PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PRQULIPTA™

atogepant tablets

Tablets, 10 mg, 30 mg, and 60 mg, oral

Calcitonin gene-related peptide (CGRP) receptor antagonist

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RECENT MAJOR LABEL CHANGES

1 Indications	05/2024
4.2 Dosage and Administration, Recommended Dose and Dosage Adjustment	05/2024

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

QULIPTA (atogepant tablets) is indicated for:

- the prevention of migraine in adults who have at least 4 migraine days per month.

1.1 Pediatrics

Pediatrics (< 18 Years of age): The safety and efficacy of QULIPTA in pediatric patients has not been studied.

1.2 Geriatrics

Clinical studies of QULIPTA did not include sufficient number of patients aged 65 years and over (N=80) to determine whether they respond differently compared to younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and maintained at the lowest effective dose, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. See **7.1 Special Populations** in **7 WARNINGS AND PRECAUTIONS** and **10.3 Pharmacokinetics** section**.**

2 CONTRAINDICATIONS

QULIPTA is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING**. Reported cases of hypersensitivity included anaphylaxis, and dyspnea (see **7 WARNINGS AND PRECAUTIONS, Hypersensitivity Reactions**).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

At the time of authorization, there are no serious warnings or precautions.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- QULIPTA is available in 10 mg, 30 mg, and 60 mg tablets.
- Dosing modifications should be considered for concomitant use of specific drugs and for patients with hepatic or renal impairment. See Table 1.

4.2 Recommended Dose and Dosage Adjustment

- Episodic migraine: The recommended dose is 10 mg, 30 mg or 60 mg orally once daily. The maximum recommended daily dose is 60 mg.
- Chronic migraine: The recommended dose is 60 mg orally once daily.

Table 1 Dose Modifications for Special Populations and for Drug Interactions

Special Populations/Drug Interactions	Recommended Daily Dose
Patients with Hepatic Impairment. See 7 WARNINGS AND PRECAUTIONS, 8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data, and 10.3 Pharmacokinetics, Special Populations and Conditions.	
Severe hepatic impairment (Child-Pugh Class C)	Should Avoid Use
Mild or moderate hepatic impairment (Child-Pugh Class A or B)	10, 30, or 60 mg
Patients with Renal Impairment. See 10.3 Pharmacokinetics, Special Populations and Conditions	
Severe Renal Impairment and end stage renal disease (CLcr <30 mL/min) only if the benefit of treatment with QULIPTA is deemed to outweigh the risk.	10 mg
Mild or moderate (CLcr 30-89 mL/min) renal impairment	10, 30, or 60 mg
Concomitant Drug. See 9 Drug Interactions	
Strong CYP3A4 Inhibitors (e.g., itraconazole, ketoconazole, clarithromycin)	10 mg
Moderate and weak CYP3A4 Inhibitors (e.g., ciprofloxacin, fluconazole, fluvoxamine, grapefruit juice, cimetidine, esomeprazole)	10, 30, or 60 mg
Strong and moderate CYP3A4 Inducers (e.g., multiple dose rifampicin, carbamazepine, phenytoin, St. John's wort, efavirenz, etravirine)	30 or 60 mg
Weak CYP3A4 Inducers (e.g., topiramate, armodafinil, rufinamide)	10, 30, or 60 mg
OATP Inhibitors (e.g., cyclosporine, single dose rifampicin)	10 or 30 mg

4.4 Administration

QULIPTA is administered orally once daily **with or without food**.

4.5 Missed Dose

A missed dose should be taken right away. If it is almost time for the next dose, patients should be instructed to skip the missed dose and take the next dose as scheduled.

5 OVERDOSAGE

Treatment of an overdose of QULIPTA should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. No specific antidote for the treatment of QULIPTA overdose is available.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 Dosage Forms Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
oral	Tablet, 10, 30 and 60 mg atogepant	colloidal silicon dioxide, croscarmellose sodium, mannitol, microcrystalline cellulose, polyvinylpyrrolidone vinyl acetate copolymer, sodium chloride, sodium stearyl fumarate, and vitamin E polyethylene glycol succinate.

