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 (5.6) 3/2017

----------INDICATIONS AND USAGE----------
VIMPAT is indicated as monotherapy or adjunctive therapy in patients with partial-onset seizures; VIMPAT Injection is indicated as short term replacement when oral administration is not feasible (1)

----------DOSAGE AND ADMINISTRATION----------
- Monotherapy: initial recommended dose is 100 mg twice daily; based on individual patient response and tolerability, increase at weekly intervals by 50 mg twice daily, up to a recommended maintenance dose of 150 mg to 200 mg twice daily (2.1)

  In patients already taking an antiepileptic drug, the VIMPAT recommended maintenance dose of 150 mg to 200 mg twice daily should be maintained for at least 3 days before initiating withdrawal of the previous antiepileptic drug (2.1)
- Adjunctive Therapy: initial recommended dose is 50 mg twice daily; based on individual patient response and tolerability, increase at weekly intervals by 50 mg twice daily, up to a recommended maintenance dose of 100 mg to 200 mg twice daily (2.1)
- VIMPAT Injection: must be administered intravenously; when switching from orally administered VIMPAT to VIMPAT Injection, the initial dosing regimen of VIMPAT Injection should be the same as that used for orally administered VIMPAT; VIMPAT Injection can be administered over a period of 15 minutes to 60 minutes; monitor closely patients with known cardiac conduction problems, on concomitant medications that prolong PR interval, or with severe cardiac disease (e.g., myocardial ischemia, heart failure), as VIMPAT may cause bradycardia or AV blocks in these patients (2.2, 5.3)
- Renal impairment: Dose adjustment is recommended for patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) (2.3, 12.3)
- Hepatic impairment: Dose adjustment is recommended for patients with mild or moderate hepatic impairment; use in severe hepatic impairment patients is not recommended (2.4, 12.3)

----------DOSAGE FORMS AND STRENGTHS----------
- 50 mg (pink), 100 mg (dark yellow), 150 mg (salmon), 200 mg (blue) film-coated tablets (3)
- 200 mg/20 mL single-use 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: ECG before beginning VIMPAT, and after VIMPAT is titrated to steady-state maintenance dose is recommended in patients with known cardiac conduction problems, taking drugs known to induce PR interval prolongation, or with severe cardiac disease (5.3)
- 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----------
- Monotherapy: Most common adverse reactions are similar to those seen in adjunctive therapy studies (6.1)
- Adjunctive therapy: Most common adverse reactions (≥10% and greater than placebo) are diplopia, headache, dizziness, nausea (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: 3/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VIMPAT is indicated in patients 17 years and older with partial-onset seizures as monotherapy or adjunctive therapy.

VIMPAT injection for intravenous use is an alternative when oral administration is temporarily not feasible.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage for VIMPAT Tablet and Oral Solution

Monotherapy

The initial recommended dose of VIMPAT is 100 mg twice daily (200 mg per day); the dose should be increased by 50 mg twice daily (100 mg per day) every week, up to a recommended maintenance dose of 150 mg twice daily to 200 mg twice daily (300 mg to 400 mg per day). Alternatively, VIMPAT may be initiated with a single loading dose of 200 mg, followed approximately 12 hours later by 100 mg twice daily (200 mg per day); this dose regimen should be continued for one week. Based on individual response and tolerability, the dose can be increased at weekly intervals by 50 mg twice daily (100 mg per day), as needed, up to the recommended maintenance dose of 150 mg twice daily to 200 mg twice daily (300 mg to 400 mg per day). The loading dose should be administered with medical supervision because of the increased incidence of CNS adverse reactions [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3)*].

For patients who are already on a single antiepileptic and will convert to VIMPAT monotherapy, the therapeutic dose of 150 mg twice daily to 200 mg twice daily (300 mg to 400 mg per day) should be maintained for at least 3 days before initiating withdrawal of the concomitant antiepileptic drug. A gradual withdrawal of the concomitant antiepileptic drug over at least 6 weeks is recommended.

Adjunctive Therapy

The initial recommended dose is 50 mg twice daily (100 mg per day). Based on individual patient response and tolerability, the dose can be increased at weekly intervals by 50 mg twice daily (100 mg per day). The recommended maintenance dose is 100 mg twice daily to 200 mg twice daily (200 mg to 400 mg per day). In clinical trials, the 300 mg twice daily (600 mg per day) dose was not more effective than the 200 mg twice daily dose (400 mg per day), but was associated with a substantially higher rate of adverse reactions [*see Clinical Studies (14.1)*].

Alternatively, VIMPAT may be initiated with a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice daily (200 mg per day); this maintenance dose regimen should be continued for one week. Based on individual patient response and tolerability, the dose can be increased at weekly intervals by 50 mg twice daily (100 mg per day), as needed, up to the maximum recommended maintenance dose of 200 mg twice daily (400 mg per day). The loading dose should be administered with medical supervision because of the increased incidence of CNS adverse reactions [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3)*]. When discontinuing VIMPAT, a gradual withdrawal over at least 1 week is recommended [*see Warnings and Precautions (5.5)*].

