PDL DRUG REVIEW

Proprietary Name: Reyvow®
Common Name: lasmiditan
PDL Category: Migraine

Comparable Products	Preferred Drug List Status
Nurtec	Non-Preferred with Conditions
Sumatriptan	Preferred
Ubrelvy	Non-Preferred with Conditions

Summary

Pharmacology/Usage: Lasmiditan, the active ingredient of Reyvow®, is a serotonin (5-HT) 1F receptor agonist. While the exact mechanism of lasmiditan is not known, it does bind with high affinity to the 5-HT 1F receptor and it presumably exerts its effects through agonist effects at this receptor.

Reyvow® is a Schedule V controlled substance, with abuse potential.

Indication: For the acute treatment of migraine with or without aura in adults. Reyvow® is not indicated for the preventive treatment of migraine.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no adequate data on the developmental risk associated with use in pregnant women. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Film-Coated Tablets: 50mg, 100mg

Recommended Dosage: Take 50mg, 100mg, or 200mg PO as needed. Do not exceed more than one dose in 24 hours and Reyvow® should not be taken unless the patient can wait at least 8 hours between dosing and driving or operating machinery. A second dose has not been shown to be effective for the same migraine attack. Furthermore, the safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established.

While dose adjustments are not required for mild or moderate hepatic impairment, use has not been studied with severe hepatic impairment and thus is not recommended in this population. Dose adjustments are not required with renal impairment.

Drug Interactions: Concomitant use of Reyvow® and drugs that are P-gp or Breast Cancer Resistant Protein (BCRP) substrates should be avoided. Use Reyvow® with caution if used in combination with alcohol or other CNS depressants. Use Reyvow® with caution in patients taking medications that increase serotonin (e.g. SSRIs, SNRIs, TCAs, MAO inhibitors, trazodone, OTC products such as dextromethorphan, or herbal supplements such as St. John's Wort).

Reyvow® has been associated with a lowering of heart rate. In a study, the addition of a single 200mg dose of Reyvow® to propranolol decreased heart rate by an additional 5 beats per minute compared to propranolol alone, for a mean maximum of 19 beats per minute. Use Reyvow® with caution in patients taking concomitant medications that lower heart rate if this magnitude of heart rate decrease may pose a concern.

Box Warning: There is no box warning with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Reyvow® 50mg/100mg/200) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included dizziness (6%/12%/14%), fatigue (3%/4%/5%), paresthesia (1%/5%/7%), sedation (4%/4%/5%), nausea and/or vomiting (1%/2%/2%), and muscle weakness (1%/1%/2%).

Reyvow® may cause CNS depression, including dizziness and sedation. Reyvow® may cause significant driving impairment. Warn against driving and other activities requiring complete mental alertness for at least 8 hours after Reyvow® is taken.

In clinical trials, reactions consistent with serotonin syndrome were reported in patients treated with Reyvow® who were not taking any other drugs associated with serotonin syndrome. Serotonin syndrome may also occur with Reyvow® during concomitant use with serotonergic drugs. The onset may occur within minutes to hours of receiving a new or a greater dose of a serotonergic medication. If serotonin syndrome is suspected, discontinue Reyvow®.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Eli Lilly and Company

Analysis: The safety and efficacy of Reyvow® in the acute treatment of migraine were assessed in 2 randomized, double-blind, placebo-controlled trials that included patients with a history of migraine with and without aura per the International Classification of Headache Disorders (ICHD-II) diagnostic criteria. Included patients were mostly female (84%) and white (78%), with a mean age of 42 years (range 18-81 years). In addition, 22% were taking preventive medication for migraine at baseline. Patients were allowed to take a rescue medication 2 hours after taking study drug; however, barbiturates, opioids, triptans, and ergots were not allowed within 24 hours of study drug administration.