QULIPTA 10 mg is supplied as white to off-white, round biconvex tablet with “A” and “10” debossed on one side.

QULIPTA 30 mg is supplied as white to off-white, oval biconvex tablet with “A30” debossed on one side.

QULIPTA 60 mg is supplied as white to off-white, oval biconvex tablet with “A60” debossed on one side.

7 WARNINGS AND PRECAUTIONS

Carcinogenesis and Mutagenesis

There was no evidence of genotoxic or carcinogenic potential in the non-clinical toxicology studies. For animal data, see **16 NON-CLINICAL TOXICOLOGY** section.

Cardiovascular

See **10.2 Pharmacodynamics**.

Dependence/Tolerance

No studies on the abuse liability of QUILIPTA have been performed in humans See **10.2 Pharmacodynamics**.

Driving and Operating Machinery

QULIPTA may cause fatigue and somnolence in some patients. Patients should be advised not to perform skilled tasks (e.g., driving, operating machinery) until they are reasonably certain that QULIPTA does not affect them adversely (see **8.2 Clinical Trial Adverse Reactions**).

Hepatic

Since atogepant is mainly metabolized by the liver through oxidation, use of this drug in patients with severe hepatic impairment should be avoided. In a small number of cases in clinical studies, a temporal association was noted between atogepant treatment and transaminase elevations greater than 3 times the upper limit of normal. In such circumstances, re-challenge is not recommended. See **4.2 Recommended Dose and Dosage Adjustment** and **8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data**.

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, rash, pruritis, urticaria, facial edema, and dyspnea, have been reported during treatment with QULIPTA. Such reactions can occur within hours to days following drug administration. If a hypersensitivity reaction occurs, QULIPTA should be discontinued and appropriate therapy instituted (see **2 CONTRAINDICATIONS and 8.5 Post-Market Adverse Reactions**).

Reproductive Health: Female and Male Potential

See **7.1.1 Pregnant Women** and **16 NON-CLINICAL TOXICOLOGY**.

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate human data on the developmental risk associated with the use of QULIPTA in pregnant women. In animal studies, oral administration of atogepant during organogenesis resulted in adverse effects on development in rats at exposures greater than those used clinically, and which were associated with maternal toxicity. QULIPTA should not be used by pregnant women unless the expected benefit to the mother outweighs the potential risk to the fetus. See **16 NON-CLINICAL TOXICOLOGY**.

Pregnancy Registry

A registry is being established to collect information about the effect of QULIPTA exposure during pregnancy. Details are forthcoming.

7.1.2 Breast-feeding

There are no data on the excretion of atogepant in the milk of lactating women. The effects of atogepant on the breastfed infant or on milk production are unknown. In lactating rats, oral administration of atogepant resulted in levels of atogepant in milk approximately 2-fold higher than plasma concentrations. As atogepant may be excreted in human milk, caution should be exercised when QULIPTA is administered to women who are breast-feeding. The potential benefit to the mother should be considered along with the potential risk to the breastfed infant. See **16 NON-CLINICAL TOXICOLOGY**.

7.1.3 Pediatrics

Pediatrics (<18 Years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Population pharmacokinetic modeling suggests no clinically significant pharmacokinetic differences between elderly and younger subjects. Based on these findings, no dose adjustment of QULIPTA is needed in elderly patients. However, the three placebo-controlled clinical studies of QULIPTA did not include adequate number of patients aged 65 years and over (N=80) to determine whether they respond differently compared to younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range. See **4 DOSAGE AND ADMINISTRATION**.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

A total of 2626 patients with episodic and chronic migraine were exposed to QULIPTA who received at least one dose, representing 1450 patient-years of exposure. Of these, 1225 were exposed to QULIPTA daily for at least 6 months and 826 patients received QULIPTA for 12 months.

