 10 registery blee daily, increase in increments of 10 mg/kg twice daily every 2 weeks to recommended dose of 30 mg/kg twice daily (2.4) Adults 16 Years and Older: S00 mg twice daily, increase by 500 mg twice daily every 2 weeks to recommended dose of 1500 mg twice daily (2.4)

Adult Patients with Impaired Renal Function • Dose adjustment is recommended, based on the patient's estimated creatinine clearance (2.5, 8.6)

DOSAGE FORMS AND STRENGTHS 250 mg, 500 mg, 750 mg, and 1000 mg film-coated, scored tablets (3)

····· CONTRAINDICATIONS ·

CONTRAINDICATIONS
 CONTRAINDICATIONS
 CONTRAINDICATIONS
 CONTRAINORATIONS
 CONTRAINED AND PRECAUTIONS
 Behavioral abnormalities including psychotic symptoms, suicial ideation, irritability, and aggressive
behavior have been observed; monitor patients for psychiatric signs and symptoms (5.1)
 Suicidal Behavior, and ideation: Monitor patients for new or ownersing depression, suicidal
thoughtsbehavior, and orunusual changes in mood or behavior (5.2)
 Monitor for somoheree and faiture and advice and they or operate machinesu until these

- thoughts/behavior, and/or unusual changes in mood or behavior (5.2) Monitor for somolence and fattigue and advise patients not to driver or operate machinery until they have gained sufficient experience on levertracetam (5.3) Serious Dermatological Reactions: Discontinule levertracetam at the first sign of rash unless clearly not drug related (5.5) Drug Reaction with Scientophila and Systemic Symptoms (DRESS)/Multiorgan Hypersensitivity: Drug Reaction and Barnatine etilogy (5.6) Coordination Difficulties: Monitor for atakia, abnormal gait, and incoordination. Advise patients to not drive or operate machinery unit they have gained experience on levetTacetam (5.7) Withdraval Seizures: Levetracetam must be gradually withdravn (5.8)

ADVERSE REACTIONS Most common adverse reactions (incidence 25% more than placebo) include: Adult patients: sommolence, asthemia, infection and dizziness (6.1) • Pediatric patients: fatigue, aggression, nasal congestion, decreased appetite, and irritability (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceutical inc. at 1-800-399-2561 or FDA at 1-800-FDA-1088 or www.rda.gov/medwatch. Pregnancy: Plasma levels of levelinicacianin major due foresand and the gregnancy: Based on animal data, may cause fetal harm (5.11, 8.1) See 17 for PATENT COUNSELING INFORMATION and Medication Guide.

Revised: 4/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Levetiracetam tablets USP are indicated for treatment of partial-onset seizures in patients 1 month of age and older.

1.2 Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy

Levetiracetam tablets USP are indicated as adjunctive therapy for the treatment of myoclonic seizures in patients 12 years of age and older with juvenile myoclonic epilepsy.

1.3 Primary Generalized Tonic-Clonic Seizures

Levetiracetam tablets USP are indicated as adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Leveti-acetant tablets USP are given orally with or without food. The levetiracetam dosing regimen depends on the indication, age group, dosage form (tablets), and renal function.

Prescribe the oral solution for pediatric patients with body weight \leq 20 kg. Prescribe the oral solution or tablets for pediatric patients with body weight above 20 kg.

When using the oral solution in pediatric patients, dosing is weight-based (mg per kg) using a calibrated measuring device (not a household teaspoon or tablespoon).

Levetiracetam tablets should be swallowed whole. Levetiracetam tablets should not be chewed or crushed.

2.2 Dosing for Partial Onset Seizures

The recommended dosing for monotherapy and adjunctive therapy is the same; as outlined below.

Adults 16 Years of Age and Older

Initiate treatment 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. There is no evidence that doses greater than 3000 mg/day confer additional benefit.

Pediatric Patients 1 Month to < 6 Months

Initiate treatment with a daily dose of 14 mg/kg in 2 divided doses (7 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 14 mg/kg to the recommended daily dose of 42 mg/kg (21 mg/kg twice daily). In the clinical trial, the mean daily dose was 35 mg/kg in this age group.

6 Months to <4 Years:

Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose in 2 weeks by an increment of 20 mg/kg to the recommended daily dose of 50 mg/kg (25 mg/kg twice daily). If a patient cannot tolerate a daily dose of 50 mg/kg, the daily dose may be reduced. In the clinical trial, the mean daily dose was 47 mg/kg in this age group.

4 Years to < 16 Years:

Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 omg/kg twice daily). If a patient cannot tolerate a daily dose of 60 mg/kg, The daily dose may be reduced. In the clinical trial, the mean daily dose was 44 mg/kg. The maximum daily dose was 3000 mg/day.

For levetiracetam tablet dosing in pediatric patients weighing 20 to 40 kg, initiate treatment with a daily dose of 500 mg given as twice daily dosing (250 mg twice daily). Increase the daily dose every 2 weeks by increments of 500 mg to a maximum recommended daily dose of 1500 mg (750 mg twice daily).

For levetiracetam tablet dosing in pediatric patients weighing more than 40 kg, initiate treatment with a daily dose of 1000 mg/day given as twice daily dosing (500 mg twice daily). Increase the daily dose every 2 weeks by increments of 1000 mg/day to a maximum recommended daily dose of 3000 mg (1500 mg twice daily).

Levetiracetam Oral Solution Weight-Based Dosing Calculation For Pediatric Patients The following calculation should be used to determine the appropriate daily dose of oral solution for pediatric patients:

Daily dose (mg/kg/day) x patient weight (kg) Total daily dose (mL/day) = -----100 mg/mL

2.3 Dosing for Myoclonic Seizures in Patients 12 Years of Age and Older with Juvenile Myoclonic Epilepsy

Initiate treatment with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Increase the dosage by 1000 mg/day every 2 weeks to the recommended daily dose of 3000 mg. The effectiveness of doses lower than 3000 mg/day has not been studied.

2.4 Dosing for Primary Generalized Tonic-Clonic Seizures

Adults 16 Years of Age and Older

Initiate treatment with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Increase dosage by 1000 mg/day every 2 weeks to the recommended daily dose of 3000 mg. The effectiveness of doses lower than 3000 mg/day has not been adequately studied.

Pediatric Patients 6 to <16 Years of Age

Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose of 60 mg/kg (30 dose every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 domg/kg twice daily). The effectiveness of doses lower than 60 mg/kg/day has not been adequately studied. Patients with body weight \leq 20 kg should be dosed with oral solution. Patients with body weight \leq 20 kg should be dosed with oral solution. Patients with body weight \leq 20 kg should be dosed with oral solution. Patients with body weight above 20 kg can be dosed with either tablets or oral solution. Patients with body weight above 20 kg can be dosed with oral solution. tablets should be administered.

2.5 Dosage Adjustments in Adult Patients with Renal Impairment

Levetiracetam tablets dosing must be individualized according to the patient's renal Level action takes dosing must be monoulaized according to the patient's final runcion status. Recommended dosage adjustments for adults are shown in Table 1. In order to calculate the dose recommended for patients with renal impairment, creatinine clearance adjusted for body surface area must be calculated. To do this an estimate of the patient's creatinine clearance (CLcr) in mL/min must first be calculated using the following formula:

~	[140-age (years)] x weight (kg)	(x 0.85 - for female
CLcr=	72 x serum creatinine (mg/dL)	patients)

Then CLcr is adjusted for body surface area (BSA) as follows: CLcr (mL/min)

BSA subject (m²) x 1.73 CLcr (mL/min/1.73m2)= -----

Group	Creatinine Clearance (mL/min/1.73 m ²)	Dosage (mg)	Frequency
Normal	>80	500 to 1,500	Every 12 hours
Mild	50 to 80	500 to 1,000	Every 12 hours
Moderate	30 to 50	250 to 750	Every 12 hours
Severe	<30	250 to 500	Every 12 hours
ESRD patients using dialysis		500 to 1,000*	Every 24 hours*
* Following dialysis, a 250 to 500	mg supplemental	dose is recomme	nded.

2.6 Discontinuation of Levetiracetam tablets

Avoid abrupt withdrawal from Levetiracetam Tablets in order to reduce the risk of

increased seizure frequency and status epilepticus [see WARNINGS AND PRECAUTIONS (5.8)]

3 DOSAGE FORMS AND STRENGTHS

Levetiracetam tablets, 250 mg are blue coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X01" on the other side.

Levetiracetam tablets, 500 mg are yellow coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on ether side of the breakline on one side and "X02" on the other side.

Levetiracetam tablets, 750 mg are orange coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X03" on the other side.

Levetiracetam tablets, 1000 mg are white to off-white coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X04" on the other side.

4 CONTRAINDICATIONS

Levetiracetam is contraindicated in patients with a hypersensitivity to levetiracetam Reactions have included anaphylaxis and angioedema [see WARNINGS AND PRECAUTIONS (5.4)].

5 WARNINGS AND PRECAUTIONS

5.1 Behavioral Abnormalities and Psychotic Symptoms

Levetiracetam may cause behavioral abnormalities and psychotic symptoms. Patients treated with levetiracetam should be monitored for psychiatric signs and symptoms. Behavioral Abnormalities

In clinical studies, 13% of adult levetiracetam-treated patients and 38% of pediatric Heritaria aduets, rearbornador to table to the deam of age) compared to 6% and 19% of adult and pediatric placebo-treated patients (4 to 16 years of age) compared to 6% and 19% of adult and pediatric placebo-treated patients, experienced non-psychotic behavioral symptoms (reported as aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, hyperkinesias, irritability, nervousness, neurosis, and personality disorder).

and personality usion use, in A randomized double-bind, placebo-controlled study was performed to assess the neurocognitive and behavioral effects of levetiracetam as adjunctive therapy in pediatric patents (4 to 16 years of age). The results from an exploratory analysis indicated a worsening in levetiracetam-treated patients on aggressive behavior (one of eight behavior dimensions) as measured in a standardized and systematic way using a validated instrument, the Achenbach Child Behavior Checklist (CBCL/6 to 18).

In clinical studies in pediatric patients 1 month to < 4 years of age, irritability was reported in 12% of the levetiracetam-treated patients compared to 0% of placebo-treated patients.

In clinical studies, 1.7% of adult levetiracetam-treated patients discontinued treatment due to behavioral adverse reactions, compared to 0.2% of placebo-treated patients. The treatment dose was reduced to 0.8% of adult levetiracetam-treated patients and in 0.5% of placebo-treated patients. Overall, 11% of levetiracetam-treated pediatric patients experienced behavioral symptoms associated with discontinuation or dose reduction, compared to 6% of placebo-treated patients.

Psychotic Symptoms

Psychotic Symptoms In clinical studies, 1% of levetiracetam-treated adult patients, 2% of levetiracetam-treated pediatric patients 4 to 16 years of age, and 17% of levetiracetam-treated pediatric patients 1 month to <4 years of age experienced psychotic symptoms, compared to 0.2%, 2%, and 5% in the corresponding age groups treated with placebo. In a controlled study that assessed the neurocognitive and behavioral effects of levetiracetam in pediatric patients 4 to 16 years of age, 1.6% of levetiracetam-treated patients experienced paranoia, compared to 0% of placebo-treated patients. In the sam study, 3.1% of levetiracetam-treated patients experienced confusional state, compared to 0% of placebo-treated patients [see USE IN SPECIFIC POPULATIONS (8.4)].

In clinical studies, two (0.3%) levetiracetam-treated adult patients were hospitalized and In clinical studies, two (0.3%) levelracetam-treated adult patients were nospitalized and their treatment was discontinued due to psychosis. Both events, reported as psychosis developed within the first week of treatment and resolved within 1 to 2 weeks following treatment discontinuation. There was no difference between drug and placebo-treated patients in the incidence of the pediatric patients who discontinued treatment due to psychotic and non-psychotic adverse reactions.

5.2 Suicidal Behavior and Ideation

Antiepileptic drugs (AEDs), including levetiracetam, increase the risk of suicidal thoughts Altebender unge (ALCO), including level action, increase the risk of subcalandoug or behavior in patients taking these drugs for any indication. Patients treated with any 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.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% cl:1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In these trials, which had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal behavior or dieaton among 27,663 AED-treated patients was 0.43%, compared to 0.24% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal thinking or behavior for every 530 patients treated. There were four suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

On survet. The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed. beyond

The risk of suicidal thoughts or behavior was generally consistent among drugs in the data analyzed. The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5 to 100 years) in the clinical trials analyzed. Table 2 shows absolute and relative risk by indication for all evaluated AEDs.

Table 2: Risk by Indication for Antiepileptic Drugs in the Pooled Analysis

Indication	Placebo Patients with Events Per	Drug Patients with Events Per	Relative Risk:Incidence of Events in Drug Patients/Incidence in Placebo Patients	Risk Difference: Additional Drug Patients with Events Per 1000 Patients
	1000	1000		
	Patients	Patients		
Epilepsy	1.0	3.4	3.5	2.4
Psychiatric	5.7	8.5	1.5	2.9
Other	1.0	1.8	1.9	0.9
Total	2.4	4.3	1.8	1.9

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

Anone considering prescribing levetiracetam or any other AED must balance the risk of suicidal thoughts or behaviors with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

5.3 So ence and Fatigue

Levetiracetam may cause somolence and fatigue. Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on levetiracetam to gauge whether it adversely affects their ability to drive or operate machinery.

Somnolence

In controlled trials of adult patients with epilepsy experiencing partial onset seizures, 15% of levetiracetam-treated patients reported somnolence, compared to 8% of placebo-treated patients. There was no clear dose response up to 3000 mg/day. In a study where there was no titration, about 45% of patients receiving 4000 mg/day reported somnolence. The somnolence was considered serious in 0.3% of levetiracetam-

treated patients, compared to 0% in the placebo group. About 3% of levetiracetam-treated patients discontinued treatment due to somnolence, compared to 0.7% of placebo-treated patients. In 1.4% of levetiracetam-treated patients and 0.9% of placebo-treated patients, the dose was reduced, while 0.3% of the levetiracetam-treated patients were hospitalized due to somnolence.

Asthenia

In controlled clinical studies of adult patients with epilepsy experiencing partial onset seizures, 15% of levetiracetam-treated patients reported asthenia, compared to 9% of placebo-treated patients. Treatment was discontinued due to asthenia in 0.8% of levetiracetam-treated patients as compared to 0.3% of placebo-treated patients. In 0.5% of levetiracetam-treated patients and in 0.2% of placebo-treated patients, the dose was reduced due to asthenia.

Somnolence and asthenia occurred most frequently within the first 4 weeks of treatment. In general, the incidences of somnolence and fatigue in the pediatric partial onset sezure studies, and in pediatric and adult myochcine and primary generalized tonic-clonic seizure studies were comparable to those of the adult partial onset seizure studies

5.4 Anaphylaxis and Angioedema

5.4 Anaprytaxis and Angloedema Levetiracteam can cause anaphylaxis or angloedema after the first dose or at any time during treatment. Signs and symptoms in cases reported in the postmarketing setting have included hypotension, hives, rash, respiratory distress, and swelling of the face. Ip, mouth, eye, tongue, throat, and feet. In some reported cases, reactions were life-threatening and required emergency treatment. If a patient develops signs or symptoms of anaphylaxis or angloedema, levetracetam should be discontinued and the patient should seek immediate medical attention. Levetracetam should be discontinued permanently if a clean atternative etiology for the reaction cannot be established [see CONTRAINDICATIONS (4)].

