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

VIMPAT® (lacosamide) film coated tablet, for oral use, CV
VIMPAT® (lacosamide) injection, for intravenous use, CV
VIMPAT® (lacosamide) oral solution, CV
Initial U.S. Approval: 2008

----------RECENT MAJOR CHANGES----------
Warnings and Precautions (5.3) 11/2018

----------INDICATIONS AND USAGE----------
VIMPAT is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.
As the safety of VIMPAT injection has not been established in pediatric patients, VIMPAT injection is indicated for the treatment of partial-onset seizures only in adult patients (17 years of age and older) (1)

----------DOSAGE AND ADMINISTRATION----------
- *Adults (17 years and older):* Initial dosage for monotherapy is 100 mg twice daily; initial dosage for adjunctive therapy is 50 mg twice daily; maximum recommended dosage for monotherapy and adjunctive therapy is 200 mg twice daily (2.1)
- *Pediatric Patients 4 Years to less than 17 years*: The recommended dosage is based on body weight and is administered orally twice daily (2.1)
- Increase dosage based on clinical response and tolerability, no more frequently than once per week (2.1)
- Injection: for intravenous and adult use only when oral administration is temporarily not feasible; dosing regimen is the same as oral regimen; administer over 15 to 60 minutes; obtaining ECG before initiation is recommended in certain patients (2.6, 5.3)
- Dose adjustment is recommended for severe renal impairment (2.3, 12.3)
- Dose adjustment is recommended for mild or moderate hepatic impairment; use in patients with severe hepatic impairment is not recommended (2.4, 12.3)

----------DOSAGE FORMS AND STRENGTHS----------
- 50 mg, 100 mg, 150 mg, 200 mg tablets (3)
- 200 mg/20 mL single-dose vial for intravenous use (3)
- 10 mg/mL oral solution (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
- Monitor patients for suicidal behavior and ideation (5.1)
- VIMPAT may cause dizziness and ataxia (5.2)
- Cardiac Rhythm and Conduction Abnormalities: Obtaining ECG before beginning and after titration to steady-state maintenance is recommended in patients with underlying proarrhythmic conditions or on concomitant medications that affect cardiac conduction; closely monitor these patients (5.3, 7.2)
- VIMPAT may cause syncope (5.4)
- VIMPAT should be gradually withdrawn to minimize the potential of increased seizure frequency (5.5)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/ Multi-Organ Hypersensitivity: Discontinue if no alternate etiology (5.6)

----------ADVERSE REACTIONS----------
- Adjunctive therapy: Most common adverse reactions in adults (≥10% and greater than placebo) are diplopia, headache, dizziness, nausea (6.1)
- Monotherapy: Most common adverse reactions are similar to those seen in adjunctive therapy studies (6.1)
- Pediatric patients: Adverse reactions are similar to those seen in adult patients (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 1-844-599-2273 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 1/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

2.1 Dosage Information

Monotherapy and Adjunctive Therapy

The recommended dosage for adults and pediatric patients 4 years to less than 17 years of age is included in Table 1. In pediatric patients 4 years to less than 17 years of age, the recommended dosing regimen is dependent upon body weight and is only recommended to be administered orally. Dosage should be increased based on clinical response and tolerability, no more frequently than once per week. Titration increments should not exceed those shown in Table 1.

Table 1: Recommended Dosage for Adults and Pediatric Patients 4 Years and Older*

Age and Body Weight	Initial Dosage	Titration Regimen	Maintenance Dosage
Adults (17 years and older)	**Monotherapy:** 100 mg twice daily (200 mg per day) **Adjunctive Therapy:** 50 mg twice daily (100 mg per day)	Increase by 50 mg twice daily (100 mg per day) every week	**Monotherapy:** 150 mg to 200 mg twice daily (300 mg to 400 mg per day) **Adjunctive Therapy:** 100 mg to 200 mg twice daily (200 mg to 400 mg per day)
	Alternate Initial Dosage: 200 mg single loading dose, followed 12 hours later by 100 mg twice daily		
Pediatric patients weighing 50 kg or more	50 mg twice daily (100 mg per day)	Increase by 50 mg twice daily (100 mg per day) every week	**Monotherapy:** 150 mg to 200 mg twice daily (300 mg to 400 mg per day) **Adjunctive Therapy:** 100 mg to 200 mg twice daily (200 mg to 400 mg per day)
Pediatric patients weighing 30 kg to less than 50 kg	1 mg/kg twice daily (2 mg/kg/day)	Increase by 1 mg/kg twice daily (2 mg/kg/day) every week	2 mg/kg to 4 mg/kg twice daily (4 mg/kg/day to 8 mg/kg/day)
Pediatric patients weighing 11 kg to less than 30 kg	1 mg/kg twice daily (2 mg/kg/day)	Increase by 1 mg/kg twice daily (2 mg/kg/day) every week	3 mg/kg to 6 mg/kg twice daily (6 mg/kg/day to 12 mg/kg/day)