In pooled placebo-controlled studies (Studies 1, 2 and 3), 2500 patients with episodic and chronic migraine received various doses of QULIPTA (N=1837) and Placebo (N=663). In these studies, 57.6% of patients treated with QULIPTA and 51.9% of patients treated with placebo experienced adverse events.

In the three placebo-controlled studies, the frequently reported adverse reactions (>1%) with QULIPTA were constipation, nausea, fatigue/somnolence, and decreased appetite, and most were mild to moderate in intensity (see table 3). No serious adverse reactions were identified with atogepant.

In these studies, 4.1%, 3.4%, and 3.1% of the patients receiving atogepant 10 mg once daily (QD), 30 mg QD, and 60 mg QD, respectively, discontinued the study (Placebo: 3.2%).

Discontinuations

The most common adverse events that led to discontinuation in QULIPTA arms of the three placebo-controlled studies included nausea (0.5%; Placebo: 0.3%), constipation (0.4%; Placebo: 0.3%), fatigue/somnolence (0.2%; Placebo: 0%), and dizziness (0.2%; Placebo: 0.2%). The most common adverse events resulting in discontinuation in the long-term safety studies were nausea (0.5%) and dizziness (0.3%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In the 12-week, placebo-controlled studies of the 2500 patients, approximately 88% were female, 74% were White, 13% were Black, 12% were Asian, and 9% were of Hispanic or Latino ethnicity.

In the three placebo-controlled studies, the following adverse events in Table 3 were observed to occur at or above 2%.

Table 3 Treatment Emergent Adverse Events Occurring with an Incidence of ≥2% in any treatment group in the Placebo-Controlled Studies of episodic and chronic migraine

	Placebo (N= 663) %	**QULIPTA 10 mg QD (N=314) %**	**QULIPTA 30 mg QD (N=411) %**	**QULIPTA 60 mg QD (N=678) %**
Gastrointestinal disorders				
Nausea	3	5	6	9
Constipation	2	6	6	8
Diarrhoea	2	1	1	2
General disorders and administration site conditions				
Fatigue	3	1	2	3

	Placebo (N= 663) %	QULIPTA 10 mg QD (N=314) %	QULIPTA 30 mg QD (N=411) %	QULIPTA 60 mg QD (N=678) %
Infections and infestations				
Upper respiratory tract infection	5	5	7	3
Nasopharyngitis	3	2	5	5
Urinary tract infection	2	2	5	3
Sinusitis	1	3	1	2
Gastroenteritis	1	1	2	1
Investigations				
Blood creatine phosphokinase increased	<1	3	1	2
Metabolism and nutrition disorders				
Decreased appetite	<1	2	1	3
Nervous system disorders				
Dizziness	2	2	2	3
Somnolence	1	3	2	2

The overall safety profile in the open-label, long-term safety studies was consistent with the placebo-controlled studies.

8.3 Less Common Clinical Trial Adverse Reactions

Adverse events reported by <2% of patients in controlled clinical studies of QULIPTA in adult patients with episodic or chronic migraine that occurred in more than 2 patients in any QULIPTA treatment arm and twice more frequently than in the placebo group are listed below. Causality to QULIPTA has not been established in every case.