5.5 Serious Dermatological Reactions

5.5 Serious Dermatological Reactions Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in both pediatric and adult patients treated with leveltracetam. The median time of onset is reported to be 14 to 17 days, but cases have been reported at least four months after initiation of treatment. Recurrence of the serious skin reactions following rechailenge with levettracetam has also been reported. Levettracetam should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered.

5.6 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan Hypersensitivity

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as Drug Reaction with Eosinophila and Systemic Symptoms (DRESS), also known as multiorgan hypersensitivity, has been reported in patients taking antiepileptic drugs, including Levetiracetam. These events can be fatal or life threatening, particularly if diagnosis and treatment do not occur as early as possible. DRESS typically, although not exclusively, presents with ever, rash, lymphadenopathy, and/or faciali swelling, in exclusively, presents with ever, rash, lymphadenopathy, and/or faciali swelling, in exclusively, presents with ever, rash, lymphadenopathy, and/or faciali swelling, in exclusively, not ther organ system involvement, such as hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis, sometimes resembiling an acute viral infection. Eosinophila is often present. Because this disorder is variable in its expression, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Levetracetam should be discontinued if an alternative etiology for the signs or symptoms cannot be established [see CONTRAINDICATIONS (4)].

5.7 Coordination Difficulties

Levetiracetam may cause coordination difficulties.

Levetiracetam may cause coordination difficulties. In controlled clinical studies in adult patients with partial onset seizure studies, 3.4% of adult levetiracetam-treated patients experienced coordination difficulties, (reported as either ataxia, abnormal gait, or incoordination) compared to 1.6% of placebo-treated patients. A total of 0.4% of patients in controlled clinical studies discontinued levetiracetam treatment due to ataxia, compared to 0% of placebo-treated patients, in 60.7% of levetiracetam-treated patients and in 0.2% of placebo-treated patients, in do 0.7% of levetiracetam-treated patients and in 0.2% of placebo-treated patients, the do was reduced due to coordination difficulties, while one of the levetiracetam-treated patients was hospitalized due to worsening of pre-existing ataxia. These events occurred most frequently within the first 4 weeks of treatment.

Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on levetiracetam to gauge whether it could adversely affect their ability to drive or operate machinery.

5.8 Withdrawal Seizures

As with most antiepileptic drugs, levetiracetam, should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus. If withdrawal is needed because of a serious adverse reaction, rapid discontinuation can be considered

5.9 Hematologic Abnormalities

Levetiracetam can cause hematologic abnormalities. Hematologic abnormalities occurred in clinical trials and included decreases in white blood cell (WBC), neutrophil, and red blood cell (RBC) counts; decreases in hemoglobin and hematocrit; and increases in biolo cell (NBC) colinis, lectreases in menoglobin ratio menadoli R, and increases in eosinophil counts. Cases of agranulocyclosis, pancytopenia, and thromocytopenia have been reported in the postmarketing setting. A complete beoure to recommended in patients experiencing significant weakness, pyrexia, recurrent infections, or coagulation disorders

Partial - Onset Seizures

Adults:

Minor, but statistically significant, decreases compared to placebo in total mean RBC count (0.03 x 10^6 /mm³), mean hemoglobin (0.09 g/dL), and mean hematocrit (0.38%), were seen in levetiracetam-treated patients in controlled trials.

were seen in leveracetam-treated patients in controlled trias. A total of 3.4% of levetriacetam-treated patients in controlled trias. A total of 3.4% of levetriacetam-treated and 1.8% of placebo-treated patients had at least one possibly significant (\leq 2.8 x 10⁹/L) decreased WBC, and 2.4% of levetriacetam-treated patients had at least one possibly significant (\leq 1.0 x 10⁹/L) decreased neutrophil count. Of the levetracetam-treated patients with a low neutrophil count, al but one rose towards or to baseline with continued treatment. No patient was discontinued secondary to low neutrophil counts.

Pediatric Patients 4 Years to < 16 Years:

Pediatic Fatterins 4 tears to 10 tears: Statistically significant decreases in WBC and neutrophil counts were seen in levetiracetam-treated patients as compared to placebo. The mean decreases from baseline in the levetiracetam-treated group were -0.4 x 10⁹L, and -0.3 x 10⁹L, respectively, whereas there were small increases in the placebo group. Mean relative lymphocyte counts increased by 1.7% in levetiracetam-treated patients, compared to a decrease of 4% in placebo patients (statistically significant).

Use lease of 4% in pacebo padents (statistically significant). In the controlled trial, more level/incacetam-treated patients had a possibly clinically significant abnormally low WBC value (3% of level/incacetam-treated patients), however, there was no apparent difference between treatment groups with respect to neutrophil count (5% of level/incacetam-treated patients), versus 4.2% of placebo-treated patients). No patient was discontinued secondary to low WBC or neutrophil counts.

In the controlled cognitive and neuropsychological safety study, 5 patients (8.6%) in the level/incactam-treated group and two patients (6.1%) in the placebo-treated group had high eosinophil count values that were possibly clinically significant (\geq 10% or \geq 0.7X10⁹L).

5.10 Increase in Blood Pressure

In a randomized, placebo-controlled study in patients 1 month to <4 years of age, a significantly higher risk of increased diastolic blood pressure was observed in the levetriacetam-treated patients (17%), compared to the placebo-treated patients (2%). There was no overall difference in mean diastolic blood pressure between the treatment groups. This disparity between the levetriacetam and placebo treatment groups was not observed in the studies of older children or in adults.

Monitor patients 1 month to <4 years of age for increases in diastolic blood pressure

5.11 Seizure Control During Pregnancy

Physiological changes may gradually decrease plasma levels of levetiracetam throughout pregnancy. This decrease is more pronounced during the third trimester. It is recommended that patients be monitored carefully during pregnancy. Close monitoring should continue through the postpartum period especially if the dose was changed during pregnancy.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more details in other sections of labeling: • Behavior Abnormalities and Psychotic Symptoms [see WARNINGS AND

- Behavior Abnormatiles and Psychotic Symptoms [see WARNINGS AND PRECAUTIONS (5.1)]
 Suicidal Behavior and Ideation [see WARNINGS AND PRECAUTIONS (5.2)]
 Somnolence and Fatigue [see WARNINGS AND PRECAUTIONS (5.3)]
 Anaphyakis and Angioedema[see WARNINGS AND PRECAUTIONS (5.4)]
 Serious Dermatological Reactions [see WARNINGS AND PRECAUTIONS (5.4)]
 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)[Multiorgan Hypersensitivity];see WARNINGS AND PRECAUTIONS (5.6)]
 Coordination Difficulties [see WARNINGS AND PRECAUTIONS (5.7)]
 Hematologic Abnormalities [see WARNINGS AND PRECAUTIONS (5.9)]
 Increase in Blood Pressure [see WARNINGS AND PRECAUTIONS (5.10)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Partial - Onset Seizures

Adults:

In controled clinical studies in adults with partial - onset seizures-, [see CLINICAL STUDIES (14.1)], the most common adverse reactions in patients receiving levetiracetam in combination with other AEDs, for events with rates greater than placebo, were sommolence, asthenia, infection, and dizziness. Of the most common adverse reactions in adults experiencing partial - onset seizures, asthenia, sommolence, and dizziness occurred predominantly during the first 4 weeks of treatment with levetiracetam.

Table 3 lists adverse reactions that occurred in at least 1% of adult epilepsy <u>patients</u> receiving level/racetam in placebo-controlled studies and were numerically more common than in patients treated with placebo. In these studies, either level/racetam or placebo was added to concurrent AED therapy.

	Levetiracetam (N = 769)	Placebo (N=439)
	%	%
Asthenia	15	9
Somnolence	15	8
Headache	14	13
Infection	13	8
Dizziness	9	4
Pain	7	6
Pharyngitis	6	4
Depression	4	2
Nervousness	4	2
Rhinitis	4	3
Anorexia	3	2
Ataxia	3	1
Vertigo	3	1
Amnesia	2	1
Anxiety	2	1
Cough Increased	2	1
Diplopia	2	1
Emotional Lability	2	0
Hostility	2	1
Paresthesia	2	1
Sinusitis	2	1

In controlled adult clinical studies, 15% of patients receiving levetiracetam and 12% receiving placebo either discontinued or had a dose reduction as a result of an adverse reaction. Table 4 lists the most common (>1%) adverse reactions that resulted in discontinuation or dose reduction and that occurred more frequently in levetiracetam-treated patients than in placebo-treated patients.

Adverse Reaction	Levetiracetam (N=769) %	Placebo (N=439) %
Somnolence	4	2
Dizziness	1	0

Pediatric Patients 4 Years to <16 Years:

The adverse reaction data presented below was obtained from a pooled analysis of two controlled pediatric clinical studies in pediatric patients 4 to 16 years of age with partial onset sezures. The most common adverse reactions in pediatric patients receiving levetiracetam in combination with other AEDs, for events with rates greater than placebo, were fatigue, aggression, nasal congestion, decreased appetite, and irritability.

Table 5 lists adverse reactions from the pooled pediatric controlled studies (4 to 16 years of age) that occurred in at least 2% of pediatric levetiracetam-treated patients and were numerically more common than in pediatric patients treated with placebo. In these studies, either levetiracetam or placebo was added to concurrent AED therapy.

	Levetiracetam	Placebo
	(N=165) %	(N=131) %
Headache	19	15
Nasopharyngitis	15	12
Vomiting	15	12
Somnolence	13	9
Fatique	11	5
Aggression	10	5
Cough	9	5
Nasal Congestion	9	2
Upper Abdominal Pain	9	8
Decreased Appetite	8	2
Abnormal Behavior	7	4
Dizziness	7	5
Irritability	7	1
Pharyngolaryngeal Pain	7	4
Diarrhea	6	2
Lethargy	6	5
Insomnia	5	3
Agitation	4	1
Anorexia	4	3
Head Injury	4	0
Altered Mood	3	1
Constipation	3	1
Contusion	3	1
Depression	3	1
Fall	3	2
Influenza	3	1
Affect Lability	2	1
Anxiety	2	1
Arthralgia	2	0
Confusional State	2	0
Conjunctivitis	2	0
Ear Pain	2	1
Gastroenteritis	2	0
oint Sprain	2	1
Mood Swings	2	1
Neck Pain	2	1
Rhinitis	2	0
Sedation	2	1

In the controlled pooled pediatric clinical studies in patients 4 to 16 years of age, 7% of patients receiving levetiracetam and 9% receiving placebo discontinued as a result of an adverse reaction.

Pediatric Patients 1 Month to < 4 Years:

In the 7-day, controlled pediatric clinical study in children 1 month to less than 4 years of age with partial - onset seizures, the most common adverse reactions in patients receiving leverifacetam in combination with other AEDs, for events with rates greater than placebo, were somnolence and irritability. Because of the shorter exposure period, incidences of adverse reactions are expected to be lower than in other pediatric studies in older patients. Therefore, other controlled pediatric data, presented above, should also be considered to apply to this age group.

Table 6 lists adverse reactions that occurred in at least 5% of pediatric epilepsy patients (ages 1 month to < 4 years) treated with levefracetam in the placebo-controlled study and were numerically more common than in patients treated with placebo. In this study, either levefracetam or placebo was added to concurrent AED therapy.

	Levetiracetam (N=60) %	Placebo (N=56) %
Somnolence	13	2
Irritability	12	0

In the 7-day controlled pediatric clinical study in patients 1 month to < 4 years of age, 3% of patients receiving level/racetam and 2% receiving placebe either discontinued or had a dose reduction as a result of an adverse reaction.

There was no adverse reaction that resulted in discontinuation for more than one patient.

Myoclonic Seizures

Although the pattern of adverse reactions in this study seems somewhat different from that seen in patients with partial-onset secures, this is likely due to the much smaller number of patients in this study compared to partial secure studies. The adverse reaction pattern for patients with JME is expected to be essentially the same as for patients with partial secures.

In the controlled clinical study in patients 12 years of age and older with myoclonic seizures, [see CLINICAL STUDIES (14.2)], the most common adverse reactions in patients receiving levetiracetam in combination with other AEDs, for events with rates greater than placebo, were somnolence, neck pain, and pharyngitis.

Table 7 lists adverse reactions that occurred in at least 5% of juvenile myoclonic epilepsy patients experiencing myoclonic seizures treated with levelriacetam and were numerically more common than in patients treated with placebo. In this study, either levetracetam or placebo was added to concurrent AED therapy.

	Levetiracetam (N=60)	Placebo (N=60)
	%	%
Somnolence	12	2
Neck Pain	8	2
Pharyngitis	7	0
Depression	5	2
Influenza	5	2
Vertigo	5	3

In the placebo-controlled study, 8% of patients receiving levet/racetam and 2% receiving placebo either discontinued or had a dose reduction as a result of an adverse reaction. The adverse reactions that led to discontinuation or dose reduction and that occurred more frequently in levet/racetam-treated patients than in placebo-treated patients are presented in Table 8.

Adverse Reaction	Levetiracetam (N=60)	Placebo (N=60)	
	%	%	
Anxiety	3	2	
Depressed mood	2	0	
Depression	2	0	
Diplopia	2	0	
Hypersomnia	2	0	
Insomnia	2	0	
Irritability	2	0	
Nervousness	2	0	
Somnolence	2	0	

Primary Generalized Tonic-Clonic Seizures

Although the pattern of adverse reactions in this study seems somewhat different from that seen in patients with partial-onset seizures, this is likely due to the much smaller number of patients in this study compared to partial seizure studies. The adverse reaction pattern for patients with primary generalized tomic-clonic (PGTC) seizures is expected to be essentially the same as for patients with partial seizures.

In the controlled clinical study that included patients 4 years of age and older with PGTC seizures, [see CLINICAL STUDIES (14.3)], the most common adverse reaction in patients receiving levetinacetam in combination with other AEDs, for events with rates greater than placebo, was nasopharyngits.

Table 9 lists adverse reactions that occurred in at least 5% of idiopathic generalized epilepsy patients experiencing PGTC seizures treated with levetiracetam and were numerically more common than in patients treated with placebo. In this study, either levetiracetam or placebo was added to concurrent AED therapy.

	Levetiracetam (N=79) %	Placebo (N=84) %
Nasopharyngitis	14	5
Fatigue	10	8
Diarrhea	8	7
Irritability	6	2
Mood swings	5	1

In the placebo-controlled study, 5% of patients receiving levetiracetam and 8% receiving placebo either discontinued or had a dose reduction during the treatment period as a result of an adverse reaction.

This study was too small to adequately characterize the adverse reactions that could be expected to result in discontinuation of treatment in this population. It is expected that the adverse reactions that would lead to discontinuation in this population would be similar to those resulting in discontinuation in other epilepsy trials (see Tables 4 and 8).

In addition, the following adverse reactions were seen in other controlled adult studies of levetracetam: balance disorder, disturbance in attention, eczema, memory impairment, myalgia, and blurred vision.