*when not specified, the dosage is the same for monotherapy and adjunctive therapy

In adjunctive clinical trials in adult patients, a dosage higher than 200 mg twice daily (400 mg per day) was not more effective and was associated with a substantially higher rate of adverse reactions [*see Adverse Reactions (6.1) and Clinical Studies (14.2)*].

VIMPAT Injection Dosage in Adult Patients (17 years and older)

VIMPAT injection may be used for adult patients when oral administration is temporarily not feasible [*see Dosage and Administration (2.6) and Warnings and Precautions (5.3)*]. VIMPAT injection can be administered intravenously to adult patients with the same dosing regimens described for oral dosing, including the loading dose. The use of VIMPAT injection in pediatric patients has not been studied.

The clinical study experience of intravenous VIMPAT is limited to 5 days of consecutive treatment.

Loading Dose in Adult Patients (17 Years and Older)

VIMPAT and VIMPAT injection may be initiated in adult patients with a single loading dose of 200 mg

2.3 Dosage Information for Patients with Renal Impairment

For patients with mild to moderate renal impairment, no dosage adjustment is necessary.

For patients with severe renal impairment [creatinine clearance (CL_{CR}) less than 30 mL/min as estimated by the Cockcroft-Gault equation for adults; CL_{CR} less than 30 mL/min/1.73m^2 as estimated by the Schwartz equation for pediatric patients] or end-stage renal disease, a reduction of 25% of the maximum dosage is recommended.

In all patients with renal impairment, the dose titration should be performed with caution.

Hemodialysis

VIMPAT is effectively removed from plasma by hemodialysis. Following a 4-hour hemodialysis treatment, dosage supplementation of up to 50% should be considered.

Concomitant Strong CYP3A4 or CYP2C9 Inhibitors

Dose reduction may be necessary in patients with renal impairment who are taking strong inhibitors of CYP3A4 and CYP2C9 [*see Drug Interactions (7.1), Use in Specific Populations (8.6), Clinical Pharmacology (12.3)*].

2.4 Dosage Information for Patients with Hepatic Impairment

For patients with mild or moderate hepatic impairment, a reduction of 25% of the maximum dosage is recommended. The dose titration should be performed with caution in patients with hepatic impairment. VIMPAT use is not recommended in patients with severe hepatic impairment.

Concomitant Strong CYP3A4 and CYP2C9 Inhibitors

Dose reduction may be necessary in patients with hepatic impairment who are taking strong inhibitors of CYP3A4 and CYP2C9 [*see Drug Interactions (7.1), Use in Specific Populations (8.7), Clinical Pharmacology (12.3)*].

2.5 Administration Instructions for VIMPAT Tablets and Oral Solution

VIMPAT may be taken with or without food.

VIMPAT Oral Solution

A calibrated measuring device is recommended to measure and deliver the prescribed dose accurately. A household teaspoon or tablespoon is not an adequate measuring device.

VIMPAT oral solution may also be administered using a nasogastric tube or gastrostomy tube.

Discard any unused VIMPAT oral solution remaining after 7 weeks of first opening the bottle.

2.6 Preparation and Administration Information for VIMPAT Injection for Adult Patients

Preparation

VIMPAT injection can be administered intravenously without further dilution or may be mixed with diluents listed below. The diluted solution should not be stored for more than 4 hours at room temperature.

Diluents:

Sodium Chloride Injection 0.9% (w/v)
Dextrose Injection 5% (w/v)
Lactated Ringer's Injection

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Product with particulate matter or discoloration should not be used.

The diluted solution should not be stored for more than 4 hours at room temperature. Any unused portion of VIMPAT injection should be discarded.

2.7 Discontinuation of VIMPAT

When discontinuing VIMPAT, a gradual withdrawal over at least 1 week is recommended [*see Warnings and Precautions (5.5)*].