Blood and lymphatic system disorders: anaemia

Cardiac disorders: palpitations, tachycardia

Gastrointestinal disorders: abdominal discomfort, dyspepsia, food poisoning, gastrooesophageal reflux disease, toothache

General disorders and administration site conditions: asthenia, non-cardiac chest pain, pyrexia

Infections and infestations: bronchitis, cellulitis, gastroenteritis viral, herpes zoster, pharyngitis streptococcal, pneumonia, viral upper respiratory tract infection

Injury, poisoning and procedural complications: foot fracture, muscle strain, skin laceration

Investigations: weight decreased

Musculoskeletal and connective tissue disorders: back pain, muscle spasms, neck pain, tendonitis

Nervous system disorders: hypoaesthesia, mental impairment

Psychiatric disorders: abnormal dreams, irritability

Renal and urinary disorders: proteinuria

Respiratory, thoracic and mediastinal disorders: nasal congestion

Skin and subcutaneous tissue disorders: dermatitis contact, pruritus

Vascular disorders: hypertension

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Hepatic

Atogepant is mainly metabolized by the liver through oxidation. In the placebo-controlled studies, similar proportion of patients in atogepant (0.9%) and placebo (1.2%) groups experienced transaminase elevations 3 times the upper limit of normal. However, there was a temporal association between atogepant treatment and reported transaminase elevations. In the majority of cases, patients had normal transaminase levels at baseline and none of the patients had a history of pre-existing liver disease. Transaminase elevations were mostly asymptomatic and resolved within 2 to 9 weeks following atogepant discontinuation. There were no reported cases of severe liver injury or jaundice. Atogepant use should be avoided in patients with severe hepatic impairment. See **4.2 Recommended Dose and Dosage Adjustment** and **7 WARNINGS AND PRECAUTIONS/Hepatic**.

Gastrointestinal

One of the most common adverse events in placebo-controlled clinical studies of atogepant was constipation, reported by 7% (96/1403) of patients (Placebo: 2% [13/663]). Constipation also led to the discontinuation in 0.4% (6/1403) of patients in the combined atogepant arms (Placebo: 0.3%, 2/663). There were no serious cases of constipation in controlled studies. Approximately 5% of patients had previous history of constipation. In a 52-week long-term safety study, constipation was reported in 7% (39/543) of patients who received atogepant 60 mg/day compared to 3% (6/196) of patients who received standard of care. In a 40-week long-term safety study, constipation was reported in 3.4%**.** (23/685) of patients who received atogepant 60 mg/day. There were no serious cases. Two patients receiving atogepant discontinued the long-term safety studies. There were 2 cases of severe constipation (one in a patient with history of constipation) that did not result in discontinuation of atogepant. See **9.4 Drug-Drug Interactions**.

Decrease in Body Weight

In the placebo-controlled studies, patients had a mean weight of 79.3 kg and mean BMI of 28.86 kg/m^2. In these studies, there was a dose-dependent decrease in mean body weight of patients who received QULIPTA 30 mg (-0.40 kg) and 60 mg (-0.90 kg). Patients receiving placebo gained a mean body weight of 0.23 kg during the course of these studies. The proportion of patients with a weight decrease ≥7% at any point during the studies was 2.5% for placebo, 3.8% for QULIPTA 10 mg, 3.2% for QULIPTA 30 mg, and 5.3% for QULIPTA 60 mg. No patients in the placebo-controlled studies discontinued treatment due to an adverse event of decreased weight.

In a 52-week open-label long-term safety study, patients had a mean weight of 83.9 kg and mean BMI of 30.55 kg/m^2. In this study, patients who were treated with QULIPTA 60 mg had a mean decrease in body weight of 1.42 kg versus those who received oral migraine preventive standard of care who had a mean body weight increase of 0.20 kg. The proportion of patients with a weight decrease ≥7% at any point during the study was 14.7% for the oral migraine preventive standard of care group and 24.1% for the QULIPTA 60 mg once daily group. Maximum weight loss of approximately 1.7 kg was also reported at 6 and 9 months. In a 40-week long-term safety study, patients had a mean weight of 84.2 kg and

mean BMI of 30.58 kg/m^2; at the end of treatment with QULIPTA 60 mg, there was a mean decrease from baseline in body weight of 1.77 kg, and 23.9% had a weight decrease ≥7% during the study. In these long-term safety studies, two QULIPTA-treated patients discontinued atogepant due to an adverse event of weight decreased.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been identified during post-approval use of QULIPTA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity (e.g., anaphylaxis, dyspnea, rash, pruritus, urticaria, facial edema).