Comparison of Gender, Age and Race

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

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of levetracetam. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Causal relacionship to drug exposure. The following adverse reactions have been reported in patients receiving marketed levetiracetam worldwide. The listing is alphabetized: abnormal liver function test, acute kidney injury, anaphylaxis, angloederna, agranulocytosis, chorocathetosis, drug reaction with eosinophilia and systemic symptoms (DRESS), dyskinesia, erythema multforme, hepatic failure, hepatitis, hyponatremia, muscular weakness, obsessive-complisive disorder (OCD), pancreatitis, pancytopenia (with bone marrow suppression identified in some of these cases), panic attack, thrombocytopenia, weight loss and worsening of seizures including in patients with SCMBA mutations. Abopecia has been reported with levetiracetam use; recovery was observed in majority of cases where levetiracetam was discontinued.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antiepileptic drugs (AEDS), including Levetiracetam, during pregnancy. Encourage women who are taking Levetiracetam during pregnancy to enrol in the North American Antiepileptic Drug (NAAED) pregnancy registry by caling 1-888-233-2334 or visiting http://www.aedpregnancy.registry.org/.

Risk Summary

Prolonged experience with Levetracetam in pregnant women has not identified a drug-associated risk of major birth defects or miscarriage, based on published literature, which includes data from pregnancy registries and reflects experience over two decades [See Human Data]. In animal studies, levetracetam produced developmental toxicity (increased embryofetal and offspring mortality, increased incidences of fetal structural abnormalities, decreased embryofetal and offspring growth, neurobehavioral alterations in offspring) at doses similar to human therapeutic doses [see Animal Data].

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is

Clinical Considerations

Levetiracetam blood levels may decrease during pregnancy [see WARNINGS AND PRECAUTIONS (5.11)].

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. Dose adjustments may be necessary to maintain clinical response.

Data

Human Data

While available studies cannot definitively establish the absence of risk, data from the published literature and pregnancy registries have not established an association with levetiracetam use during pregnancy and major birth defects or miscarriage.

Animal Data

When levetiracetam (0, 400, 1200, or 3600 mg/kg/day) was administered orally to pregnant rats during the period of organogenesis, reduced fetal weights and increase incidence of fetal skeletal variations were observed at the highest dose tested. There was no evidence of maternal toxicity. The no-effect dose for adverse effects on embryofetal developmental in rats (1200 mg/kg/day) is approximately 4 times the maximum recommended human dose (MRHD) of 3000 mg on a body surface area (mg/m²) basis.

(Ingim') Juda: Oral administration of levetiracetam (0, 200, 600, or 1800 mg/kg/day) to pregnant rabbits during the period of organogenesis resulted in increased embryofetal mortality and incidences of fetal skeletal abnormalities at variations at the mid and high dose and decreased fetal weights and increased incidence of fetal malformations at the high dose, which associated with maternal toxicity. The no effect dose for adverse effects on embryofetal development in rabbits (200 mg/kg/day) is approximately equivalent to the MRHD on a mg/m² basis.

Oral administration of leveliracetam (0, 70, 350, or 1800 mg/kg/day) to female rats throughout pregnancy and lactation led to an increased incidence of fetal skeletal variations, reduced fetal body weight, and decreased growth in offspring at the mid and high doses and increased pup mortality and neurobehavioral alterations in offspring at the highest dose tested. There was no evidence of maternal toxicity. The no-effect dose for adverse effects on pre- and postnatal development in rats (70 mg/kg/day) is less than the MRHD on a mg/m² basis.

Oral administration of levetiracetam to rats during the latter part 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).

8.2 Lactation

The effect of levetiracetam on labor and delivery in humans is unknown

8.4 Pediatric Use

The safety and effectiveness of levetiracetam for the treatment of partial-onset seizures in patients 1 month to 16 years of age have been established [see CLINICAL STUDIES (14.1)]. The dosing recommendation in these pediatric patients varies according to age group and is weight-based [see CLINICAL PHARMACOLOGY (12.3) and CLINICAL STUDIES (14.1)].

The safety and effectiveness of levetiracetam as adjunctive therapy for the treatment of myoclonic seizures in adolescents 12 years of age and older with juvenile myoclonic epilepsy have been established [see CLINICAL STUDIES (14.2)].

The safety and effectiveness of levelrizectam as adjunctive therapy for the treatment of primary generalized tonic- clonic seizures in pediatric patients 6 years of age and older with idiopathic generalized epilepsy have been established [see CLINICAL STUDIES (14-3)].

Safety and effectiveness for the treatment of partial-onset seizures in pediatric patients below the age of 1 month; adjunctive therapy for the treatment of myoclonic seizures in pediatric patients below the age of 12 years; and adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in pediatric patients below the age of 6 years have not been established.

have not been established. A 3-month, randomized, double-bilind, placebo-controlled study was performed to assess the neurocognitive and behavioral effects of levetriacetam as adjunctive therapy in 98 (levetracetam N=64, placebo N=34) pediatric patients, ages 4 to 16 years old, with partial seizures that were inadequately controlled. The target dose was 60 mg/kg/day. Neurocognitive effects were measured by the Leter-R Attention and Memory (AM) Battery, which measures various aspects of a child's memory and attention. Although no substantive differences were observed between the placebo and drug treated groups in the median change from baseline in this battery, the study was not adequate to assess formal statistical non-interfority of the drug and placebo. The Achenbach Child Behavior Checklist (CBCL/6 to 18), a standardized validated tool used to assess formal childr commercies and hebavioral/emotional grobplems, was also assessed Achenoach Child Benavor Checkis (LBCL/b to 16), a standardized validated tool used to assess a child's competencies and behavioral/emotional problems, was also assessed in this study. An analysis of the CBCL/b to 18 indicated on average a worsening in levetiracetam-treated patients in aggressive behavior, one of the eight syndrome scores. [see WARNINGS AND PRECAUTIONS (5.1)].

Iuvenile Animal Toxicity Data

Studies of levetiracetam in juvenile rats (dosed on postnatal days 4 through day 52) and dogs (dosed from postnatal weeks 3 through 7) at doses of up to 1800 mg/kg/day (approximately 7 and 24 times, respectively, the maximum recommended pediatric dose of 60 mg/kg/day on a mg/m² basis) did not demonstrate adverse effects on postnatal development. developmen

8.5 Geriatric Use

There were 347 subjects in clinical studies of levetiracetam that were 65 and over. No overall differences in safety were observed between these subjects and younger subjects. There were insufficient numbers of elderly subjects in controlled trials of epilepsy to adequately assess the effectiveness of levetiracetam in these patients.

Levetracetam is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in does election, and it may be useful to monitor renal function [see CLINICAL PHARMACOLOGY (12.3)].

8.6 Renal Impairment

Clearance of leverifacetam is decreased in patients with renal impairment and is correlated with creatinine clearance [see CLINICAL PHARMACOLOGY (12.3)]. Dose adjustment is recommended for patients with impaired renal function and supplemental doses should be given to patients after dialysis [see DOSAGE AND ADMINISTRATION (2.5)].

10 OVERDOSAGE

10.1 Signs, Symptoms and Laboratory Findings of Acute Overdosage in

The highest known dose of leveliracetam received in the clinical development program The injust known buss or eventual and the constraint of the initial development program was 6000 mg/day. Other than drowsiness, there were no adverse reactions in the few known cases of overdose in clinical trials. Cases of somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed with leveltracetam overdoses in postmarketing use.

10.2 Management of Overdose

There is no specific antidate for overdose with levetiracetam. If indicated, elimination of unabsorbed drug should be attempted by emesis or gastric lavage; usual precautions should be observed to maintain airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the patient's clinical status. A Certified Poison Control Center should be contacted for up to date information on the management of overdose with levetiracetam.

10.3 Hemodialysis

Standard hemodialysis procedures result in significant clearance of levetiracetam Janua di Henodajas procedures i poste il sugini and cedrance or levera decari (approximate/50% in 4 houst) be considered in cases of overdose. Although hemodiajsis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal impairment.

11 DESCRIPTION

Levetiracetam USP is an antiepileptic drug available as 250 mg (blue), 500 mg (yellow), 750 mg (orange), and 1000 mg (white) tablets for oral administration.

The chemical name of level fractant, values in 0 narounning data. In the chemical name of level fractant, as ingle enantomer, is $(-iS)_{-c}$ -ethyl-2-oxo-1-pyrrolidine acetamide, its molecular formula is CaH₁₂N₂O₂ and its molecular weight is 170.21. Level tractant is chemically unrelated to existing antiepileptic drugs (AEDs). It has the following structural formula:



Levetiracetam USP is a white to off-white crystaline powder with a faint odor and a bitter taste. It is very soluble in water (104.0 g/100 mL). It is freely soluble in chloroform (65.3 g/100 mL) and in methanol (53.6 g/100 mL), soluble in ethanol (16.5 g/100 mL), sparingly soluble in actorbitrie (6.7 g/100 mL) and practically insoluble in n-hexane. (Solubility limits are expressed as g/100 mL solvent).

Levetiracetam tablets USP contain the labeled amount of levetiracetam.

For 250 mg, 500 mg and 750 mg strengths:

Inactive ingredients: colloidal silicon dioxide, corn starch, crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, taic, titanium dioxide, and additional agents listed below:

250 mg tablets: FD&C Blue No. 2/indigo carmine Aluminum Lake

500 mg tablets: Yellow Iron Oxide 750 mg tablets: FD&C Blue No. 2/indigo carmine Aluminum Lake, FD&C Yellow No. 6/sunset yellow FCF Aluminum Lake, iron oxide red

For 1000 mg strength:

Inactive ingredients: colloidal silicon dioxide, corn starch, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, talc and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism(s) by which levetiracetam exerts its antiepileptic effect is unknov

A saturable and stereoselective neuronal binding site in rat brain tissue has been described for levetiracetam. Experimental data indicate that this binding site is the synaptic vesicle protein SV2A, though to be involved in the regulation of vesicle exocytosis. Although the molecular significance of levetiracetam binding to SV2A is not understood, levetiracetam and related analogs showed a rank order of affinity for SV2A which correlated with the potency of their antisezure activity in audiogenic seizure-prone mice. These findings suggest that the interaction of levetiracetam with the SV2A protein may contribute to the antiepileptic mechanism of action of the drug.

12.2 Pharmacodynamics

Effects on OTc Interval

The effect of levelracetam on QTc prolongation was evaluated in a randomized, double-blind, positive-controlled (moxifbxacin 400 mg) and placebo-controlled crossover study of levetracetam (1000 mg or 5000 mg) in 52 healthy subjects. The upper bound of the 90% confidence interval for the largest placebo-adjusted, baseline-corrected QTc was below 10 milliseconds. Therefore, there was no evidence of significant QTc prolongation in this study.

12.3 Pharmacokinetics

The pharmacokinetics of levetiracetam are similar when used as monotherapy or as adjunctive therapy for the treatment of partial-onset seizures.

Absorption and Distribution

Absorption and Distribution Absorption of leveltracteam is rapid, with peak plasma concentrations occurring in about an hour following oral administration in fasted subjects. The oral bioavailability of leveltracetam tablets is 100% and the tablets and oral solution are bioequivalent in rate and extent of absorption. Food does not affect the extent of absorption of leveltracetam but it decreases C_{max} by 20% and delays T_{max} by 1.5 hours. The pharmacokinetics of leveltracetam are linear over the dose range of 500 to 500 mg. Steady state is achieved after 2 days of multiple twice-daily dosing. Leveltracetam and its major metabolite are less than 10% bound to plasma proteins; clinically significant interactions with other drugs through competition for protein binding sites are therefore unlikely.

Metabolism

Levetiracetam is not extensively metabolized in humans. The major metabolic pathway is Level accessing in the extensively interaordized in munihits the map threadout plankey is the azymatic hydrolysis of the accelended group, which produces the carboxylic acid metabolite, ucb L057 (24% of dose) and is not dependent on any liver cytochrome P450 more activities of the accelended activities in animal sector models. Two minor liver accelended acc social grines, the map/ interactione is indexide a matchine model. The map/ metabolites were identified as the product of hydroxylation of the 2-oxo-pyrrolidine ring (2% of dose) and opening of the 2-oxo-pyrrolidine ring in position 5 (1% of dose). There is no enantiomeric interconversion of levet/inacetam or its map reabolite.

Elimination

Levertiracted and plasma half-life in adults is 7 ± 1 hour and is unaffected by either dose or repeated administration. Levetiractam is eliminated from the systemic circulation by renal excretion as unchanged drug which represents 66% of administratered dose. The total body clearance is 0.96 mL/min/kg and the renal clearance is 0.6 mL/min/kg. The mechanism of excretion is glomerular filtration with subsequent partial tubular reabsorption. The metabolite ucb L057 is excreted by glomerular filtration administration with subsequent partial tubular reabsorption. The metabolite ucb L057 is excreted by glomerular filtration administration with subsequent partial tubular reabsorption with a renal clearance of 4 mL/min/kg. Levetiracetam elimination is correlated to creatione clearance. Levetiracetam clearance is reduced in patients with renal impairment (*see USE IN SPECIFIC POPULATIONS (8.6) and DOSAGE AND ADMINISTRATION (2.5)*].

Specific Populations

Elderly:

Pharmacokinetics of levetiracetam were evaluated in 16 elderly subjects (age 61 to 88 years) with creatinine clearance ranging from 30 to 74 mL/min. Following oral administration of twice-daily dosing for 10 days, total body clearance decreased by 38% and the half-life was 2.5 hours longer in the elderly compared to healthy adults. This is most likely due to the decrease in renal function in these subjects.

Pediatric Patients:

Pharmacokinetics of levetiracetam were evaluated in 24 pediatric patients (age 6 to 12 years) after single dose (20 mg/kg). The body weight adjusted apparent clearance of levetiracetam was approximately 40% higher than in adults.

A repeat dose pharmacokinetic study was conducted in pediatric patients (age 4 to 12 years) at doses of 20 mg/kg/day, 40 mg/kg/day, and 60 mg/kg/day. The evaluation of

the pharmacokinetic profile of levetiracetam and its metabolite (ucb L057) in 14 pediatric The phain deconstrated rapid extendection and is freedowing (ucb CD) in the period patients demonstrated rapid extended in the previous of the patients demonstrated rapid extended in the previous of the patients of the pa Levetiracetam had no significant effect on the plasma concentrations of carbamazepine. Leven aced in his no significant effect of the positive concentrations of Carlo analoge of appoint acid, topramate or lamotrigine. However, there was about a 22% increase of apparent clearance of leveliracetam when it was co-administered with an enzyme-inducing AED (e.g. carbamazepine).

Following single dose administration (20 mg/kg) of a 10% oral solution to children with epileps (1 month to < 4 years), levetinacter mass 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).

Population pharmacokinetic analysis showed that body weight was significantly correlated to the clearance of levetiracetam in pediatric patients; clearance increased with an increase in body weight.

Pediatric Patients with Obesity

Pediatric Patients with Obesity A population PK analysis of levetiracetam was conducted in 164 obese and non-obese pediatric patients 2 to <18 years of age with median (range) weight 39.2 (11.3-134) kg to evaluate the potential impact of obesity on plasma levetiracetam exposures. Obesity was defined as BMI = 2561 hercentile for age and sex based on CDC 2000 growth chart recommendations. Simulations were conducted for obese and non-obese pediatric patients ages 4 to <16 years. • When the recommended tablet dose is administered to pediatric patients weighing < 40 kg, obese pediatric patients have 27% higher median Cmax,ss and 19% higher median Cmin,ss compared to non-obese patients.

- median Cmin,ss compared to non-obese patients. When the recommended tablet dose is administered to pediatric patients weighing \geq 40 kg, obese pediatric patients have 10-11% lower median Cmax,ss and 2% lower median Cmax,ss compared to non-obese patients. When the recommended oral solution dose is administered to pediatric patients across the full weight range, obese pediatric patients across and 41% higher median Cmin,ss compared to non-obese pediatric patients.

