Prescriber’s Guide to Lasmiditan
What You Need to Know: Reyvow (lasmiditan) for Acute Treatment of Migraine

By Karen Berger, PharmD

On October 11, 2019, the FDA approved lasmiditan (Reyvow; Eli Lilly) tablets for the acute (active, short-term) treatment of migraine with or without aura in adults. Lasmiditan is indicated only for acute treatment, and is not used for preventive treatment.¹

Lasmiditan is the first FDA-approved drug from the new class of serotonin (5-HT)1F receptor agonists. The drug binds to 5-HT1F receptors with high affinity, and although the precise mechanism is unknown, the therapeutic effects are likely mediated by agonist effects at the receptor.²

Migraine Overview

As the third most prevalent illness in the world, migraine affects 39 million men, women, and children in the United States, and 1 billion worldwide. Over 4 million people suffer from chronic daily migraine, with at least 15 migraine days per month.³

Migraine is a neurological disease with incapacitating neurological symptoms. It presents as a severe, throbbing, recurring pain, usually on one side of the head. Attacks often occur with visual disturbances (some patients experience an aura), nausea, vomiting, dizziness, sensitivity to light, touch, and sound, and tingling or numbness. An attack usually lasts anywhere from 4 to 72 hours.

Migraine can lead to depression, anxiety, and sleep disturbances. Women are more affected than men, with 85% of chronic sufferers being women. Migraine leads to healthcare and lost productivity costs as high as $36 billion each year in the United States.³

Dosing and Administration

The recommended doses of lasmiditan are 50 mg, 100 mg, or 200 mg tablets (taken as two 100 mg tablets) taken orally once every 24 hours, with or without food. Only one dose should be taken in 24 hours; a second dose is not effective.

This medication should only be taken if the patient can wait at least 8 hours after taking the medication before driving or operating machinery.

Notably, the safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established.⁴
How Supplied

Lasmiditan is available in 50 mg (NDC 0002-4312-08) and 100 mg (NDC 0002-4491-08) tablets; each strength comes in a package of 8 tablets.

Storage

Lasmiditan tablets should be stored at room temperature (68°F to 77°F); excursions are permitted to 59°F to 86°F. Keep out of the reach of children.4

Contraindications

There are no contraindications to use of lasmiditan.4

Drug Interactions4

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
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<tbody>
<tr>
<td>Alcohol/CNS Depressants</td>
<td>Has not been studied, but lasmiditan should be used with caution due to the potential of lasmiditan to cause sedation and other cognitive and/or neuropsychiatric reactions</td>
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<tr>
<td>Serotonergic Drugs</td>
<td>Lasmiditan should be used with caution in patients taking SSRIs, SNRIs, TCAs, MAO inhibitors, trazodone, dextromethorphan, or St. John’s Wort, due to increased risk of serotonin syndrome</td>
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<tr>
<td>Heart Rate-Lowering Drugs</td>
<td>Because lasmiditan may lower heart rate, use with caution in patients taking medications that can lower heart rate</td>
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<tr>
<td>P-gp and Breast Cancer-Resistant Protein (BCRP)</td>
<td>Avoid concomitant use with lasmiditan</td>
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Adverse Reactions

Clinically Significant Reactions:

- Driving Impairment: Lasmiditan can cause significant driving impairment and sleepiness up to 8 hours following administration. Patients should not engage in potentially hazardous activities that require complete mental alertness, such as driving or operating machinery, for at least 8 hours after a dose of lasmiditan.

- CNS Depression: Lasmiditan may cause CNS depression, including dizziness and sedation, and should be used with caution in patients using alcohol or other CNS depressants.

- Serotonin Syndrome: In clinical trials, serotonin syndrome symptoms were reported in patients who were not taking any other drugs associated with serotonin syndrome, as well as patients also taking serotonergic drugs such as SSRIs, SNRIs, TCAs, and MAOIs. Symptoms of serotonin syndrome may include: mental status changes such as agitation, hallucinations, or coma, as well as autonomic instability (tachycardia, labile blood pressure, hyperthermia), or neuromuscular signs (hyperreflexia, incoordination), and/or GI symptoms (nausea, vomiting, diarrhea). Lasmiditan should be discontinued if serotonin syndrome is suspected.

- Medication Overuse Headache: Overuse of any acute migraine drug or combination of drugs for 10 or more days monthly, may lead to medication overuse headache, which presents as migraine-like daily headaches or increased frequency of migraine attacks. Patients experiencing this will need to discontinue the overused drug(s) and be treated for withdrawal symptoms.

