PDL DRUG REVIEW

Proprietary Name: Qulipta®
Common Name: atogepant
PDL Category: CGRP Inhibitors

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

Summary

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

Indication: For the preventive treatment of episodic migraine in adults.

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. Clinical considerations include that published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Tablets: 10mg, 30mg, 60mg.

Recommended Dosage: Take one tablet (10mg, 30mg, or 60mg) PO QD with or without food.

Dose adjustments are not recommended for patients with mild or moderate hepatic impairment. Avoid the use of Qulipta® with severe hepatic impairment. Dose adjustments are not recommended for patients with mild or moderate renal impairment. In patients with severe renal impairment and in patients with end-stage renal disease (ESRD), the recommended dosage is 10mg PO QD. For patients with ESRD undergoing intermittent dialysis, Qulipta® should preferably be taken after dialysis.

Drug Interactions: Coadministration of Qulipta® with itraconazole, a strong CYP3A4 inhibitor, resulted in a significant increase in exposure of atogepant in healthy subjects. The recommended dosage of Qulipta® with concomitant use of strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin) is 10mg PO QD. No dosage adjustment of Qulipta® is needed with concomitant use of moderate or weak CYP3A4 inhibitors.

Coadministration of Qulipta® with steady state rifampin, a strong CYP3A4 inducer, resulted in a significant decrease in exposure of atogepant in healthy subjects. Concomitant administration of Qulipta® with moderate inducers of CYP3A4 can also result in decreased exposure of atogepant. The recommended dosage of Qulipta® with concomitant use of strong or moderate CYP3A4 inducers (e.g. rifampin, carbamazepine, phenytoin, St. John's wort, efavirenz, etravirine) is 30mg or 60mg QD. Dosage adjustment of Qulipta® is not required with concomitant use of weak CYP3A4 inducers.

Coadministration of Qulipta® with single dose rifampin, an OATP inhibitor, resulted in a significant increase in exposure of atogepant in healthy subjects. The recommended dosage of Qulipta® with concomitant use of OATP inhibitors (e.g. cyclosporine) is 10mg or 30mg QD.

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

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Qulipta® 10mg/30mg/60mg) 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 (2%/3%/6%), constipation (5%/5%/5%), fatigue/somnolence (1%/1%/3%), and decreased appetite (<2%/<1%/<2%).

In studies 1 and 2, the proportion of patients with a weight decrease of at least 7% at any point was 2.8% with placebo, 3.8% for Qulipta® 10mg, 3.2% for Qulipta® 30mg, and 4.9% for Qulipta® 60mg.

In studies 1 and 2, the rate of transaminase elevations over 3 times the upper limit of normal was similar between patients treated with Qulipta® (1%) and those treated with placebo (1.8%). However, there were cases with transaminase elevations over 3 times the upper limit of normal that were temporally associated with Qulipta® treatment; these were asymptomatic and resolved within 8 weeks of discontinuation. There were no cases of severe liver injury or jaundice.

Contraindications: There are no contraindications listed with this product.

Manufacturer: AbbVie.

Analysis: The safety and efficacy of Qulipta® for the preventive treatment of episodic migraine were assessed in two randomized, multicenter, double-blind, placebo-controlled studies that included adults with at least a 1-year history of migraine with or without aura, per the International Classification of Headache Disorders (ICHD-3) diagnostic criteria. In both 12 weeks studies, adults were permitted to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, acetaminophen, or opioids) as needed. The use of a concomitant medication that acts on the CGRP pathway was not permitted for either acute or preventive treatment of migraine. The studies excluded patients with myocardial infarction, stroke, or transient ischemic attacks within 6 months prior to screening.

Study 1 included patients with a mean age of 42 years (range 18 to 73), while 89% were female, 83% were white, and the mean migraine frequency at baseline was about 8 migraine days per month. A total of 805 patients (88%) completed the 12-week study. The primary endpoint was the change from baseline in mean monthly migraine days (MMD) across the 12-week treatment period. Secondary endpoints included the change from baseline in mean monthly headache days, the change from baseline in mean monthly acute medication use days, the proportion of patients achieving at least a 50% reduction from baseline in mean MMD (3-month average), the change from baseline in mean monthly Activity Impairment in Migraine-Diary (AIM-D) Performance of Daily Activities (PDA) domain scores, the change from baseline in mean monthly AIM-D Physical Impairment (PI) domain scores, across the 12-week treatment period, and the change from baseline at week 12 for Migraine Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1) Role Function-Restrictive (RFR) domain scores.

The AIM-D evaluates difficulty with performance of daily activities (PDA domain) and physical impairment (PI domain) due to migraine, with scores ranging from 0 to 100. Higher scores indicate greater impact of migraine and reductions from baseline indicate improvement. The MSQ v2.1 Role Function-Restrictive (RFR) domain score assesses how often migraine impacts function related to daily social and work-related activities over the past 4 weeks, with scores ranging from 0 to 100. Higher scores indicate lesser impact of migraine on daily activities and increases from baseline indicate improvement.