However, differences in exposures between obese and non-obese pediatric patients are not expected to be clinically meaningful because the recommended dose titration at initiation of leverincetant therapy would establish an appropriate dose for each individual patient.

Pregnancy:

Levetiracetam levels may decrease during pregnancy. [see WARNINGS AND PRECAUTIONS (5.11) and USE IN SPECIFIC POPULATIONS (8.1)].

Gender:

Levetiracetam C_{max} and AUC were 20% higher in women (N=11) compared to men (N=12). However, clearances adjusted for body weight were comparable. Race:

Formal pharmacokinetic studies of the effects of race have not been conducted. Cross-study comparisons involving Caucasians (N=12) and Asians (N=12), however, show that pharmacokinetics of leveltracetam were comparable between the two races. Because levettracetam is primarily renally excreted and there are no important racial differences in creatinine clearance, pharmacokinetic differences due to race are not expected.

Renal Impairment:

The disposition of levetiracetam was studied in adult subjects with varving degrees of The upposition to relate the deviate status of the status subjects with variety and upper status to the renal function. Total body clearance of leveltracetam is preduced in patients with impaired renal function by 40% in the mild group (CLcr = 50 to 80 mL/min), 50% in the moderate group (CLcr = 30 to 50 mL/min) and 60% in the severe renal impairment group (CLcr = 30 mL/min). Clearance of leveltracetam is correlated with creatinine clearance.

In anuric (end stage renal disease) patients, the total body clearance decreased 70% compared to normal subjects (CLcr >80 mL/min). Approximately 50% of the pool of levetracetam in the body is removed during a standard 4- hour hemodialysis procedure [see DOSAGE AND ADMINISTRATION (2.5)].

Hepatic Impairment:

In subjects with mid (Child-Pugh A) to moderate (Child-Pugh B) hepatic impairment, the pharmacokinetics of levetiracetam were unchanged. In patients with severe hepatic impairment (Child-Pugh C), total body clearance was 50% that of normal subjects, but decreased renal clearance accounted for most of the decrease. No dose adjustment is needed for patients with hepatic impairment.

Drug Interactions

In vitro data on metabolic interactions indicate that levetiracetam is unlikely to produce, In this order of the control in the actions inducted that level the certain is unitkely to produce, or be subject to, pharmacokinetic interactions. Level acteatam and its major metabolite, at concentrations well above $C_{\rm maxi}$ levels achieved within the therapeutic dose range, are neither inhibitors of, nor high affinity substrates for, human liver cytochrome P450 isoforms, epoxide hydrolase or UDP-glucuronidation enzymes. In addition, leveliracetam does not affect the *in vitro* glucuronidation of valproic acid.

Potential pharmacokinetic interactions of or with levetiracetam were assessed in clinical pharmacokinetic studies (phenytoin, valproate, warfarin, digoxin, oral contraceptive, probenecid) and through pharmacokinetic screening in the placebo-controlled clinical studies in epilepsy patients.

Phenvtoin:

Levetiracetam (3000 mg daily) had no effect on the pharmacokinetic disposition of phenytoin in patients with refractory epilepsy. Pharmacokinetics of levetiracetam w also not affected by phenytoin.

Valproate:

Levetiracetam (1500 mg twice daily) did not alter the pharmacokinetics of valproate in healthy volunteers. Valproate 500 mg twice daily did not modify the rate or extent of levetiracetam absorption or its plasma clearance or urinary excretion. There also was no effect on exposure to and the excretion of the primary metabolite, ucb L057.

Other Antiepileptic Drugs:

Potential drug interactions between levetiracetam and other AEDs (carbamazepine, gabapentin, lamotrigine, phenobarbtal, phenytoin, primidone and valproate) were a assessed by evaluating the serum concentrations of levetiracetam and these AEDs during placebo-controlled clinical studies. These data indicate that levetiracetam do ere also during placebo-controlled clinical studies. These data indicate that levetiracetam does no influence the plasma concentration of other AEDs and that these AEDs do not influence es not the pharmacokinetics of levetiracetam.

Effect of AEDs in Pediatric Patients:

There was about a 22% increase of apparent total body clearance of levetiracetam when it was co-administered with enzyme-inducing AEDs. Dose adjustment is not recommended. Levetiracetam had no effect on plasma concentrations of carbamazepine, valproate, topiramate, or lamotrigine.

Oral Contraceptives:

Levetiracetam (500 mg twice daily) did not influence the pharmacokinetics of an oral Leven action (300 mg vite Gary vib nitv invitence vite primit/vitence so a nor al contraceptive containing (0.3 mg ethni) ethnic invitence of 0.15 mg levenoreserved or of the luteinizing hormone and progesterone levels, indicating that impairment of contraceptive efficacy is unlikely. Coadministration of this oral contraceptive din on tinfluence the pharmacokinetics of levetiracetam

Digoxin:

Levetiracetam (1000 mg twice daily) did not influence the pharmacokinetics and pharmacodynamics (ECG) of digoxin given as a 0.25 mg dose every day. Coadministration of digoxin did not influence the pharmacokinetics of levetiracetam.

Warfarin:

Levetiracetam (1000 mg twice daily) did not influence the pharmacokinetics of R and S warfarin. Prothrombin time was not affected by levetiracetam. Coadministration of warfarin did not affect the pharmacokinetics of levetiracetam.

Probenecid:

Probenetic, a renal tubular secretion blocking agent, administered at a dose of 500 mg four times a day, did not change the pharmacokinetics of levetiracetam 1000 mg bwice daily. $\rm C^{55}_{max}$ of the metabolite, ucb L057, was approximately doubled in the presence of probenecid while the fraction of drug excreted unchanged in the urine remained the same. Renal clearance of ucb L057 in the presence of probenecid decreased 60%, probably related to compettive inhibition of tubular secretion of ucb L057. The effect of levetiracetam on probenecid was not studied.

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. Plasma exposure (AUC) at the highest dose was approximately 6 times that in humans at the maximum recommended daily human dose (MRHD) of 3000 mg. The winner and the index number of the index an increase in tumors. The highest dose tested in mice for 2 years (3000 mg/kg/day) is approximately 5 times the MRHD on a body surface area (mg/ m²) basis.

Mutagenesis

Levetiracetam was negative in in vitro (Ames, chromosomal aberration in mammalian cells) and in vivo (mouse micronucleus) assays. The major human metabolike of levetiracetam (ucb US7) was negative in *in vitro* (Ames, mouse *ymphoma*) assay. Impairment of Fertility

No adverse effects on male or female fertility or reproductive performance were

observed in rats at oral doses up to 1800 mg/kg/day, which were associated with plasma exposures (AUC) up to approximately 6 times that in humans at the MRHD.

14 CLINICAL STUDIES

14.1 Partial Onset Seizures

Effectiveness in Partial-Onset Seizures in Adults

Effectiveness in Partial-Onset Seizures in Adults The effectiveness of levetracetam for the treatment of partial-onset seizures in adults was established in three multicenter, randomized, double-bilnd, placebo-controlled clinical studies in patients who had refractory partial-onset seizures with or without secondary generalization. The tablet formulation was used in all these studies. In these studies, 904 patients were randomized to placebo, 1000 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 classical AEDs. Patients enrolled in Study 3 had refractory partial-onset seizures for at least 1 year and had taken one classical AED. At the time of the study, patients were taking a stable dose regimen of at least 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.

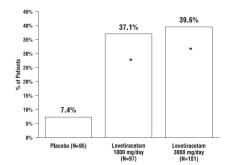
Study 1:

Study 1 was a double-blind, placebo-controlled, parallel-group study conducted at 41 stess in the lunded States comparing level*acetam 1000 mg/day (N=70), kevetracetam 3000 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 thration period, followed by a 12-week fixed dose evaluation period, diving which concomitant AED regimens were held constant. The primary measure of effectiveness was a between group comparison of the percent reduction in weekly partial seture frequency relative to placebo over the entire randomized threatment period (thration + evaluation period). Secondary outcome variables included the responder rate (incidence of patients with \pm 50% reduction from baseline in partial-onset seture frequency). The analysis of Study 1 are displayed in Table 10. Study 1 was a double-blind, placebo-controlled, parallel-group study conducted at 41

	Placebo (N=95)	Levetiracetam 1000 mg/day (N=97)	Levetiracetam 3000 mg/day (N=101)
Percent reduction in partial seizure frequency over placebo	-	26.1%*	30.1%*

The percentage of patients (y-axis) who achieved \geq 50% reduction in weekly seizure rates from baseline in partial onset-seizure frequency over the entire randomized treatment period (thration + evaluation period) within the three treatment groups (x-axis) is presented in Figure 1.

Figure 1: Responder Rate (≥50% Reduction from Baseline) in Study 1



*statistically significant versus placebo

Study 2:

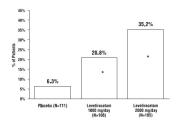
Study 2 was a double-blind, placebo-controlled, crossover study conducted at 62 centers in Europe comparing levetiracetam 1000 mg/day (N=106), levetiracetam 2000 mg/day (N=105), and placebo (N=111) given in equally divided doses twice daily.

mgraay (v=1us), and placebo (v=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 concomtant AED regimens were held constant. The primary measure of effectiveness was a between group comparison of the percent reduction in weekly partial 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 \pm 50% reduction from baseline in partial-onset seizure frequency). The results of the analysis of Period A are displayed in Table 11.

	Placebo (N=111)	Levetiracetam 1000 mg/day (N=106)	Levetiracetam 2000 mg/day (N=105)
Percent reduction in partial seizure frequency over placebo	-	17.1%*	21.4%*

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-axb) is presented in Figure 2.

Figure 2: Responder Rate (≥50% Reduction from Baseline) in Study 2: Period



*statistically significant versus placebo

The comparison of levetiracetam 2000 mg/day to levetiracetam 1000 mg/day for responder rate was statistically significant (P=0.02). Analysis of the trial as a cross-over yielded similar results.

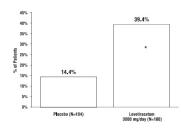
Studv 3:

Study 3: Study 3: Study 3 was a double-blind, placebo-controlled, parallel-group study conducted at 47 centers in Europe comparing levetiracetam 3000 mg/day (N=180) and placebo (N=104) in patients with refractory partial-onset seizures, with or without secondary generalization, receiving only one concomitant AED. Study drug was given in two divided doses. After a prospective baseline period of 12 weeks, patients were randomized to one of two treatment groups described above. The 16-week treatment period consisted of a 4-week titration period, followed by a 12-week fixed dose evaluation period, during which concomitant AED doses 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). Secondary outcome variables included the responder rate (incidence of patients with =50% reduction from baseline in partial-onset seizure frequency). Table 12 displays the results of the analysis of Study 3.

	Placebo (N=104)	Levetiracetam 3000 mg/day (N=180)
Percent reduction in partial seizure frequency over placebo	-	23.0%*

The percentage of patients (y-axis) who achieved \geq 50% reduction in weekly seizure rates from baseline in partial-onset seizure frequency over the entire randomized treatment period (thration + evaluation period) within the two treatment groups (x-axis) is presented in Figure 3.

Figure 3: Responder Rate (≥50% Reduction from Baseline) in Study 3



*statistically significant versus placebo

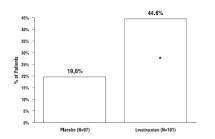
Effectiveness in Partial-Onset Seizures in Pediatric Patients 4 to 16 Years

The effectiveness of levetiracetam as adjunctive therapy for the treatment of partial-onset sekures in pediatric patients was established in one multicenter, randomized double-blind, placebo-controlled study (Study 4), conducted at 60 stes in North America, in pediatric patients 4 to 16 years of age with partial sekures uncontrolled by standard antieplieptic drugs (AEDs). Eligible patients on a stable dose of 1 to 2 AEDs, who still experienced at least 4 partial onset sekures during the 4 weeks prior to screening, as well as at least 4 partial onset sekures in each of the two 4-week baseline periods, were randomized to receive either levetiracetam or placebo. The enrolled population included 198 patients (levetiracetam N=101, placebo N=97) with refractory partial-onset sekures, whether or not secondarily generalized. The study consisted of n 8-week baseline period and 4-week thration period followed by a 10-week valuation period. Dosing was initiated at a dose of 20 mg/kg/day in two divided doses. During the reatment period, levetracetam doses were adjusted in 20 mg/kg/day increments, at 2-week intervals to the target dose of 60 mg/kg/day. The primary measure of effectiveness was a between group comparison of the percent reduction in weekly partial sekure frequency relative to placebo over the entire 14-week randomized treatment period (lavetracet + evaluation period). Secondary outcome variables included the responder rate (incidence of patients with \ge 50% reduction from baseline in partial-onset sekure frequency per week). Table 13 displays the results of this study. The effectiveness of levetiracetam as adjunctive therapy for the treatment of partial-

	Placebo (N=97)	Levetiracetam (N=101)
Percent reduction in partial seizure frequency over placebo	-	26.8%*

The percentage of patients (y-axis) who achieved \geq 50% reduction in weekly seizure rates from baseline in partial-onset seizure frequency over the entire randomized treatment period (thration - evaluation period) within the two treatment groups (x-axis) is presented in Figure 4.

Figure 4: Responder Rate (≥ 50% Reduction from Baseline) in Study 4

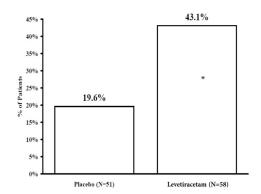


*statistically significant versus placebo

Effectiveness in Partial-Onset Seizures in Pediatric Patients 1 Month to <4 Years of Age

The effectiveness of leveliracetam for the treatment of partial-onset seizures therapy in The encloweness on reveal actual for the treatment of part darks interacy in pediatric patients was established in one multicenter, randomized double-blind, placebo-controlled study (Study 5), conducted at 62 sites in North America, South America, and Europe in pediatric patients 1 month to less than 4 years of age with partial seizures, uncontrolled by standard epileptic drugs (AEDs). Eligible patients on a stable dose of 1 to 2 AEDs, who experienced at less 12 partial-onset seizures during the 48-hour baseline video EEG were randomized to receive either levetiracetam or placebo. The enrolled population included 116 patients (levetiracetam N=60, placebo N=56) with refractory partial onset-seizures, whether or not secondariy generalized. Randomization was stratified by age range as follows: 1 month to less than 6 months of age (N=4 treated with levetiracetam). J year to less than 2 years of age (N=20 treated with levetiracetam), and 2 years to less than 2 years of age (N=20 treated with levetiracetam). The study consisted of a 5-day evaluation period which included a 1-day tration period followed by a 4-day maintenance period. Levetiracetam dosing was determined by age and weight as follows: children 1 month to less than 4 years of effectiveness was the responder rate (percent of patients with \ge 50% reduction from baseline in average daily partial-onset seizure frequency) assessed by a binded central reader using a 48-hour video rate (percent or pateness win 2 50% reduction) from baseme in average daily partial-onset sekure frequency) assessed by a blinded central reader using a 48-hour video EEG performed during the last two days of the 4-day maintenance period. A total of 109 patients were included in the timot average of the 4-day maintenance period. A total of total between leveltracetam and placebo was observed (see Figure 5). The treatment effect associated with leveltracetam was consistent across age groups.