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Atogepant is primarily metabolized by CYP3A4. Atogepant is a substrate of P-gp, BCRP, OATP1B1, OATP1B3 and OAT1. See **10.3 Pharmacokinetics**; **9.4 Drug-Drug Interactions,** and Table 1 in **4.2 Recommended Dose and Dosage Adjustment**.

9.4 Drug-Drug Interactions

CYP3A4 Inhibitors

Co-administration of 60 mg QULIPTA with itraconazole, a strong CYP3A4 inhibitor, resulted in a 5.5-fold increase in the exposure of atogepant in healthy subjects (see **10.3 Pharmacokinetics**). Maximum dose of QULIPTA 10 mg is recommended with concomitant use of strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin). Data from physiologically based pharmacokinetic (PBPK) modeling suggest that co-administration of QULIPTA with moderate CYP3A4 inhibitors (e.g., ciprofloxacin, fluconazole, fluvoxamine, grapefruit juice) increases atogepant exposure by 1.7-fold. No dose adjustment is required when QULIPTA is co-administered with moderate or weak CYP3A4 inhibitors (e.g., cimetidine, esomeprazole). See **4 DOSAGE AND ADMINISTRATION** and Table 1.

CYP3A4 Inducers

Co-administration of QULIPTA with **multiple 600 mg doses** of rifampicin, a strong CYP3A4 inducer, resulted in a significant decrease in exposure of atogepant in healthy subjects (see **10.3 Pharmacokinetics**). QULIPTA 30 or 60 mg is recommended when co-administered with strong and moderate CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin, St. John's wort, efavirenz, etravirine). No dose adjustment is required when QULIPTA is co-administered with weak CYP3A4 inducers (e.g., topiramate). See **4 DOSAGE AND ADMINISTRATION** and Table 1.

OATP Inhibitors

Single doses of rifampicin affect atogepant pharmacokinetics mainly by inhibition of organic anion transporter polypeptide (OATP). In a drug interaction study in healthy adult subjects, co-administration of QULIPTA with a **single 600 mg dose** of rifampicin resulted in a 2-fold and 3-fold increase in atogepant C_{max} and AUC, respectively (see **10.3 Pharmacokinetics**). When co-administered with OATP inhibitors (e.g., cyclosporin), maximum recommended daily dose of QULIPTA is 30 mg. See **4 DOSAGE AND ADMINISTRATION** and Table 1.

Potential for Other Drugs to Affect Atogepant Exposure

Table 4 Summary of Potential Effects of Co-administered Drugs on Atogepant Exposure

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Atogepant Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
Itraconazole (strong CYP3A4 inhibitor)	CT	200 mg QD for 7 days	single 60 mg dose	Increased 2.15-fold	Increased 5.5-fold	Administer maximum 10 mg atogepant.
Moderate CYP3A4 inhibitors	PBPK Modeling[a]	Fluconazole 400 mg on Day 1, 200 mg QD on Days 2-10	single 60 mg dose	Increased 1.21-fold	Increased 1.68-fold	No atogepant dose adjustment is anticipated.
Mild CYP3A4 inhibitors	PBPK Modeling[a]	Cimetidine 400 mg BID for 10 days	single 60 mg dose	No change	No change	No atogepant dose adjustment is anticipated.
Rifampicin (strong CYP3A4 inducer)	CT	**(multiple doses)** 600 mg QD for 7 days	single 60 mg dose	Decreased by 30%	Decreased by 60%	Administer 30 mg or 60 mg atogepant dose. See text under OATP Inhibitors above table 4.
Topiramate (weak CYP3A4 inducer)	CT	100 mg BID for 5 days after uptitration	60 mg QD for 17 days	Decreased by 24%	Decreased by 25%	No atogepant dose adjustment required
Rifampicin (strong OATP inhibitor)	CT	(**single dose**) 600 mg	single 60 mg dose	Increased 2.23-fold	Increased 2.85-fold	Administer maximum 30 mg atogepant dose. See text under OATP Inhibitors above table 4.
Quinidine (P-gp inhibitor) Not currently marketed in Canada	CT	Quinidine gluconate 324 mg BID for 1 day, 648 mg BID for 4 days	single 60 mg dose	Increased by 4%	Increased by 26%	No atogepant dose adjustment required. See section 9.2.
BCRP inhibitors	PBPK Modeling[a]	NA	single 60 mg dose	Increased 1.29-fold	Increased 1.18-fold	No atogepant dose adjustment is anticipated.