3 DOSAGE FORMS AND STRENGTHS

VIMPAT Tablets

- 50 mg: pink, oval, film-coated, debossed with "SP" on one side and "50" on the other
- 100 mg: dark yellow, oval, film-coated, debossed with "SP" on one side and "100" on the other
- 150 mg: salmon, oval, film-coated, debossed with "SP" on one side and "150" on the other
- 200 mg: blue, oval, film-coated, debossed with "SP" on one side and "200" on the other

VIMPAT Injection

- 200 mg/20 mL: clear, colorless sterile solution in single-dose vials

VIMPAT Oral Solution

- 10 mg/mL: clear, colorless to yellow or yellow-brown, strawberry-flavored liquid

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Suicidal Behavior and Ideation

Antiepileptic drugs (AEDs), including VIMPAT, increase the risk of suicidal thoughts 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) of 11 different AEDs showed that patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI: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 of suicidal behavior or ideation among 27,863 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 of events is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting 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.

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 (5-100 years) in the clinical trials analyzed.

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.

Anyone considering prescribing VIMPAT or any other AED must balance this risk with the risk of untreated illness. Epilepsy and many other illnesses for which antiepileptics 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.

5.2 Dizziness and Ataxia

VIMPAT may cause dizziness and ataxia. In adult patients with partial-onset seizures taking 1 to 3 concomitant AEDs, dizziness was experienced by 25% of patients randomized to the recommended doses (200 to 400 mg/day) of VIMPAT (compared with 8% of placebo patients) and was the adverse event most frequently leading to discontinuation (3%). Ataxia was experienced by 6% of patients randomized to the recommended doses (200 to 400 mg/day) of VIMPAT (compared to 2% of placebo patients). The onset of dizziness and ataxia was most commonly observed during titration. There was a substantial increase in these adverse events at doses higher than 400 mg/day [*see Adverse Reactions (6.1)*]. Dizziness and ataxia were also observed in pediatric clinical trials.

5.3 Cardiac Rhythm and Conduction Abnormalities

PR Interval Prolongation, Atrioventricular Block, and Ventricular Tachyarrhythmia

Dose-dependent prolongations in PR interval with VIMPAT have been observed in clinical studies in adult patients and in healthy volunteers [*see Clinical Pharmacology (12.2)*]. In adjunctive clinical trials in adult patients with partial-onset seizures, asymptomatic first-degree atrioventricular (AV) block was observed as an adverse reaction in 0.4% (4/944) of patients randomized to receive VIMPAT and 0% (0/364) of patients randomized to receive placebo. One case of profound bradycardia was observed in a patient during a 15-minute infusion of 150 mg VIMPAT.When VIMPAT is given with other drugs that prolong the PR interval, further PR prolongation is possible.

In the postmarketing setting, there have been reports of cardiac arrhythmias in patients treated with VIMPAT, including bradycardia, AV block, and ventricular tachyarrhythmia, which have rarely resulted in asystole, cardiac arrest, and death. Most, although not all, cases have occurred in patients with underlying proarrhythmic conditions, or in those taking concomitant medications that affect cardiac conduction or prolong the PR interval. These events have occurred with both oral and intravenous routes of administration and at prescribed doses as well as in the setting of overdose [*see Overdosage (10)*].

Vimpat should be used with caution in patients with underlying proarrhythmic conditions such as known cardiac conduction problems (e.g., marked first-degree AV block, second-degree or higher AV block and sick sinus syndrome without pacemaker), severe cardiac disease (such as myocardial ischemia or heart failure, or structural heart disease), and cardiac sodium channelopathies (e.g., Brugada Syndrome). VIMPAT should also be used with caution in patients on concomitant medications that affect cardiac conduction, including sodium channel blockers, beta-blockers, calcium channel blockers, potassium channel blockers, and medications that prolong the PR interval [*see Drug Interactions (7.2)*]. In such patients, obtaining an ECG before beginning VIMPAT, and after VIMPAT is titrated to steady-state maintenance dose, is recommended. In addition, these patients should be closely monitored if they are administered VIMPAT through the intravenous route [*see Adverse Reactions (6.1), Drug Interactions (7.2)*].

Atrial Fibrillation and Atrial Flutter

In the short-term investigational trials of VIMPAT in adult patients with partial-onset seizures there were no cases of atrial fibrillation or flutter. Both atrial fibrillation and atrial flutter have been reported in open label partial-onset seizure trials and in postmarketing experience. In adult patients with diabetic neuropathy, for

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