Figure 5: Responder Rate for All Patients Ages 1 Month to < 4 Years ($\geq 50\%$ Reduction from Baseline) in Study 5



*statistically significant versus placebo

14.2 Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy

14.2 Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy The effectiveness of levetiracetam as adjunctive therapy in patients 12 years of age and older with Juvenile myoclonic epilepsy (JME) experiencing myoclonic seizures was established in one multicenter, randomized, double-bind, placebo-controlled study (Study 6), conducted at 37 sites in 14 countries. Eigible patients on a stable dose of 1 antiepilepit drug (AED) experiencing one or more myoclonic seizures per day for at least 8 days during the prospective 8-week baseline period were randomized to ether levetracetam or placebo (levetracetam N=60, placebo N=60). Patients were thrated over 4 weeks to a target dose of 3000 my/day and treated at a stable dose of 3000 mg/day over 12 weeks (evaluation period). Study drug was given in 2 divided doses.

The primary measure of effectiveness was the proportion of patients with at least 50% reduction in the number of days per week with one or more myoclonic seizures during the treatment period (thration + evaluation periods) as compared to baseline. Of the 120 patients enrolled, 113 had a diagnosis of confirmed or suspected JME. Table 14 displays the results for the 113 patients with JME in this study.

Table 14: Responder Rate (≥50% Reduction from Baseline) in Myoclonic Seizure Days per Week for Patients with IME in Study 6

Seizure Duys per We	Seizure Days per week for racients with jine in Study o		
	Placebo (N=59)	Levetiracetam (N=54)	
Percentage of responders	23.7%	60.4%*	

14.3 Primary Generalized Tonic-Clonic Seizures

The effectiveness of levelracetam as adjunctive therapy in patients 6 years of age and older with idiopathic generalized epilepsy experiencing primary generalized tonic-clonic (PGTC) setures was established in one multicenter, randomized, double-blind, placebo-controlled study (Study 7), conducted at 50 sites in 8 countries. Eligible patients on a stable dose of 1 or 2 antelpieptic drugs (AEDs) experiencing a teast 3 PGTC setures during the 8-week combined baseline period (at least one PGTC seture during the 4-week prospective baseline period (at least one PGTC seture during the 4-week prospective baseline period at at least one PGTC seture during the 4-week prospective baseline period at at least one PGTC seture during the 4-week prospective baseline period at a teast one PGTC seture during the 6-week prospective baseline period at a teast baseline' in the remainder of this section. Patients were titrated over 4 weeks (sevaluation period). Study drug was given in 2 equally divided doses per day. The primary measure of effectiveness was the percent reduction from baseline in weekly PGTC setures frequency for levelracetam and placebo treatment groups over the treatment period (titration + evaluation period). Studied of pelipsy, utilisation section. Patients were thereat equiles y divided doses per day. The primary measure of effectiveness was the percent reduction from baseline in weekly PGTC sectures. Each of these syndromes of idiopathic generalized epilepsy (predominate) juvenile myoclonic epilepsy, juvenile absence epilepsy, or fand Mai sectures on awkening) experiencing primary generalized tonic-clonic setures. Each of these syndromes of idiopathic generalized epilepsy was well represented in this patient population. The effectiveness of levetiracetam as adjunctive therapy in patients 6 years of age and

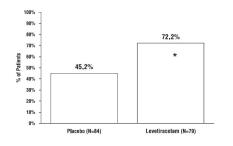
There was a statistically significant decrease from baseline in PGTC frequency in the levetiracetam-treated patients compared to the placebo-treated patients.

Table 15: Median Percent Reduction from Baseline in PGTC Seizure Frequency per Week in Study 7

	Placebo (N=84)	Levetiracetam (N=78)
Percent reduction in PGTC seizure frequency	44.6%	77.6%*

The percentage of patients (y-axis) who achieved \geq 50% reduction in weekly seizure rates from baseline in PGTC seizure frequency over the entire randomized treatment period (titration + evaluation period) within the two treatment groups (x-axis) is presented in Figure 6.

Figure 6: Responder Rate (\geq 50% Reduction from Baseline) in PGTC Seizure Frequency per Week in Study 7



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Levetriacetar tablets USP, 250 mg are blue coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X01" on the other side.

They are supplied as follows: NDC 68180-112-09 Bottles of 90's NDC 68180-112-16 Bottles of 120's NDC 68180-112-02 Bottles of 500's Levetiracetam tablets USP, 500 mg are yellow coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X02" on the other side. They are supplied as follows: NDC 68180-113-09 Bottles of 90's NDC 68180-113-16 Bottles of 120's

NDC 68180-113-02 Bottles of 500's Levetiracetam tablets USP, 750 mg are orange coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X03" on the other side. They are supplied as follows:

NDC 68180-114-09 Bottles of 90's NDC 68180-114-16 Bottles of 120's

NDC 68180-114-02 Bottles of 500's Levetiracetam tablets USP, 1000 mg are white to off-white coloured, oblong-shaped, biconvex, film-coated tablets debossed with "L" and "U" on either side of the breakline on one side and "X04" on the other side. They are supplied as follows:

NDC 68180-115-07 Bottles of 60's NDC 68180-115-02 Bottles of 500's

16.2 Storage

Store at $25^{\circ}C$ (77°F); excursions permitted to $15^{\circ}C$ to $30^{\circ}C$ (59° F to $86^{\circ}F$) [see USP Controlled Room Temperature].

Pharmacist: Dispense in a tight, light-resistant container with child-resistant closure along with medication guide provided separately.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide). For Medication Guide, please visit: www.lupin.com/levetiracetamtab-mg.pdf

Psychiatric Reactions and Changes in Behavior

Advise patients that levetiracetam may cause changes in behavior (e.g. aggression, agitation, anger, anxiety, apathy, depression, hostility, and irritability) and psychotic symptoms [see WARNINGS AND PRECAUTIONS (5.1)].

Suicidal Behavior and Ideation

Counsel patients, their caregivers, and/or families that antiepleptic drugs (AEDs), including levetiracetam, may increase the risk of suicidal thoughts and behavior and advise patients to be alert for the emergence or worsening of symptoms of depression; unusual changes in mood or behavior; or suicidal thoughts, behavior, or thoughts about self-harm. Advise patients, their caregivers, and/or families to immediately report behaviors of concern to a healthcare provider [see WARNINGS AND PRECAUTIONS (5.2)].

Effects on Driving or Operating Machinery

Inform patients that levetiracetam may cause dizziness and somnolence. Inform In the packets of the accessed and the second accessed and the second accessed accesed accessed accessed accessed accessed accesed accesse

Anaphylaxis and Angioedema

Advise patients to discontinue leveltracetam and seek medical care if they develop signs and symptoms of anaphylaxis or angioedema [see WARNINGS AND PRECAUTIONS [5.4]].

Dermatological Adverse Reactions

Advise patients that serious dermatological adverse reactions have occurred in patients treated with levetiracetam and instruct them to call their physician immediately if a rash develops [see WARNINGS AND PRECAUTIONS (5.5)].

DRESS/Multiorgan Hypersensitivity

Instruct patients and caregivers that a fever or rash associated with signs of other organ system involvement (e.g., jymphadenopathy, hepatic dysfunction) may be drug-related and should be reported to their healthcare provider immediately. Levetiracetam should be discontinued immediately if a serious hypersensitivity reaction is suspected (see WARNINGS AND PRECAUTIONS (5.6)).

Withdrawal of Levetiracetam Tablets

Advise patients and caregivers not to discontinue use of Levetiracetam Tablets without consulting with their healthcare provider Levetracetam Tablets should normally be gradually withdrawn to reduce the potential of increased seizure frequency and status epilepticus (see Warnings and Precautions (5.8)).

Pregnancy

Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during levelracetam therapy. Encourage patients to enrol in the North American Antiepileptic Drug (NAAED) pregnancy registry if they become pregnant. Isee USE IN SPECIFIC POPULATIONS (8.1).

ID# 276499

Alert for dispensers : Medication Guide will need to be printed and dispensed

Manufactured for:

Lupin Pharmaceuticals, Inc.

Baltimore, Maryland 21202 United States

MADE IN INDIA

Revised: April 2024

Dispense with Medication Guide available at: www.lupin.com/levetiracetamtab-mg.pdf MEDICATION GUIDE

LEVETIRACETAM (LEE-ve-tye-RA-se-tam)

TABLETS USP 250 mg, 500 mg, 750 mg and 1000 mg Rx only

Read this Medication Guide before you start taking levetiracetam tablets and each time you get a refill. There may be new information. This information does not take the place of taking to your healthcare provider about your medical condition or treatment.

What is the most important information I should know about levetiracetam tablets?

Like other antiepileptic drugs, levetiracetam tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500 people taking it.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you: thoughts about suicide or dying attempts to commit suicide new or worse depression enew or worse depression feallow and add or creates

- feeling agitated or restless

- acting aggressive, being angry, or violent acting on dangerous impulses an extreme increase in activity and talking (mania) other unusual changes in behavior or mood

Do not stop levetiracetam tablets without first talking to a healthcare

- Stopping levetiracetam tablets suddenly can cause serious problems. Stopping a seizure medicine suddenly can cause seizures that will not stop (status epilepticus). Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other
- How can I watch for early symptoms of suicidal thoughts and actions?
 Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
 Keep all follow-up visits with your healthcare provider as scheduled.
- Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

What are levetiracetam tablets

Levetiracetam tablets are a prescription medicine taken by mouth that is used to treal partial-onset seizures in people 1 month of age and older.

Levetiracetam tablets are a prescription medicine taken by mouth that is used with other medicines to treat:

myoclonic seizures in people 12 years of age and older with juvenile myoclonic epilepsy

primary generalized tonic-clonic seizures in people 6 years of age and older with certain types of generalized epilepsy.

It is not known if levetiracetam tablets are safe or effective in children under

- 1 month of age to treat partial-onset seizures
- 12 years of age to treat myoclonic seizures
- 6 years of age to treat primary generalized tonic-clonic seizures

Before taking your medicine, make sure you have received the correct medicine. Compare the name above with the name on your bottle and the appearance of your medicine with the description of levetriacetam tablets provided below. Tell your pharmacist immediately if you think you have been given the wrong medicine.

Who should not take levetiracetam tablets?

Do not take levetiracetam tablets if you are allergic to levetiracetam

What should I tell my healthcare provider before starting levetiracetam tablets?

- tablets?
 Before taking levetiracetam tablets, tell your healthcare provider about all of your medical conditions, including if you:
 have vor have had depression, mood problems or suicidal thoughts or behavior
 have kindney problems
 are pregnant or planning to become pregnant. It is not known if levetiracetam tablet will harm your unborn baby. You and your healthcare provider will have to decide if you should take levetiracetam tablets withile you are pregnant. If you become pregnant tablet will harm your unborn baby. You and your healthcare provider will have to decide if you should take levetiracetam tablet while you are pregnant. If you become pregnant while taking bectracetam tablets, tak to your healthcare provider about registering with the North American Antepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334 or go to http://www.aedpregnancyregistry.org. The purpose of this registry is to collect information about the safety of levetiracetam and other antiepileptic medicine during pregnancy.
 are breast feeding or plan to breastfeed. Levetiracetam can pass into your breast milk can harm your baby. Tak to your doctor about the best way to feed your baby while you receive levetiracetam. during

Tell your healthcare provider about all the medicines you take, including prescription and over-the counter medicines,vitamins, and herbal supplements. Do not start a new medicine without first talking with your healthcare provider.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine.

How should I take levetiracetam tablets?

- ow should I take levetracetam tablets exactly as your healthcare provider tells you to take it. Your healthcare provider will tell you how much levetriacetam tablets to take and when to take it. Levetriacetam tablets are usually taken 2 times each day. Your healthcare provider may change your dose. Do not change your dose without talking to your healthcare provider. Take levetriacetam tablets with or without food.

- Swallow the tablets whole. Do not chew or crush tablets. Ask your healthcare provider for levetracetam oral solution if you cannot swallow tablets. If you take too much levetracetam tablets, call your local Poison Control Center or go to the nearest emergency room right away.

What should I avoid while taking levetiracetam tablets?

Do not drive, operate machinery or do other dangerous activities until you know how levetiracetam tablet affects you. Levetiracetam tablets may make you dizzy or sleepy.

What are the possible side effects of levetiracetam tablets?

can cause serious side effects including: See "What is the most important information I should know about levetiracetam tablets?"

- Call your healthcare provider right away if you have any of these symptoms:
 mood and behavior changes such as aggression, agitation, anger, anxiety, apathy, mood swings, depression, hostility, and irritability. A few people may get psychotic symptoms such as hallucinations (seeing or hearing things that are really not there), delusions (false or strange thoughts or beliefs) and unusual behavior.
 extreme sleepiness, tiredness, and waekness
 allergic reactions such as swelling of the face, lips, eyes, tongue, and throat, trouble swallowing or breathing, and hives.
 a skin rash. Serious skin rashes can happen after you start taking levetiracetam tablets. There is no way to tell if a mild rash will become a serious reaction.
 a serious allergic reaction that may affect your skin or other parts of your body such as your liver, kidneys, heart, or blood cells. This allergic reaction can be life-threatening and can cause death, particularly if it is not treated as early as possible.

	ider right away if you have:
a skin rash	 fever or swollen glands that do not

	go away
 swelling of your face 	 shortness of breath
 dark urine 	 yellowing of the skin or whites of
	the eyes

probl ns with muscle coordination (problems walking and moving)

The most common side effects seen in people who take levetiracetam tablets include: sleepiness
infection
weakness
dizziness

The most common side effects seen in children who take levetiracetam tablets include, in addition to those listed above

 tiredness decreased appetite

- decreased appetit
 irritability
 acting aggressive
 nasal congestion

Tell your healthcare provider if you have any side effect that bothers you or that does not go away

These are not all the possible side effects of leveliracetam tablets. For more information,

ask your healthcare provider or pharmackit. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1:e00-FDA:1088, You may also report side effects to Lupin Pharmaceuticals, Inc. at 1:800-399-2561.

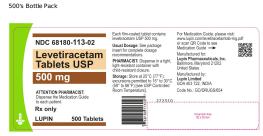
Levetiracetam Tablets USP Rx Only 1000 mg NDC 68180-115-02 500's Bottle Pack



Levetiracetam Tablets USP Rx Only 750 mg NDC 68180-114-02 500's Bottle Pack

Levetiracetam Tablets USP

Rx Only 500 ma NDC 68180-113-02



Each film-coated tablet cont levetiracetam USP 250 mg. For Medication Guide, please www.lupin.com/levetiracetam or scan QR Code to see Medication Guide --> NDC 68180-112-02 Usual Dosage: See package insert fo complete dosage recommendations. Levetiracetam Tablets USP PHARMACIST: Dispense in a tight, light-resistant container with child-resistant closure. Manufactured for: Lupin Pharmaceuticals, Inc. Baltimore, Maryland 21202 250 mg Storage: Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Manufactured by: Lupin Limited GOA 403 722, INDIA ATTENTION PHARMACIST: Dispense the Medication Guide Code No.: GO/DRUGS/654 272307 Rx only Unvarnish Area 75 x 20 mm LUPIN 500 Tablets



ID#:

750 mg tablets: FD & C Blue No. 2/indigo carmine Aluminum Lake, FD & C Yellow No. 6/sunset yellow FCF Aluminum Lake, iron oxide red For 1000 mg strength: Inactive ingredients: colloidal silicon dioxide, corn starch, croscarmeliose sodium, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, tai cand titanium dioxide. Levetiracetam tablets do not contain lactose or gluten. This Medication Guide has been approved by the US Food and Drug Administration. Manufactured for: Lupin Pharmaceuticals. Inc.