Results for study 1 can be observed in the table below, which was adapted from the prescribing information.

Efficacy Endpoints in Study 1	Qulipta® 10mg (N=214)	Qulipta® 30mg (N=223)	Qulipta® 60mg (N=222)	Placebo (N=214)
Monthly Migraine Days (MMD) across 12 weeks				
Baseline	7.5	7.9	7.8	7.5
Mean change from baseline	-3.7	-3.9	-4.2	-2.5
Difference from placebo; p-value	-1.2; <0.001	-1.4; <0.001	-1.7; <0.001	
Monthly Headache Days across 12 weeks				
Baseline	8.4	8.8	9.0	8.4
Mean change from baseline	-3.9	-4.0	-4.2	-2.5
Difference from placebo; p-value	-1.4; <0.001	-1.5; <0.001	-1.7; <0.001	
Monthly Acute Medication Use Days across 12 weeks				
Baseline	6.6	6.7	6.9	6.5
Mean change from baseline	-3.7	-3.7	-3.9	-2.4
Difference from placebo; p-value	-1.3; <0.001	-1.3; <0.001	-1.5; <0.001	
≥50% MMD Responders across 12 weeks				
% Responders	56%	59%	61%	29%
Difference from placebo (%); p-value (*NNT calculated by CHC*)	27%; <0.001 (NNT 4)	30%; <0.001 (NNT 4)	32%; <0.001 (NNT 4)	
MSQ v2.1 RFR Domain at week 12				
Baseline	44.9	44.0	46.8	46.8
Mean change from baseline	30.4	30.5	31.3	20.5
Difference from placebo; p-value	9.9; <0.001	10.1; <0.001	10.8; <0.001	
AIM-D PDA Domain across 12 weeks				
Baseline	15.5	16.9	15.9	15.2
Mean change from baseline	-7.3	-8.6	-9.4	-6.1
Difference from placebo; p-value	-1.2; NS	-2.5; <0.001	-3.3; <0.001	
AIM-D PI Domain across 12 weeks				
Baseline	11.7	13.0	11.6	11.2
Mean change from baseline	-5.1	-6.0	-6.5	-4.0
Difference from placebo; p-value	-1.1; NS	-2.0; 0.002	-2.5; <0.001	

Study 2 included patients with a mean age of 40 years (range 18 to 74), while 87% were female, 76% were white, and the mean migraine frequency at baseline was about 8 migraine days per month. A total of 541 patients (83%) completed the 12-week double-blind period. The primary endpoint was the change from baseline in mean monthly migraine days across the 12-week treatment period.

Results suggested that there was a significantly greater reduction in mean monthly migraine days across the 12-week treatment period in all Qulipta® treatment groups as compared with placebo. Results can be seen in the table below, which was adapted from the prescribing information.

Efficacy Endpoints in Study 1	Qulipta® 10mg (N=92)	Qulipta® 30mg (N=182)	Qulipta® 60mg (N=177)	Placebo (N=178)
Monthly Migraine Days (MMD) across 12 weeks				
Baseline	7.6	7.6	7.7	7.8
Mean change from baseline	-4.0	-3.8	-3.6	-2.8
Difference from placebo; p-value	-1.1; 0.024	-0.9; 0.039	-0.7; 0.039	
Monthly Headache Days across 12 weeks				
Baseline	8.9	8.7	8.9	9.1
Mean change from baseline	-4.3	-4.2	-3.9	-2.9
Difference from placebo; p-value	-1.4; 0.024	-1.2; 0.039	-0.9; 0.039	

Place in Therapy: Qulipta®, an oral once daily CGRP receptor antagonist, is indicated for the preventive treatment of episodic migraine in adults. Dose modifications are indicated for severe renal impairment and ESRD, as well as when used concomitantly with certain medications. In two randomized, double-blind, placebo-controlled trials, the primary efficacy endpoint assessed was the change from baseline in mean monthly migraine days (MMD) across the 12-week treatment period. In both studies, results suggested that there was a significantly greater reduction in mean monthly migraine days across the 12-week treatment period in all three Qulipta® treatment doses as compared with placebo. Qulipta® is now the second FDA approved oral CGRP receptor antagonist indicated for the preventive treatment of episodic migraine.

There is no evidence at this time to support that Qulipta® is safer or more effective than the other currently available medications. It is therefore recommended that Qulipta® remain non-preferred and require prior authorization to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Qulipta [package insert]. Dublin, Ireland: Forest Laboratories Ireland Ltd; 2021. (Manufactured by Forest Laboratories Ireland Ltd; Qulipta is a trademark of Allergan Pharmaceuticals International Limited, an AbbVie company)