The primary endpoints were assessed in patients treated for a migraine with moderate to severe pain within 4 hours of the onset of the attack. The efficacy of Reyvow® was established by an effect on pain freedom at 2 hours and Most Bothersome Symptom (MBS) freedom at 2 hours compared to placebo in both studies. Pain freedom was defined as a reduction of moderate or severe headache pain to no pain, and MBS freedom was defined as the absence of the self-identified MBS (photophobia, phonophobia, nausea). Of patients who selected an MBS, the most commonly selected MBS was photophobia (54%), followed by 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 in the Reyvow® group at all doses compared to those in the placebo group. Results can be seen in the table below, which was adapted from the prescribing information.

	Study 1			Study 2			
	Reyvow® 100mg	Reyvow® 200mg	placebo	Reyvow® 50mg	Reyvow® 100mg	Reyvow® 200mg	placebo
Pain Free at 2 hours							
N	498	503	515	544	523	521	534
% Responders	28.3%	31.8%	15.3%	28.3%	31.4%	38.8%	21%
Difference from placebo	13%	16.5%		7.3%	10.4%	17.8%	
p-value	<0.001	<0.001		0.006	<0.001	<0.001	
NNT per CHC	8	7		14	10	6	
Most Bothersome Symptom (MBS) Free at 2 hours							
N	464	467	480	502	491	478	509
% Responders	41.2%	40.7%	29.6%	40.8%	44.0%	48.7%	33.2%
Difference from placebo	11.6%	11.1%		7.6%	10.8%	15.5%	

	Study 1			Study 2			
	Reyvow® 100mg	Reyvow® 200mg	placebo	Reyvow® 50mg	Reyvow® 100mg	Reyvow® 200mg	placebo
p-value	<0.001	<0.001		0.014	<0.001	<0.001	
NNT per CHC	9	10		14	10	7	

Pain relief at 2 hours, defined as a reduction in migraine pain from moderate or severe to mild or none, was also assessed. Results can be found in the table below, which was adapted from the prescribing information.

	Study 1			Study 2			
	Reyvow® 100mg	Reyvow® 200mg	placebo	Reyvow® 50mg	Reyvow® 100mg	Reyvow® 200mg	placebo
Pain Relief at 2 hours							
N	498	503	515	544	523	521	534
% Responders	54.0%	55.3%	40.0%	55.9%	61.4%	61.0%	45.1%
Difference from placebo	14%	15.3%		10.8%	16.3%	15.9%	
NNT per CHC	8	7		10	7	7	

In addition, driving performance was assessed at 90 minutes after administration of Reyvow® 50mg, 100mg, 200mg, alprazolam 1mg, and placebo in a randomized, double-blind, placebo- and active-controlled, five-period crossover study in healthy volunteers with a mean age of 34.9 years (N=90) using a computer-based driving simulation. The primary outcome was the difference from placebo in the Standard Deviation of Lateral Position (SDLP), a measure of driving performance. A dose-dependent impairment of computer-based simulated driving performance was noted across all doses of Reyvow® at 90 minutes after administration.

In a separate randomized, double-blind, placebo- and active-controlled, four-period crossover study, driving performance was also assessed at 8, 12, and 24 hours after administration of Reyvow® 100mg or 200mg in healthy volunteers with a mean age of 32.8 years (N=67). Computer-based simulated driving performance using SDLP was the primary endpoint and diphenhydramine was the used as a positive control. The mean SDLP did not reach the threshold for driving impairment at 8 hours or later after Reyvow® administration.

Place in Therapy: Reyvow® is a Schedule V controlled substance indicated for the acute treatment of migraine with or without aura in adults. It is not indicated for the preventive treatment of migraine. Reyvow® is the first and only FDA-approved treatment in a new class called the serotonin 1F receptor agonists. In clinical trials compared with placebo, Reyvow® significantly improved the proportion achieving headache pain freedom and freedom from most bothersome symptoms at 2 hours. Comparator studies with other active agents were not found.

There is no evidence at this time to support that Reyvow® is safer or more effective than the currently preferred medications. It is therefore recommended that Reyvow® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred with Conditions**
- ☒ **Refer to DUR for PA Criteria**

References

[1]Reyvow [package insert]. Indianapolis, IN: Lilly; 2020.

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