PDL DRUG REVIEW

Proprietary Name: Ubrelvy®
Common Name: ubrogepant
PDL Category: CGRP Inhibitors

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

Summary

Pharmacology/Usage: Ubrogepant, the active ingredient of Ubrelvy®, is a calcitonin gene-related peptide (CGRP) receptor antagonist.

Indication: For the acute treatment of migraine with or without aura in adults. This 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: Tablets: 50mg, 100mg

Recommended Dosage: Take 50mg or 100mg PO with or without food. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200mg, and the safety of treating more than 8 migraines in a 30-day period has not been established.

Dose adjustments are not required with mild to moderate hepatic or mild to moderate renal impairment. Use 50mg as the initial dose and 50mg for the second dose (if needed) with severe hepatic or severe renal impairment. Use should be avoided in end-stage renal disease.

Drug Interactions: Ubrogepant is a substrate of BCRP and P-gp efflux transporters. Use of BCRP and/or P-gp only inhibitors (e.g. quinidine, carvedilol, eltrombopag) may increase the exposure of ubrogepant. Dose adjustment of ubrogepant is recommended with BCRP and/or P-gp only inhibitors (50mg initial dose, 50mg second dose if needed).

Concomitant use of ubrogepant with strong CYP3A4 inducers (e.g. phenytoin, barbiturates, rifampin, St. John's Wort) should be avoided. The coadministration of ubrogepant with moderate or weak CYP3A4 inducers was not assessed in a clinical study; however, ubrogepant dose adjustments are recommended (100mg initial dose, 100mg second dose if needed).

Ubrogepant should not be used concomitantly with strong CYP3A4 inhibitors; however, ubrogepant dose adjustments are recommended with concomitant use of ubrogepant and moderate CYP3A4 inhibitors (e.g. cyclosporine, ciprofloxacin, fluconazole, fluvoxamine, grapefruit juice). The recommended ubrogepant dosing is 50mg for the initial dose while avoiding a second dose within 24 hours. With concomitant use with weak CYP3A4 inhibitors, reduce the ubrogepant dose to 50mg for the initial dose and 50mg for the second dose if needed.

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

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Ubrelvy® 50mg/100mg) 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 nausea (0%/2%), somnolence (1%/2%), and dry mouth (0%/1%). Note that somnolence includes the adverse reaction-related terms sedation and fatigue.

Contraindications: Concomitant use of strong CYP3A4 inhibitors

Manufacturer: Allergan

Analysis: The safety and efficacy of Ubrelvy® for the acute treatment of migraine were assessed in 2 randomized, double-blind, placebo-controlled trials. In both studies, patients were instructed to treat a migraine with moderate to severe headache pain intensity; a second dose of study medication, or the patient's usual acute treatment for migraine, was permitted between 2 to 48 hours after the initial treatment for a non-responding or recurrent migraine headache. There were up to 23% of patients taking preventive medications for migraine at baseline.

The efficacy of Ubrelvy® was established by an effect on pain freedom at 2 hours post-dose and most bothersome symptom (MBS) freedom at 2 hours post-dose compared to placebo. 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 (i.e. photophobia, phonophobia, or nausea). Of patients who selected an MBS, the most commonly selected was photophobia (56%), followed by phonophobia (24%), and nausea (19%).

In both studies, the % of patients achieving headache pain freedom and MBS freedom at 2 hours post-dose was significantly higher in the Ubrelvy® group compared to the placebo group. Results can be seen in the table below, which was adapted from the prescribing information. In addition, the table includes results of the % of patients achieving pain relief at 2 hours post-dose (defined as a reduction in migraine pain from moderate or severe to mild or none) and the % of patients achieving sustained pain freedom between 2 to 24 hours post-dose. The incidence of photophobia and phonophobia was reduced after Ubrelvy® administration at both doses compared with placebo.

	Study 1			Study 2	
	Ubrelvy® 50mg	Ubrelvy® 100mg	placebo	Ubrelvy® 50mg	placebo
Pain Free at 2 hours					
N	422	448	456	464	456
% Responders	19.2%	21.2%	11.8%	21.8%	14.3%
Difference from placebo	7.4%	9.4%		7.5%	
p-value	0.002	<0.001		0.007	
NNT per CHC	14	11		14	
Most Bothersome Symptom (MBS) Free at 2 hours					
N	420	448	454	463	456
% Responders	38.6%	37.7%	27.8%	38.9%	27.4%

	Study 1			Study 2	
	Ubrelvy® 50mg	Ubrelvy® 100mg	placebo	Ubrelvy® 50mg	placebo
Difference from placebo	10.8%	9.9%		11.5%	
p-value	<0.001	<0.001		<0.001	
NNT per CHC	10	11		9	
Pain Relief at 2 hours					
N	422	448	456	464	456
% Responders	60.7%	61.4%	49.1%	62.7%	48.2%
p-value	<0.001	<0.001		<0.001	
NNT per CHC	9	9		7	
Sustained Pain Freedom 2-24 hours					
N	418	441	452	457	451
% Responders	12.7%	15.4%	8.6%	14.4%	8.2%
p-value	NS	0.002		0.005	
NNT per CHC	25	15		17	

Place in Therapy: Ubrelvy® is the first oral calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine with or without aura in adults. It is not indicated for the preventive treatment of migraine. In 2 clinical trials compared with placebo, Ubrelvy® significantly increased the proportion of patients achieving headache pain freedom and most bothersome symptom freedom at 2 hours post-dose.

There is no evidence at this time that Ubrelvy® is safer or more effective than the currently preferred, more cost-effective medications. It is therefore recommended that Ubrelvy® 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]Ubrelvy [package insert]. Madison, NJ: Allergan; 2019.