2.2 Dosage for VIMPAT Injection

Intravenous VIMPAT can be administered in the same dosing regimens described for oral dosing, including the loading dose. These dosages may be infused intravenously over a period of 15 minutes to 60 minutes. Intravenous infusion of 30 to 60 minutes is preferable, and should be used when a 15 minute administration is

Monitor closely patients with known cardiac conduction problems, on concomitant medications that prolong PR interval, or with severe cardiac disease (e.g., myocardial ischemia, heart failure), as intravenous infusion of VIMPAT may cause bradycardia or AV blocks in these patients [*see Warnings and Precautions (5.3)*].

When switching from oral to intravenous VIMPAT, the initial total daily intravenous dosage regimen of VIMPAT should be equivalent to the dosage regimen of oral VIMPAT. The clinical study experience of intravenous VIMPAT is limited to 5 days of consecutive treatment. At the end of the intravenous treatment period, the patient may be switched to VIMPAT oral administration at the equivalent daily dosage and frequency of the intravenous administration.

2.3 Dosage Information in Patients with Renal Impairment

No dose adjustment is necessary in patients with mild to moderate renal impairment. A maximum dose of 300 mg per day VIMPAT is recommended for patients with severe renal impairment [creatinine clearance (CL_{CR}) less than or equal to 30 mL/min] and in patients with endstage renal disease. VIMPAT is effectively removed from plasma by hemodialysis. Following a 4-hour hemodialysis treatment, dosage supplementation of up to 50% should be considered. In all renally impaired patients, the dose titration should be performed with caution. Patients with renal impairment who are taking strong inhibitors of CYP3A4 and CYP2C9 may have a significant increase in exposure to VIMPAT. Dose reduction may be necessary in these patients [*see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)*].

2.4 Dosage Information in Patients with Hepatic Impairment

The dose titration should be performed with caution in patients with hepatic impairment. A maximum dose of 300 mg per day is recommended for patients with mild or moderate hepatic impairment.

VIMPAT use is not recommended in patients with severe hepatic impairment. Patients with hepatic impairment who are taking strong inhibitors of CYP3A4 and CYP2C9 may have a significant increase in exposure to VIMPAT. Dose reduction may be necessary in these patients [*see Use in Specific Populations (8.7), Clinical Pharmacology (12.3)*].

2.5 Administration Instructions

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 Injection

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

Product with particulate matter or discoloration should not be used.
Any unused portion of VIMPAT injection should be discarded.

3 DOSAGE FORMS AND STRENGTHS

- 50 mg (pink), 100 mg (dark yellow), 150 mg (salmon), and 200 mg (blue) film-coated tablets

- 10 mg/mL oral solution

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.

Table 1 shows absolute and relative risk by indication for all evaluated AEDs.

Table 1 Risk by Indication for Antiepileptic Drugs in the Pooled Analysis

Indication	Placebo Patients with Events Per 1000 Patients	Drug Patients with Events Per 1000 Patients	Relative Risk: Incidence of Events in Drug Patients/Incidence in Placebo Patients	Risk Difference: Additional Drug Patients with Events Per 1000 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.

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.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

5.2 Dizziness and Ataxia

VIMPAT may cause dizziness and ataxia.

In 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)*].

5.3 Cardiac Rhythm and Conduction Abnormalities

PR interval prolongation

Dose-dependent prolongations in PR interval with VIMPAT have been observed in clinical studies in patients and in healthy volunteers [*see Clinical Pharmacology (12.2)*]. In adjunctive clinical trials in patients with partial-onset epilepsy, 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. In clinical trials in patients with diabetic neuropathy, asymptomatic first-degree AV block was observed as an adverse reaction in 0.5% (5/1023) of patients receiving VIMPAT and 0% (0/291) of patients receiving placebo. Second degree and complete AV block have been reported in patients in pain studies and in patients with seizures. When VIMPAT is given with other drugs that prolong the PR interval, further PR prolongation is possible.

VIMPAT should be used with caution in patients with known conduction problems (e.g., marked first-degree AV block, second-degree or higher AV block and sick sinus syndrome without pacemaker), sodium channelopathies (e.g., Brugada Syndrome), on concomitant medications that prolong PR interval, or with severe cardiac disease such as myocardial ischemia or heart failure, or structural heart disease. 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. One case of profound bradycardia was observed in a patient during a 15-minute infusion of 150 mg VIMPAT. There were two postmarketing reports of third degree AV block in patients with significant cardiac history and also receiving metoprolol and amlodipine during infusion of VIMPAT injection at doses higher than recommended [*see Adverse Reactions (6.1), Drug Interactions (7.2)*].

Atrial fibrillation and Atrial flutter

In the short-term investigational trials of VIMPAT in epilepsy patients, there were no cases of atrial fibrillation or flutter. Both atrial fibrillation and atrial flutter have been reported in open label epilepsy trials and in postmarketing experience. In patients with diabetic neuropathy, 0.5% of patients treated with VIMPAT experienced an adverse reaction of atrial fibrillation or atrial flutter, compared to 0% of placebo-treated patients. VIMPAT administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients

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