Other side effects seen in clinical studies included dizziness, fatigue, paresthesia, sedation, nausea/vomiting, and muscle weakness.

Lasmiditan is also associated with the following vital sign changes:

- Decreased Heart Rate (of 5 to 10 bpm): Consider evaluating heart rate in patients who may not tolerate this decrease, especially if taking other medications that lower heart rate

- Increased Blood Pressure following a single dose: Consider evaluating blood pressure after lasmiditan administration in patients who may not tolerate this increase
### Special Populations

<table>
<thead>
<tr>
<th>Special Population</th>
<th>Effect of Lasmiditan</th>
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<tbody>
<tr>
<td>Pediatrics</td>
<td>Safety and efficacy not established</td>
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<tr>
<td>Pregnancy/Lactation</td>
<td>- No data in pregnant women</td>
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<tr>
<td></td>
<td>- In animal studies, high doses caused maternal toxicity and birth defects; highest dose increased risk of stillbirth and neonatal death.</td>
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<td></td>
<td>- No data on lactation in humans</td>
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<td>- In rats, high levels of drug were found in milk</td>
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<tr>
<td>Renal Impairment</td>
<td>No dosage adjustment needed</td>
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<tr>
<td>Hepatic Impairment</td>
<td>- Mild/Moderate: No dosage adjustment needed</td>
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<tr>
<td></td>
<td>- Severe: not studied; do not use lasmiditan</td>
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<tr>
<td>Geriatrics</td>
<td>More frequent dizziness, greater increase in BP: start at lower doses and monitor closely</td>
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</table>
Abuse

The United States Drug Enforcement Agency is currently reviewing the controlled substance schedule of lasmiditan. At the time of publication, a human abuse potential study showed that lasmiditan had abuse potential; the drug is more likely than placebo to cause euphoria and hallucinations (but occurred in only 1% of patients). Patients should be evaluated for risk of drug abuse and observed for signs of lasmiditan abuse.

Clinical Studies

Lasmiditan efficacy for acute treatment of migraine was demonstrated in 2 randomized, double-blind, placebo-controlled trials.

The studies enrolled patients with a history of migraine with and without aura. The patients were mostly female (84%) and white (78%), with a mean age of 42 years. At baseline, 22% of patients were taking preventive medication for migraine.

Study 1 randomly assigned patients to lasmiditan 100 mg or 200 mg or placebo. Study 2 randomly assigned patients to lasmiditan 50 mg, 100 mg, 200 mg, or placebo.

Patients were allowed to take a rescue medication 2 hours after taking lasmiditan, but not allowed to take opioids, barbiturates, triptans, or ergots within 24 hours of lasmiditan administration.

The efficacy of lasmiditan was established by an effect on pain freedom and freedom from most bothersome symptom (MBS) at 2 hours compared with placebo for both studies. Pain freedom was defined as a “reduction of moderate or severe headache pain to no pain,” and freedom from MBS was defined as the “absence of the self-identified MBS (photophobia, phonophobia, or nausea).”

Of those patients who selected a most bothersome symptom, the most commonly selected symptoms were: photophobia (54%), nausea (24%), and phonophobia (22%). “In both studies, the percentage of patients achieving pain freedom and MBS freedom 2 hours after treatment was significantly greater among patients receiving Reyvow at all doses compared to those receiving placebo.”

Also, driving performance was assessed in 90 healthy volunteers with a computer-based driving
simulation. An impairment was seen with all doses of lasmiditan 90 minutes after administration. In another study, driving impairment was assessed in 67 healthy volunteers with a computer-based simulation, and there was no driving impairment at 8 hours or later after lasmiditan administration.

Patient Counseling

- Do not drive or operate machinery for at least 8 hours after taking lasmiditan; do not take lasmiditan if you cannot wait at least 8 hours before driving or operating machinery
- Do not take more than one dose in 24 hours, even if your headache goes away and then returns
- Do not drink alcohol or take any other medications that make you sleepy
- Some people experience medication overuse headache, especially if you take lasmiditan for 10 or more days per month. If your headaches get worse, contact your healthcare provider
- Keep a headache journal
- Be aware of the possibility of serotonin syndrome: mental changes (hallucinations), agitation, coma, rapid heartbeat, changes in BP, increased temperature, tight muscles, trouble walking, nausea, vomiting, diarrhea

Availability and Cost

Lasmiditan will be available in retail pharmacies in January 2020, pending controlled substance classification.* Price will be determined closer to this time. Lilly will work with payors, providers, and patients through a patient support program for financial assistance.

*Per the Lilly Answer Team for healthcare professionals
References