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Atogepant Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
Famotidine	CT	20 mg famotidine twice	single 60 mg dose	Decreased by 49%	Decreased by 21%	No atogepant dose adjustment required.
Esomeprazole	CT	40 mg QD for 7 days	single 60 mg dose	Decreased by 23%	Decreased by 8%	No atogepant dose adjustment required.
Acetaminophen	CT	single 1000 mg dose	single 60 mg dose	No change	Increased by 13%	No atogepant dose adjustment required.
Naproxen	CT	single 500 mg dose	single 60 mg dose	No change	Decreased by 1%	No atogepant dose adjustment required.
Sumatriptan	CT	single 100 mg dose	single 60 mg dose	Decreased by 22%	Decreased by 5%	No atogepant dose adjustment required.
Ubrogepant (Another CGRP receptor antagonist)	CT	100 mg on Day 1 and every third day on Days 7-28	60 mg QD, Days 2-28	No change	No change	Atogepant and ubrogepant combination therapy led to increase in reported cases of constipation. Concomitant use is not recommended.
(Inhibitors of) other CYP enzymes (CYP1A2, CYP2D6, CYP2C9, CYP2C19)	In vitro[a]	N/A	N/A	Inhibitors of CYP1A2, CYP2D6, CYP2C9 and CYP2C19 are not expected to significantly alter atogepant metabolism.		No atogepant dose adjustment is anticipated.
Inhibitors of transporters (P-gp, BCRP, OATP1B1, OATP1B3, OAT1, OAT3,	In vitro[a]	N/A	N/A	Atogepant is a substrate of P-gp, BCRP, OATP1B1, OATP1B3, and OAT1 and inhibitors of these may increase atogepant exposure.		Maximum 30 mg atogepant dose when coadministered with strong OATP inhibitors. No atogepant dose

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Atogepant Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
OCT2, or MATE1)				Atogepant was not a substrate of OAT3, OCT2, or MATE1.		adjustment is anticipated with other transporter inhibitors. See text under OATP Inhibitors above table 4.

Legend: CT = Clinical Trial; PBPK = physiologically based pharmacokinetic
a: As clinical drug-drug interaction studies were not conducted except with P-gp and OATP (see above in Table 4), caution is advised (e.g., monitor adverse reactions).

Table 5 Summary of Potential Effects of Atogepant on the Exposure of Co-administered Drugs

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Co-administered Drug Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
Ethinyl estradiol	CT	single 0.03 mg dose	60 mg atogepant once daily for 17 days	Decreased by 10%	No change	No ethinyl estradiol dose adjustment required.
Levonorgestrel	CT	single 0.15 mg dose	60 mg atogepant once daily for 17 days	Increased by 9%	Increased by 19%	No levonorgestrel dose adjustment required.
Acetaminophen	CT	single 1000 mg dose	single 60 mg dose	Decreased by 11%	Decreased by 6%	No acetaminophen dose adjustment required.
Naproxen	CT	single 500 mg dose	single 60 mg dose	Decreased by 6%	Decreased by 2%	No naproxen dose adjustment required.
Sumatriptan	CT	single 100 mg dose	single 60 mg dose	Decreased by 5%	Increased by 2%	No sumatriptan dose adjustment required.