250 mg tablets: FD & C Blue No. 2/indigo carmine Aluminum Lake 500 mg tablets: Yellow Iron Oxide

active ingredient: levetiracetam For 250 mg, 500 mg and 750 mg strengths: Inactive ingredients: colloidal silicon dioxide, corn starch, crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, talc, titanium dioxide, and additional agents listed below:

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature] away from heat and light. Keep Levetiracetam tablets and all medicines out of the reach of

General information about safe and effective use of Levetiracetam Tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use leveltracetam tablets for a condition for which it was not prescribed. Do not give leveltracetam tablets to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacts or healthcare provider information about leveltracetam tablets that is written for health professionals.

What are the ingredients of levetiracetam tablets?

How should I store Levetiracetam tablets?

Levetiracetam tablets

Baltimore, Maryland 21202 United States. MADE IN INDIA. Revised: April 2024 276500

childre

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 68180-115-02 Levetiracetam Tablets USP 1000 mg ATTENTION PHARMACIST:	Each film-coaled lablet contains levelinozehn USP 1000 mg. Usual Dosage: See package insert for complete dosage recommendations PHARMACIS: Dispense in a light, drild-resistant dosure Storage: Stora 25°C (77°F); excursions permitted to 15° b 30°C (5° to 85°F) base USP Controled Room Temperature, - 272315	For Medication Guide, please visit: www.lipit.com/fore/tites/atmid-ing.pdf Medication Guide - Medication Guide Manufactured for: Lupin Pharmaceuticals, Inc. Bailmore, Manyland 21:002 United Saltis Manufactured by: Lupin Limited GGA 430 728, INDA GGA 430 728, INDA
Dispense the Medication Guide to each patient. Rx only	20511	Unamith Area
LUPIN 500 Tablets	98180	#2 x 25 mm

	ablet, film coat				
Product Info Product Type	ormation	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC-68180-117
Route of Admi	inistration	ORAL	item code (source)	NDC.08180-112
Active Ingre	dient/Active	Moiety edient Name	Ba	asis of St	rength Streng
EVETIRACETAN		55) (LEVETIRACETAM - UNII:44YRR		ETIRACETAN	
nactive Ing	redients				
		Ingredient Name IE (UNII: OP1R32D61U)			Strength
D&C BLUE NO.	(UNII: 257830E5 2 (UNII: L06K8R7	DQK)			
) (UNII: 0VUT3PMY82)) (UNII: 0WZ8WG20P6)			
	GLYCOL 4000 (097M6I30) UNII: 4R4HFI6D95)			
POLYVINYL ALC		FIED (UNII: 532B59J990)			
SILICON DIOXID	E (UNII: ET)7Z6XE (UNII: 08232NY35				
TALC (UNII: 75EV					
TTANION DIOX		(2)*)			
Product Cha					
	BLUE (Blue) OVAL (Oblong-sha	ped, Biconvex, Film-Coated)		core ize	2 pieces 15mm
Flavor			In	nprint Cod	ie L;U;X01
Jondanis					
Packaging					
# Item Code	e Pa	ckage Description	Marketing Date	Start	Marketing End Date
16	Product	LE; Type 0: Not a Combination	01/15/2009		
2 NDC:68180-11 09	2- 90 in 1 BOTTL Product	E; Type 0: Not a Combination	01/15/2009		
B NDC:68180-11	2- 500 in 1 BOTT Product	LE; Type 0: Not a Combination	01/15/2009		
	lnformat				
Marketing Category		tion Number or Monograph Citation	Dat	ig Start te	Marketing En Date
NDA	ANDA07815	4	01/15/2009		
vetiracetam t Product Info	ablet, film coat				
evetiracetam t Product Info Product Type	ablet, film coat	ed HUMAN PRESCRIPTION DRUG ORAL	Item Code (Source)	NDC:68180-113
evetiracetam t Product Info Product Type	ablet, film coat	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:68180-113
evetiracetam t Product Info Product Type Route of Admi	ablet, film coat ormation Inistration dient/Active	HUMAN PRESCRIPTION DRUG ORAL Moiety			
evetiracetam t Product Info Product Type Route of Admi Active Ingre	ablet, film coat cormation inistration dient/Active Ingro	HUMAN PRESCRIPTION DRUG	Ba		rength Streng
evetiracetam t Product Info Product Type Route of Admi Active Ingre	ablet, film coat prmation inistration dient/Active Ingn 4 (UNII: 44YRR345	HUMAN PRESCRIPTION DRUG ORAL Moiety edient Name	Ba	asis of St	rength Streng
evetiracetam t Product Info Product Type Route of Admi Active Ingre	ablet, film coat ormation inistration dient/Active Ingn 4 (UNII: 44YRR345 redients	HUMAN PRESCRIPTION DRUG ORAL Molety delient Name S5) (LEVETRACETAN - UNIL-44YRR	Ba	asis of St	rength Streng
evetiracetam t Product Info Product Type Route of Admi Active Ingre LeveTIRACETAM Inactive Ingr	ablet, film coat prmation inistration dient/Active ingn 4 (UNII: 44YRR345 redients CROCRYSTALLIN	HUMAN PRESCRIPTION DRUG ORAL Molecty Solicet Name Ingredient Name Ingredient Name E (UNI: 0918320610)	Ba	asis of St	rength Streng 4 500 mg
evetiracetam t Product Info Product Type Route of Admi Active Ingre LeveTIRACETAM Inactive Ingr CELLUOSE, MIL CROSPOVIDONE	ablet, film coat ormation inistration dient/Active ingn 4 (UNII: 44YRR345 redients cRoCRYSTALLIN 2 (UNII: 257830E5 "ELLOW (UNII: EX	HUMAN PRESCRIPTION DRUG ORAL Molecty Solutevent Name Ingredient Name Ingredient Name (UNII: 0°1/12061U) Soluti: 0°1/12061U) Soluti: 0°1/12061U)	Ba	asis of St	rength Streng 4 500 mg
evetiracetam t Product Info Product Type Route of Admi Active Ingre LEVETIRACETAM Inactive Ingre CELLULOSE, MHI CROSPOVIDOB-LIOSE YMPROMELLOSE YMPROMELLOSE	ablet, film coat ormation inistration dient/Active Ingr 4 (UNI: 44YRB35 redients ccoccrystallin (UNI: 2378057 rellow (UNI: 278057 2110 (UNI: 258057) 210 (INI: 258057) 210 (INI: 258057)	HUMAN PRESCRIPTION DRUG ORAL Molecty dident Name Ingredient Name Ingredient Name (UNI: 09182061U) 61) 48020MRT) 1 (UNI: 001789/W22) 1 (UNI: 001789/W22)	Ba	asis of St	rength Streng 4 500 mg
Product Infe Product Infe Product Type Route of Admi Active Ingre LeveTIRACETAM Inactive Ingre CELLULOSE, MIN CELLULOSE, MIN CELLULOSE, MIN FERRIC OXIDE Y MYPROMELLOSE MAGNESIUM ST POLYETHYLEME	abilet, film coat prmation inistration dient/Active Ingr 4 (UNII: 44YBR345 redients CROCRYSTALLIA CROCRYSTALLIA CROCRYSTALLIA CROCRYSTALLIA 23016 (MPAS 23016 (MPAS 23016 (MPAS) CROCRYSTALLIA GUYCOL 4000 (CMI): 70	HUMAN PRESCRIPTION DRUG ORAL Molecy defent Name Ingredient Name Ingredient Name Ingredient Name Ingredient Name Ingredient Name (UNI: 00178/VT2) 1 (UNI: 00178/VT2) 1 (UNI: 00178/VT2) 1 (UNI: 00178/VT2) 0 (UNI: 00178/VT2) 1 (UNI: 001	Ba	asis of St	rength Streng 4 500 mg
evetiracetam t Product Info Product Type Route of Admi Active Ingre Leveriracetam inactive Ingre cellulose, Min cellulose, Min cellul	ablet, film coat ormation inistration dient/Active ingr (UNII: 44YR345 redients croccrystallin (UNII: 257805) ELLOW (UNII: 257805) ELLOWIN: COMPARISON E 2910 (BMPAS) E 291	HUMAN PRESCRIPTION DRUG OPAL Molecy defent Name Ingredient Name Ingredient Name III (UNI: 001182061U) 61) 8302MRT) 1 (UNI: 00178/W32) 1 (UNI: 00178/W32) 1 (UNI: 00178/W32) 0 (UNI: 00178/W32) 1 (Ba	asis of St	rength Streng 4 500 mg
evetiracetam t Product Info Product Type Route of Admi Active Ingre Leveriracetam Inactive Ingre Cellulose, Mir RosPovidone Machine Ingre Cellulose, Mir RosPovidone Machine Ingre Cellulose, Mir Promotellose Machine Ingre Columna Machine Ingre Columna Machine Ingre Machine Ingre Machin	ablet, film coat ablet, film	HUMAN PRESCRIPTION DRUG ORAL Moiety edient Name Ingredient Status Ingredient	Ba	asis of St	rength Streng 4 500 mg
Product Infe Product Infe Product Type Route of Admi Active Ingre Leveriractive Ingre Leveriractive Ingre Cellulose, Mir Reservo Xub Y MyROMELLOS MAGNESIUM ST POLYETHYLENE POLYETHYLENE ONLYWIT ALC: ONLYWICH ALC:	ablet, film coat ablet, film	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name IN (DRUCK NAME) (UNE OVERACETAN - UNIL-44YRR IN (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 1000-000000000000000000000000000000000	Ba	asis of St	rength Streng 4 500 mg
Product Infr Product Infr Product Type Route of Admi Active Ingre Leverinacetae Inactive Ingre Cellulose, Mir Reservo Xub Pry MyrpoMeLLOSS Magnesum ST Anoly Pry Net All Productione Units Stance, Com	ablet, film coat ablet, film coat anistration dient/Active ing nedients (UNE 2378035 2310 (d MPA. 2310 (d	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name IN (DRUCK NAME) (UNE OVERACETAN - UNIL-44YRR IN (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 1000-000000000000000000000000000000000	Ba	asis of St	rength Streng 4 500 mg
evetiracetam t Product Info Product Type Route of Admi Active Ingre LeverIRACETAM Inactive Ingre CellULOSE, MIR CROSPOVIDOR CROSPOVIDOR VERNELOSE MACHESIN SULCON DIXIN SULCON DIXIN SULCON DIXIN SULCON DIXIN CONTRACT, CONTRACT, CON	ablet, film coat symmetric dient/Active instration dient/Active ing redients (UNE 2378062 2390 (3 MPAS 2390 (3 MPAS 2300 (3 MPAS 23	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name IN (DRUCK NAME) (UNE OVERACETAN - UNIL-44YRR IN (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 1000-000000000000000000000000000000000	83 34555) LEV	nsis of Sti	strength Strength Strength Strength
evetiracetam t Product Info Product Type Route of Admi Active Ingre LEVETIRACETAM Inactive Ingre CELLULOSE, MI ROSPOVIDONE CELLULOSE, MI ROSPOVIDONE CELLULOSE, MI ROSPOVIDONE CELLULOSE, MI ROSPOVIDONE CELLULOSE, MI ROSPOVIDONE CELLULOSE, MI PROTOCOLOSE, MI MI PROTOCOLOSE MI Product Cha Color Shape	ablet, film coat ablet, film coat inistration dient/Active Ingr (UNIE: 44YRR345 redients redients init (UNIE: 2730527 init (UNI	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name IN (DRUCK NAME) (UNE OVERACETAN - UNIL-44YRR IN (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 4360-20487) (UNIL OVERACETAN - UNIL-44YRR 1000-000000000000000000000000000000000	834555) LEV	asis of Sti etiracetaw core ize	2 pieces 13mm
Product Infe Product Infe Product Type Route of Admi Active Ingre LeverirActeration Inactive Ingre LeverirActeration Terration Could be reading to the terration reading to	ablet, film coat ablet, film coat inistration dient/Active Ingr (UNIE: 44YRR345 redients redients init (UNIE: 2730527 init (UNI	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name Ingredient Name Ingr	834555) LEV	asis of Sti etiracetaw core ize	strength Strength 500 mg
Active Ingree Route of Admi Active Ingree Leveriracteran Inactive Ingree Leveriracteran Inactive Ingree Cellulose, Mir Rasponio Ingree Resto Color Machine See Machine See Mac	ablet, film coat ablet, film coat inistration dient/Active Ingr (UNIE: 44YRR345 redients redients init (UNIE: 2730527 init (UNI	HUMAN PRESCRIPTION DRUG ORAL Molecty edient Name Ingredient Name Ingr	834555) LEV	asis of Sti etiracetaw core ize	2 pieces 13mm
Product Info Product Info Product Type Route of Admi Active Ingre Leverinacetan Inactive Ingre Leverinacetan Inactive Ingre Inactive Ingre Cellulose, Min Consorvitoous (UMII Suicon DioXin Product Cha Color Diversion (UMII Stacc) (UC) (C) (C) Product Cha Color Diversion (C) Product Cha Contains Packaging	ablet, film coat symmetric dient/Active instration dient/Active ing redients crocersystallin (UNIE 25780557 2190 (G MPAS 2190 (G MPA	HUMAN PRESCRIPTION DRUG ORAL Molecty addent Name Ingredient Name (UNE OPIALSOFIC) S5) (LEVETRACETAN - UNIL-84YRR MODIFICIAL STREAM (UNIL: 00470789/VS2) 1) (UNIL: 004789/VS2) 1) (UNIL: 004789/VS2)	8 34555) LEV S S S In	ETRACETAN ETRACETAN CORE CORE ZZE Apprint Coc	strength Str
Product Info Product Info Product Type Route of Admi Active Ingre LeverInacetar Inactive Ingre LeverInacetar Inactive Ingre Inactive Ingre In	ablet, film coat ablet, film coat amount of the second of	ними PRESCRIPTION DRUG ORAL Molecty edient Name Ingredient Name IE (UNI: 0718/2001) 61) 438/02/MT/1 10(UNI: 00/UT/20178/1732) 10(UNI: 00/UT/20178/	34555) LEV S Marketing Date	core ize Start	strength Str
Product Info Product Info Product Info Product Type Reute of Admi Active Ingre LeverirRACETAN Inactive Ingre Ingre LeverirRACETAN Inactive Ingre Ingre Leve	ablet, film coat ablet, film coat and ablet, film coat and ablet, film coat ablet, film coa	HUMAN PRESCRIPTION DRUG OPAL Molety Solution Sol	8 34555) LEV 5 5 5 10 01/15/2009	core ize Start	2 pieces Billion Ie LUX02
Product Info Product Info Product Info Product Type Route of Admi Active Ingre LeverirRACETAN Inactive Ingre LeverirRACETAN LeverirRACETAN Contains Contain	ablet, film coat ablet, film coat armation inistration dient/Active Ingr dingr dient/Active Ingr dient/Active Ingr dient	HUMAN PRESCRIPTION DRUG OPAL Molecty Solient Name Ingredient Name (LUNE: 071823061U) (UNE: 0017874782) (UNE: 071823061U) (UNE: 071874787) (UNE: 07187478787) (UNE: 0718747878787) (UNE: 07187478787878787878787878787878787878787	34555) LEV S Marketing Date	core ize Start	2 pieces Billion Ie LUX02
Product Info Product Info Product Info Product Type Route of Admi Active Ingre LeverirRACETAN Inactive Ingre LeverirRACETAN LeverirRACETAN Contains Contain	ablet, film coat ablet, film coat armation inistration dient/Active Ingr dingr dient/Active Ingr dient/Active Ingr dient	HUMAN PRESCRIPTION DRUG OPAL Molety Solution Sol	Bi 34555) LEV S S S S S S In Date 01/15/2009 01/15/2009	core ize Start	2 pieces Billion Ie LUX02
Product Info Product Type Route of Admi Active Ingre LeverIIRACETAM Inactive Ingre CellULOSE, MI Inactive Ingre CellULOSE, MI Inactive Ingre Proversion Info Proversion Info State Portry Active Proversion Info Shape Product Cha Color Shape Color Shape Color Shape Product Cha Color Shape Color Shape Color Shape Info Contains Packaging Item Code Info Contains Packaging Item Code Info Info Info Info Info Info Info Info	abilet, film coat ormation inistration dient/Active inistration dient/Active inistration dent/Active redients construction constrestruction constrestruction<	HUMAN PRESCRIPTION DRUG OPAL OPAL Ingredient Name Ingredient Nam	Bi 34555) LEV S S S S S S In Date 01/15/2009 01/15/2009	core ize Start	2 pieces Billion Ie LUX02
Activation to the second	abilet, film coat srmation inistration dient/Active ing inistration dient/Active ing redients convertigit convertigit convertigit convertigit initiation convertigit	HUMAN PRESCRIPTION DRUG OPAL OPAL Ingredient Name Ingredient Nam	Br 34555) LEV S S S S S S In Date 01/15/2009 01/15/2009 01/15/2009	sis of Start	rength Strength 500 mg Strength 2 pieces 18mm 1e LUX02 Marketing Enc
Product Info Product Info Product Type Route of Admi Active Ingre EVETIRACETAN Inactive Ingre Ingre EVETIRACETAN Inactive Ingre Ingre EVETIRACETAN Info Ingre EVETIRACETAN Ingre EVETIRACETAN Ingre	abilet, film coat srmation inistration dient/Active ing inistration dient/Active ing redients convertigit convertigit convertigit convertigit initiation convertigit	HUMAN PRESCRIPTION DRUG ORA. Molety addent Name (RUNE OPLICATION DRUG S5) (LEVETRACETAN - UNIL-44YRR (RUNE OPLICATION DRUG S4020M7) (UNIL OUTSPAYED) (UNIL OUTS	Br 34555) LEV S S S S S S In Date 01/15/2009 01/15/2009 01/15/2009	core treatment of start	rength Strengt Strength Strength Strength Imm te LUX02
Product Info Product Info Product Type Route of Admi Active Ingre EVETIRACETAN Inactive Ingre Ingre EVETIRACETAN Inactive Ingre Ingre EVETIRACETAN Info Ingre EVETIRACETAN Ingre EVETIRACETAN Ingre	abilet, film coat ormation inistration dient/Active Ing inistration dient/Active Ing redients redients constraint	HUMAN PRESCRIPTION DRUG ORA. Molety addent Name (RUNE OPLICATION DRUG S5) (LEVETRACETAN - UNIL-44YRR (RUNE OPLICATION DRUG S4020M7) (UNIL OUTSPAYED) (UNIL OUTS	Bi 34555) LEV S S S S II II 01/15/2009 01/15/2009 01/15/2009 01/15/2009	sis of Start	rength Strength 500 mg Strength 2 pieces 18mm 1e LUX02 Marketing Enc
Product Infe Product Infe Product Type Route of Admi Active Ingre LeverIRACETAN Active Ingre LeverIRACETAN Inactive Ingre LeverIRACETAN Inactive Ingre CellUloSE, Min ProsponeLLOSE Market Ingre Colores Anno Provident Char Product Colores Analysis of the Colores Shape Colores Tranch, Colore Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores	abilet, film coat ormation inistration dient/Active Ing dient/Active Ing dent/Active Ing dent/Active Ing dent/Active Ing cedients de (unit: 1000000000000000000000000000000000000	HUMAN PRESCRIPTION DRUG ORA. Molecty solution of the second se	Bi 34555) LEV S S S S II II 01/15/2009 01/15/2009 01/15/2009 01/15/2009	sis of Start	rength Strength 500 mg Strength 2 pieces 18mm 1e LUX02 Marketing Enc
Product Info Product Info Product Type Route of Admi Active Ingre EVETIRACETAN Active Ingre EVETIRACETAN Incomposition Prosposition Prosposition Product Char Product Char Pro	abiet, film coat orm ation inistration inistration inistration idient/Active ingr (UUNE 44YRR35 redients redie	HUMAN PRESCRIPTION DRUG ORA. Molecty solution of the second se	Bi 34555) LEV S S S S II II 01/15/2009 01/15/2009 01/15/2009 01/15/2009	sis of Start	rength Streng 500 mg Strength 2 pices 18mm 18mm 10m 10m 10m 10m 10m 10m 10m 1
Product Infe Product Infe Product Type Route of Admi Active Ingre LeverIRACETAN Active Ingre LeverIRACETAN Inactive Ingre LeverIRACETAN Inactive Ingre CellUloSE, Min ProsponeLLOSE Market Ingre Colores Anno Provident Char Product Colores Analysis of the Colores Shape Colores Tranch, Colore Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores Shape Colores Tranch, Colores		HUMAN PRESCRIPTION DRUG ORA. Molecty solution of the second se	34555) LEV 34555) LEV S S S II D215/2009 01/15/2009 01/15/2009 01/15/2009	core core is start	rength Strength 500 mg Strength 2 pieces 18mm 1e LUX02 Marketing Enc

