NEW DRUG APPROVAL

Brand Name	Qulipta™
Generic Name	atogepant
Drug Manufacturer	Abbvie Inc.

New Drug Approval

FDA Approval Date: September 28, 2021
Review Designation: Priority
Type of Review: Type 1 - New Molecular Entity; New Drug Application (NDA): 215206
Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Migraine is an episodic disorder, the centrepiece of which is a severe headache generally associated with nausea and/or light and sound sensitivity. It is one of the most common complaints encountered by neurologists in day-to-day practice.

Migraine is a common neurological disorder that affects both children and adults in the United States. It is a known cause of significant disability, ranked sixth by the World Health Organization for years lost to disability.

Approximately 39 million Americans (12% of the population) suffer from migraine in the United States; 28 million are women. Migraine is most common between the ages of 18 and 44 years. About 90% of people with migraine have a family history.

About 50% of female migraine sufferers have more than 1 attack each month, and 25% experience 4 or more severe attacks per month.

Efficacy

The efficacy of Qulipta™ for the preventive treatment of episodic migraine in adults was demonstrated in two randomized, multicenter, double-blind, placebo-controlled studies (Study 1 and Study 2). The studies enrolled patients with at least a 1-year history of migraine with or without aura, according to the International Classification of Headache Disorders (ICHD-3) diagnostic criteria.

The FDA approval of Qulipta™ was based on results from AbbVie's atogepant clinical trial program, including the Phase 3 ADVANCE study, in which Qulipta™ demonstrated statistically significant reductions in mean monthly migraine days compared with placebo across all dosages.

Study 1:

Study 1, also known as the Phase 3 ADVANCE trial (NCT03777059), was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study designed to assess the efficacy and safety of 10-mg, 30-mg, and 60-mg daily doses of Qulipta. Patients in Study 1 were excluded if they had an inadequate response to more than 4 medications (2 with different mechanisms of action) previously prescribed for the prevention of migraine.

Study 2:

Study 2 was a similarly designed Phase 2/3 clinical trial (NCT02848326) with the same primary efficacy endpoint.

Both trials enrolled patients with at least a 1-year history of migraine headaches (with or without aura) according to the ICHD-3 diagnostic criteria, with 4–14 migraine days per month in the 3 months prior to the first study visit.

Patients were permitted to use treatments for acute migraine headaches including triptans, ergotamine derivatives, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids, but were not permitted to use any concomitant CGRP inhibitor (oral or injectable).

Study Group	Qulipta 10 mg		Qulipta 30 mg		Qulipta 60 mg		Placebo	
Study	Study 1 n = 214	Study 2 n = 92	Study 1 n = 223	Study 2 n = 182	Study 1 n = 222	Study 2 n = 177	Study 1 n = 214	Study 2 n = 178
MMDs across 12 weeks*								
Baseline	7.5	7.6	7.9	7.6	7.8	7.7	7.5	7.8
Mean change from baseline	−3.7	−4.0	−3.9	−3.8	−4.2	−3.6	−2.5	−2.8
Difference from placebo	−1.2	−1.1	−1.4	−0.9	−1.7	−0.7	–	–
P value	<0.001	0.024	<0.001	0.039	<0.001	0.039	–	–
Monthly headache days across 12 weeks								
Baseline	8.4	8.9	8.8	8.7	9.0	8.9	8.4	9.1
Mean change from baseline	−3.9	−4.3	−4.0	−4.2	−4.2	−3.9	−2.5	−2.9
Difference from placebo	−1.4	−1.4	−1.5	−1.2	−1.7	−0.9	–	–
P value	<0.001	0.024	<0.001	0.039	<0.001	0.039	–	–
≥50% reduction in MMDs								
Percentage of participants	56	58	59	53	61	52	29	40
Difference from placebo (%)	27	18	30	13	32	12	–	–
P value	<0.001	0.11	<0.001	0.11	<0.001	0.15	–	–

Sources: Qulipta Prescribing Information

Abbreviations: MMD, monthly migraine day.

*Primary endpoint in both trials.

Safety

ADVERSE EVENTS

The most common adverse reactions (at least 4% and greater than placebo) are nausea, constipation, and fatigue.

WARNINGS & PRECAUTIONS

None.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS OF ACTION

Atogepant is a calcitonin gene-related peptide (CGRP) receptor antagonist]. CGRP is distributed throughout the nervous system, and it is concentrated at anatomical sites, such as the trigeminovascular system, which are

involved in migraine pathophysiology. Centrally, CGRP is involved in nociceptive transmission through second and third-order neurons and pain modulation in the brainstem. Peripherally, CGRP mediates vasodilation through smooth muscle receptors. CGRP concentrations are elevated during acute migraine attacks and may be chronically elevated in chronic migraineurs.

Dose & Administration

ADULTS

- The recommended dosage is 10 mg, 30 mg, or 60 mg taken orally once daily with or without food.
- Severe renal impairment or end-stage renal disease: 10 mg once daily.

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

The recommended dosage of Qulipta™ is 10 mg once daily. For patients with ESRD undergoing intermittent dialysis, Qulipta™ should preferably be taken after dialysis. No dose adjustment is recommended for patients with mild or moderate renal impairment. No dose adjustment is recommended for patients with mild or moderate renal impairment.

HEPATIC IMPAIRMENT

No dose adjustment of Qulipta™ is recommended for patients with mild or moderate hepatic impairment. Avoid use of Qulipta™ in patients with severe hepatic impairment.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Tablets: 10 mg, 30 mg, and 60 mg.