Active Ingredient/Active Moiety

		555) (LEVETIRACETAM - UNII:44YRR		EVETIRACETA	trength Strength M 750 mg
	edients	Ingredient Name			Strength
		NE (UNII: OP1R32D61U)			Screngen
ROSPOVIDONE D&C BLUE NO.					
D&C YELLOW M	O. 6 (UNII: H77	VEI93A8)			
ERRIC OXIDE R		3G675) S) (UNII: 0VUT3PMY82)			
IYPROMELLOSE		S) (UNII: 0WZ 8WG20P6)			
		(UNII: 4R4HFI6D95)			
OLYVINYL ALCO		IFIED (UNII: 532859j990)			
SILICON DIOXIDI	E (UNII: ETJ7Z6)				
TARCH, CORN (TALC (UNII: 75EV) TITANIUM DIOXI	7J4R1U)				
Product Cha	RANGE (Orange			Score	2 pieces
	VAL (Oblong-sh	aped, Biconvex, Film-Coated)		Size	20mm
lavor Contains				Imprint Co	de L;U;X03
Packaging					
# Item Code		ackage Description	Marketi Da	ng Start te	Marketing End Date
NDC:68180-114	- 120 in 1 BOT Product	TLE; Type 0: Not a Combination	01/15/2009		
2 NDC:68180-114	 90 in 1 BOTT Product 	LE; Type 0: Not a Combination	01/15/2009		
NDC:68180-114	- 500 in 1 BOT Product	TLE; Type 0: Not a Combination	01/15/2009		
02	Product				
Marketing	Informa	tion			
Marketing Category		ation Number or Monograph Citation		ting Start Date	Marketing End Date
NDA	ANDA0781		01/15/200		Jac
EVETIRAC					
evetiracetam ta	ıblet, film coa	ted			
Product Info	rmation				
Product Type		HUMAN PRESCRIPTION DRUG	Item Cod	e (Source)	NDC:68180-115
Route of Admi	nistration	ORAL			
Active Ingree	dient/Active	Moietv			
	Ing	redient Name		Basis of S	trength Strength
EVETIRACETAM	(UNII: 44YRR34	555) (LEVETIRACETAM - UNII:44YRR	34555) I	EVETIRACETA	M 1000 mg
Inactive Ingr	edients				
	BOCRYSTALL	Ingredient Name NE (UNII: OP1R32D61U)			Strength
MAGNECUM	SE SODIUM (U	NII: M28OL1HH48)			
	ARATE (UNII: 7	0097M6I30)			
POLYETHYLENE	ARATE (UNII: 7 GLYCOL 6000				
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII:	ARATE (UNII: 7 GLYCOL 6000 DHOL, UNSPEC FZ 989GH94E)	0097M6I30) (UNII: 30IQX730WE) (IFIED (UNII: 532859J990)			
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII: SILICON DIOXIDI	ARATE (UNII: 7 GLYCOL 6000 DHOL, UNSPEC FZ 989GH94E) E (UNII: ETJ7Z6)	0097M6I30) (UNII: 30IQX730WE) IFIED (UNII: 532B59J990) (BU4)			
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (FALC (UNII: 75EV)	ARATE (UNII: 7 GLYCOL 6000 DHOL, UNSPEC FZ989GH94E) E (UNII: ETJ7Z6) UNII: 08232NY3 7J4R1U)	0097M6I30) (UNII: 30IQX730WE) IFFED (UNII: 532859J990) (BU4) SJ)			
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (FALC (UNII: 75EV)	ARATE (UNII: 7 GLYCOL 6000 DHOL, UNSPEC FZ989GH94E) E (UNII: ETJ7Z6) UNII: 08232NY3 7J4R1U)	0097M6I30) (UNII: 30IQX730WE) IFFED (UNII: 532859J990) (BU4) SJ)			
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (FALC (UNII: 75EV) FITANIUM DIOXI	EARATE (UNII: 7 GLYCOL 6000 DHOL, UNSPEC FZ 989GH94E) E (UNII: ETJ7Z 6> UNII: 08232NY3 7J4R1U) DE (UNII: 15FIXS	0097/M6I30) (UMII: 30(Qx730WE) IFFED (UMII: 532859(9990) (BU4) (SJ) (YZJP)			
POLYETHYLENE POLYVINYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (FALC (UNII: 75EV) FITANIUM DIOXII Product Chai Color	Contemporation of the second s	000794600) (UINE 300(X730/KE) (#FED (UNII: 532859)990) (BU4) (S) (V2)P) ((frwhite)		Score	2 pieces 32mm
POLYETHYLENE POLYUNYL ALCC POVIDONE (UNII: SILICON DIOXID STARCH, CORN (TALC (UNI: 75EV: TITANIUM DIOXI Product Chai Color V Shape C	Contemporation of the second s	003746(30) (UNII: 30(2x/30WE) (HERD (UNII: 532859)990) (BU4) (S)) (S))		Score Size Imprint Co	22mm
POLYETHYLENE POLYUNYL ALCC POVIDONE (UNIL SILICON DIOXID STARCH, CORN (ALC (UNIL 75EV) TITANIUM DIOXI Product Chai Color V Shape C Flavor	Contemporation of the second s	000794600) (UINE 300(X730/KE) (#FED (UNII: 532859)990) (BU4) (S) (V2)P) ((frwhite)		Size	22mm
POLYETHYLENE POLYUNYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (UNII: SILICON DIOXIDI STARCH, CORN (UNII: STARCH, CORN (UNII: Product Chai Solor (UNII: Shape (Caroline) Shape (Caroline) Shape (Caroline)	Contemporation of the second s	000794600) (UINE 300(X730/KE) (#FED (UNII: 532859)990) (BU4) (S) (V2)P) ((ff-white)		Size	22mm
POLYETHYLENE POLYUNYL ALCO POVIDONE (UNII: SILICON DIOXIDI STARCH, CORN (UNII: SILICON DIOXIDI STARCH, CORN (UNII: STARCH, CORN (UNII: Product Cha Color (UNII: Shape Ci Shape	ARATE (UNI: 7 GYCOL 6000 HOL, UNSPEC F2989GH94E) (UNI: E172F6 (UNI: E172F6 UNI: 08222NY3 7/4R1U) DE (UNI: 15FXS PACLED (UNI: 15FXS WHTE (White to VVAL (Oblong-s)	00074600) (UNI: 30(2730/E) IFIED (UNI: 532859(990) (8U4) 5)) (V/2)P off-white) aped, Biconvex, Film-Coated)	Marketi	Size Imprint Co ng Start	22mm de L;U;X04
POLYETHYLENE COLYMINY ALCO OVIDONE (UNII: SILICON DIOXIDI SILICON DIOXIDI FAACH, CORN (TALC (UNII: 75EV: TITANIUM DIOXI Product Chai Color y Shape C Flavor C Contains Packaging # Item Code	ARATE (UNIE 7 GLYCOL 6000 MOL, UNSPEC 72989CH94E) E (UNIE 7298CH94E) E (UNIE 7298CH94E) E (UNIE 7276 MITE (UNIE 15FIXS Patter (UNIE 15FIXS WHTE (UNIE 15FIXS WHTE (UNIE 16 MITE (UNIE 16 MITE (UNIE 17 MITE (UNIE 17	00079600) (UNI: 30(2x30x6) IFFED (UNI: 532859(990) (8844) 5) (7) (7) (7) (7) (7) (7) (7) (7) (7) (7	Da	Size Imprint Co ng Start	22mm de L;U;X04
VOLYETHYLENE VOLYETHYLENE VOLYENTYL ALCCOVENTYL ALCCOVENTYL ALCCOVENTY ILLCON DIOXIDISTI ILLCON DIOXIDISTI ILLCON DIOXIDISTI ILLCON DIOXIDISTI VALC (UNII: 75EV. TITANIUM DIOXI VALCOVENTYLENE VIETNICA V	IARATE (UNI: 7 GLYCOL 6000 MOL, UNSPECT T2989CH94E) E (UNI: ET)726 MII: C0232N7 JARLU) DE (UNI: STSIX) DE (UNI: STSIX) WHTE (White to VVAL (Oblong-sh VVAL (Oblong-sh + + 60 in 1 BOTT	uckage Description LE: Type 0: Not a Combination	01/15/2009	Size Imprint Co ng Start	22mm de L;U;X04
VOLYETHYLENE VOLYETHYLENE VOLYENTYL ALCCOVENTYL ALCCOVENTYL ALCCOVENTY ILLCON DIOXIDISTI ILLCON DIOXIDISTI ILLCON DIOXIDISTI ILLCON DIOXIDISTI VALC (UNII: 75EV. TITANIUM DIOXI VALCOVENTYLENE VIETNICA V	IARATE (UNI: 7 GLYCOL 6000 MOL, UNSPECT T2989CH94E) E (UNI: ET)726 MII: C0232N7 JARLU) DE (UNI: STSIX) DE (UNI: STSIX) WHTE (White to VVAL (Oblong-sh VVAL (Oblong-sh + + 60 in 1 BOTT	00079600) (UNI: 30(2x30x6) IFFED (UNI: 532859(990) (8844) 5) (7) (7) (7) (7) (7) (7) (7) (7) (7) (7	Da	Size Imprint Co ng Start	22mm de L;U;X04
POLYETHYLENE POLYETHYLENE SOLVONE SILICON DIOXIDI SILICON DIOXIDI SILICON DIOXIDI SILICON DIOXIDI SILICON DIOXIDI Product Cha Color k Shape C Contains Packaging # Item Code 1 070Cc68180-1112 070Cc68180-1120	LARATE (UNI: 7 GLYCOL 5000 GLYCOL 5000 FOL, UNSPECT CSUM: ETJ2C6(H94E) LUMI: TO2232NY3 TACKET (UNI: 1 DE (UNI: 15FX VAL (Oblong-sP VAL (Oblong-sP F 60 in 1 BOTT Product 50 00 IN 1807	uckage Description LE: Type 0: Not a Combination	01/15/2009	Size Imprint Co ng Start	22mm de L;U;X04
POLYTIYLENE POLYMIPLALE POLYMIPLALE POLYMIPLALE POLYMIPLALE SILCON DISVIDUS STARCH, CORN STARCH, CORN TALE (UME 75E// TITANUM DISVIDUS Product Char Contains Packaging # Item Code MCC-68180-111 Marketing	ARATE (UNIE 7 GUYCE) 6000 HOL, UNISPEC 739305(H945) (UNIE: 01260 UNIE: 00220 (UNIE: 157050 CUNIE: 022047 PARU) DE (UNIE: 157050 CUNIE: 157050	0097M6(20) (UNE 30(X730KE) UPIED (UNE 532859(990) (BU4) (S) (BU4) (S) (BU4) (S) (BU4) (S) (BU4) (S) (S) (S) (S) (S) (S) (S) (S	01/15/2009 01/01/2040	Size Imprint Co ng Start te	22mm LUX04
POLYTIYLENE POLYTIYLENE POLYTIYLENE POLYTIYLENE (JME) POLYTYYLINE	IARATE (UNIE ? GUYCOL 6000 HOL, UNISPEC 72 9905(H945) (UNIE 172 60) IQUINE 172 60 INTER (WHE 15 FIX COLOR 15 FIX INTER (WHE 15 FIX INTER (WHE 16 IN 18 OT INTER (WHE 10 IN 18 OT	0007H6(0) (UNE 30(X730KE) (FFED (UNE 532859(900) (UNE 30(X730KE) (UN2)P) off-white) aped, Biconvex, Film-Coated) ackage Description LE: Type 0: Not a Combination TLE: Type 0: Not a Combination TLE: Type 0: Not a Combination	01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm de L;U;X04
oLYTTYLE HE OLYTYLL ALC DIVONUT ALC DIVON	ARATE (UNIE 7 GUYCOL 6000 HOL, UNISPEC 79905(HAE), UNISPEC 19905(HAE), UNISPEC 19905(HAE), UNISPEC 19905(HAE), UNISPECTION 1947100 INIC 001101 CONTRACTOR 1947100 INIC 00110 Product Product Product Informat Applic	0007H6(0) (UNE 30(X730KE) (FFED (UNE 532859(900) (UNE 30(X730KE) (UN2)P) off-white) aped, Biconvex, Film-Coated) ackage Description LE: Type 0: Not a Combination TLE: Type 0: Not a Combination TLE: Type 0: Not a Combination	01/15/2009 01/01/2040	Size Imprint Co ng Start te ting Start ate	22mm LUX04
POLYTIYLE NE POLYMYLA LACE POVDORE (UME) STARCH, CORN (E STARCH, C) (C) (C) (C) (C) (C) (C) (C) (C) (C) (IARATE (UNIE ? GUYCOL 6000 HOL, UNISPEC 72 9905(H945) (UNIE 172 60) IQUINE 172 60 INTER (WHE 15 FIX COLOR 15 FIX INTER (WHE 15 FIX INTER (WHE 16 IN 18 OT INTER (WHE 10 IN 18 OT	0007H6(0) (UNE 30(X730KE) (FFED (UNE 532859(900) (UNE 30(X730KE) (UN2)P) off-white) aped, Biconvex, Film-Coated) ackage Description LE: Type 0: Not a Combination TLE: Type 0: Not a Combination TLE: Type 0: Not a Combination	01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm LUX04
DUCTIVILENE DOLVINITALCO DOLVINITALCO DOLVINITALCO DICON DUZNIC DICON DUZNIC DIC	ARATE (UNIE : CUNIE : CLYCOL 6000 HOL, UNISPEC F2996CH4021 F2996CH4021 E (UNIE : E7226/UNIE : EVAIE: E7226/UNIE : VIMIE: 02222W7 DE (UNIE : 15FIXS Pacteristics Factoristics VIMIE: 0212W7 DE (UNIE : 15FIXS Pacteristics Factoristics Factoristics Factoristics 56 (In 1 BOTORistics) Fooduct 50 (In 1 BOTORistics) Fooduct BOTORistics Fooduct Fooduct Informal Applic	0007M6(0) (UNE 30(X730/E) UPIED (UNE 532859(980) (2014) (2	01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm LUX04
DOLYTIYILENE POLYWIYLALC POYDORE (UME SILCON DIZXING SILCON DIZXING STARCH, CORN OF TARCH, CORN OF TARCH, CORN OF TARAVOT Contains Packaging # Incode Packaging # Incode Naccession Naccession Marketing Category Nac	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC F2995(H404) E (UNIE 17256) E (UNIE 17256) CUNIE 17257 Participation (UNIE 1571X) Participation (UNIE 1571X) Partici	0007H6(0) (UNE 30(X730/E) (FFED (UNE 532855(990)) (BU4) (S)) (BU4) (S)) (C) (BU4) (S)) (C) (C) (C) (C) (C) (C) (C) (C) (C) (01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm LUX04
DOLYTIYILENE POLYWIYLALC POYDORE (UME SILCON DIZXING SILCON DIZXING STARCH, CORN OF TARCH, CORN OF TARCH, CORN OF TARAVOT Contains Packaging # Incode Packaging # Incode Naccession Naccession Marketing Category Nac	ARATE (UNIE ; CUNIE ; GLYCOL 6000 ; NUSPEC ; F299C;H402 ; NUSPEC ; F299C;H402 ; NUE: 02322W17 DE (UNIE : 5712G) NUE: 02522W17 JPE (UNIE : 1571XG) NUE: 02522W17 JPE (UNIE : 1571XG) NUE: 02522W17 JPE (UNIE : 1571XG) NUE: 0252W17 JPE (UNIE : 1571XG) STATE STATE (WHITE (White to 'VAIL (Obligges)') NUE: 0571XG) STATE (WHITE (White to 'STATE)) STATE STATE (WHITE (WHITE (WHITE (WHITE to 'STATE))) STATE STATE (WHITE (WHITE (WHITE to 'STATE)) STATE STATE (WHITE to 'STATE)) STATE STATE (WHITE TO 'STATE) STATE STATE STAT	0007M6(0) (UNE 30(X730/E) UPIED (UNE 532859(980) (2014) (2	01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm LUX04
DOLYTIYLENE POLYWIYLALC POYDORE (UME SUICON DIZXING STARCH, CORN (CONN STARCH, CONN (CONN STARCH, CONN (CONN TITANUUM DIXXII Product Cha Scolar v Contains Product Cha Boccission 11 (DCC-68180-11 (DC	ARAFE (UNIE : Z GLYCOL 6000 HOL, UNISPEC F2996(H4G) (UNISPEC F2996(H4G) (UNIE E (UNIE : ET7260 INIE: 02322N7 7)AR1U) DE (UNIE: 15FIXS Product INIE: 000000000 Product E07 Product E07 Prod	0007M600) (UNE 30(X730/E) (FFED (UNE 5328559900) (2014) (2	01/15/2009 01/01/2040 Marke	Size Imprint Co ng Start te ting Start ate	22mm LUX04
POLYTIYLENE POLYMINA LAC: POVDORE (UME) STARCH, CORN (CORN STARCH, CORN (CORN TTARCUME) Product Chai Stape (Constant) Stape (Constant) (Constan	ARATE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC 7299C(H42) E (UNIE 17256) UNIE (UNIE 17256) INIE (UNIE 17256) INIE (UNIE 17256) INIE (UNIE 1716) Product 101 Product 101	0007ME(0) (UNE 30(X)30KE) (PHED (UNE 532859(900) (BH4) (S)) (BH4) (S)) (BH4) (S)) (BH4) (S)) (S)) (S)) (S)) (S)) (S)) (S)) (S	01/15/2009 01/01/2040 01/01/2040 01/15/200 iness Oper	Size Imprint Co ng Start te ting Start Jate 9	22mm de LUX04
DOLYTIYLENE POLYWIYLALC POYDORE (UME SUICON DIZXING STARCH, CORN (CONN STARCH, CONN (CONN STARCH, CONN (CONN TITANUUM DIXXII Product Cha Scolar v Contains Product Cha Boccission 11 (DCC-68180-11 (DC	ARATE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC 7299C(H42) E (UNIE 17256) UNIE (UNIE 17256) INIE (UNIE 17256) INIE (UNIE 17256) INIE (UNIE 1716) Product 101 Product 101	0007M600) (UNE 30(X730/E) (FFED (UNE 5328559900) (2014) (2	01/15/2009 01/01/2040 01/01/2040 01/15/200 iness Oper	Size Imprint Co ng Start te ting Start Jate 9	22mm de LUX04
POLYTIYLENE POLYTIYLENE POLYDIYLAL SULCON DUXDUE UNDE STARCH, CORN IN STARCH, CORN IN STARCH, CORN IN Product Chai Stabus Product Chai Stabus Product Chai Not Stabus Product Chai Not Product Chai Not Not Product Chai Not Not Product Chai Not Not Product Chai Not Not Not Not Not Not Not Not Not Not	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC F2996(H4G) II (UNIE 17260) III (UNIE 17260) IIII (UNIE 17260) IIIII (UNIE 1571X5) IIIII (UNIE 1571X5) IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	0007ME(0) (UNE 30(X)30KE) (PHED (UNE 532859(900) (BH4) (S)) (BH4) (S)) (BH4) (S)) (BH4) (S)) (S)) (S)) (S)) (S)) (S)) (S)) (S	01/15/2009 01/01/2040 01/01/2040 01/15/200 iness Oper	Size Imprint Co ng Start te ting Start Jate 9	22mm de LUX04
POLYTIYLENE POLYNIYL ALC POYDORE (JWH: SUCON DIXING STARCH, CORN T TARCH, CORN T Product Chai Color 4 4 Product Chai Color 4 4 Product Chai Color 4 4 Product Chai Color 4 4 Product Chai Shape C TarAnium Doxi I tem Code 1 100-0010-111 100-0010-000-00	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC 7299C/HOL UNISPEC E (UNIE : 17256 LE (UNIE : 17257 LE (UNIE : 17257) LE (UNIE : 172577) LE (UNIE : 172577) LE (UNIE : 172577) LE (UNIE : 1725777)	0097M620) (UNE 300/X300/E) UPIED (UNE 5328259990) (BU4) (S) (BU4) (S) (BU4) (S) (BU4) (S) (S) (S) (S) (S) (S) (S) (S	01/15/2009 01/01/2040 01/01/2040 01/15/2000 intess Oper 113, 68180-1 3)	Size Imprint Co ng Start te ting Start 9 9 ations 14, 68180-115	22mm de LUX04
POLYTIYLENE POLYNINY ALC: POYDORY (JWHE WITH SUCON DIXING STARCH, CORN IN TARCH, CORN IN TARCHINE, TOTALINA POLYTITANIUM DIXIN Product Cha Shape C TITANIUM DIXIN Shape C TITANIUM DIXIN PACKABING I Iben Code I INC-68180-112 I Iben Code I Iben Code	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC F299CH4041 E (UNIE 17260 UNIE 0222V1 JARIU) DE (UNIE 17260 UNIE 0222V1 JARIU) DE (UNIE 17260 CONTRACTOR Product Product DE (UNIE 1000 Product B01 Product B01	009746(20) (UNE 30(2730/E) UPIED (UNE 5328559990) (BU4) 5() (BU4) 5() 01 01 01 01 01 01 01 01 01 01	01/15/2009 01/01/2040 Marke 01/15/200 01/15/200 iness Oper 113, 68180-1 i))	Size Imprint Co ng Start te ting Start Pate 9 ations 14, 68180-111 ations	22mm de LUX04
DUCTIVILENE DUCYNILLENE DUCYNI	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC F299CH4041 E (UNIE 17260 UNIE 0222V1 JARIU) DE (UNIE 17260 UNIE 0222V1 JARIU) DE (UNIE 17260 CONTRACTOR Product Product DE (UNIE 1000 Product B01 Product B01	0097M620) (UNE 300/X300/E) UPIED (UNE 5328259990) (BU4) (S) (BU4) (S) (BU4) (S) (BU4) (S) (S) (S) (S) (S) (S) (S) (S	01/15/2009 01/01/2040 Marke 01/15/200 01/15/200 iness Oper 113, 68180-1 i))	Size Imprint Co ng Start te ting Start Pate 9 ations 14, 68180-111 ations	22mm de LUX04
DUCTIVILENE POLVINIVA LAC: POVDORE (UME) SILCON DUZNIE SILCON DUZNIE SILCON DUZNIE TARCH, COMP. 152- TITTANIUM DIOXID Product Cha Contains Product Cha Contains Product Cha Stabus Product Cha Contains Product Cha Stabus Product Cha Contains Product Cha Stabus Product Product Cha Stabus Product Product Cha Stabus Product Product Produ	ARATE (UNIE ; Z ARATE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC 2599C(H42) E (UNIE : 17226 UNIE : 02322W) Pactoristics Pactoristics WAL (Obling sh Pactoristics WAL (Obling sh Pactoristics WAL (Obling sh Pactoristics WAL (Obling sh Pactoristics WAL (Obling sh Pactoristics Pactoristics Pactoristics WAL (Obling sh Pactoristics WAL (Obling sh Pactoristics Pactoris	009746(20) (UNE 30(2730/E) (FFED (UNE 5328559990) (BU4) 5() (BU4) 5() 01 01 01 01 01 01 01 01 01 01	01/15/2009 01/01/2040 Marke 01/15/200 01/15/200 iness Oper 113, 68180-1 i))	Size Imprint Co ng Start te ting Start Pate 9 ations 14, 68180-111 ations	22mm de LUX04
POLYTIYLENE POLYTIYLENE POLYDIYLAL SULCON DUXIDI STARCH, CORN T Product Chai Starch, Conn T Product Chai Starc (unit: 75°C TrtAnium DuXi Shape C TrtAnium DuXi (DCC0100111 (DCC0100111) (DCC010011) (DCC010011) (DCC010111) (DCC010111) (DCC010	ARAFE (UNIE ; Z GLYCOL 6000 HOL, UNISPEC 2799C/HOL E (UNIE : 5799C/HOL E (UNIE : 5799C/HOL MIE : 02322W/ Pactoristics WHITE (White iso 2004 (Oblong st Pactoristics WHITE (White iso 2004 (Oblong st Pactoristics Pa	0007H6(D) (UNE 30(X730KE) IFIED (UNE 5328559900) IBU4) 5() 1BU4) 5() 1BU4) 5() 1BU4) 5() 1BU4) 5() 1BU4) 1B	D2 D1/5/2009 D1/5/2009 D1/5/2009 D1/5/200 D1/5/200 Marke E D2 D1/5/200 Iness Oper 113, 68180-1 D1 D1 D1/5/200 Iness Oper Iness Oper	Size Imprint Co ng Start te ting Start size 9 9 ations 14, 68180-112 ations	22mm de LUX04 Marketing End Date 5), PACK(68180-112, 5), PACK(68180-112,

Revised: 4/2024

Lupin Pharmaceuticals, Inc.