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Co-administered Drug Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
Ubrogepant	CT	100 mg on Day 1 and every third day on Days 7-28	60 mg QD, Days 2-28	Increased by 26%	Increased by 19%	Atogepant and ubrogepant combination therapy led to increase in reported cases of constipation. Concomitant use is not recommended.
Topiramate	CT	100 mg BID for 5 days after uptitration	60 mg QD for 17 days	Decreased by 6%	Decreased by 5%	No topiramate dose adjustment required
(Induction of) CYP isoforms	In vitro[a]	N/A	N/A	Atogepant did not significantly induce CYP2B6 or CYP1A2. Atogepant induced CYP3A4, but is not expected to have a clinically significant effect on pharmacokinetics of CYP3A4 substrates.		No dose adjustment of coadministered CYP substrates is anticipated.
(Inhibition of) CYP isoforms, MAO-A, and UGT1A1	In vitro[a]	N/A	N/A	Atogepant did not directly inhibit CYP1A2 or 3A4, and displayed weak inhibition of CYP2B6, CYP2C8, CYP2C9, CYP2D6 and CYP2C19. Atogepant is not a potent inhibitor of MAO-A or UGT1A1.		No dose adjustment of co-administered CYPs, MAO-A or UGT1A1 substrates is anticipated.
(Inhibition of) hepatic uptake transporters OATP1B1,	In vitro[a]	N/A	N/A	Atogepant inhibited OATP1B1, OATP1B3, OCT1 and MATE1 but is not anticipated to interact significantly		No dose adjustment of coadministered OATP1B1, OATP1B3, OCT1

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Co-administered Drug Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C_{max}	AUC	
OATP1B3, OCT1 and MATE1				with concomitant medications that are substrates.		and MATE1 substrates is anticipated.
(Inhibition of) efflux transporters P-gp, BCRP, BSEP and MRPs	In vitro[a]	N/A	N/A	Atogepant does not significantly inhibit P-gp, BCRP, BSEP or MRPs.		No dose adjustment of co-administered P-gp, BCRP, BSEP or MRPs substrates is anticipated.

Legend: CT = clinical trial
a: As clinical drug-drug interaction studies were not conducted, caution is advised (e.g., monitor adverse reactions).

9.5 Drug-Food Interactions

Grapefruit juice is a moderate CYP34A inhibitor and may increase atogepant exposure. See **9.4 Drug-Drug Interactions**.

See **10.3 Pharmacokinetics**.

9.6 Drug-Herb Interactions

See **10.3 Pharmacokinetics**.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been studied.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Atogepant is an orally administered, small molecule, selective calcitonin gene-related peptide (CGRP) receptor antagonist that blocks the binding of the CGRP to its receptor. CGRP is a neuropeptide that may play a role in migraine pathophysiology.

10.2 Pharmacodynamics

Cardiac Electrophysiology

In a randomized, double-blind, placebo- and positive-controlled, 3 period crossover ECG assessment study in healthy subjects (N=60), atogepant at a single supratherapeutic dose of 300 mg (5X multiple of maximum recommended daily dose), was not observed to have any noteworthy effect on the QTcF interval, the QRS duration, or the PR interval.

Dependence Liability

Atogepant has not been studied in humans for its dependence liability. In a self-administration study conducted in male rats, atogepant was not reinforcing at the highest dose tested (C_{max} 0.7 times the maximum human recommended dose). In a physical dependence study, no new behaviors were observed in male rats following cessation of a 28 day repeat dosing period.

10.3 Pharmacokinetics

Absorption

Following oral administration of QULIPTA, atogepant is rapidly absorbed with plasma concentrations >14 nM (EC_{90} based on capsaicin induced dermal vasodilation model [CIDV]) within 0.5 hours and median T_{max} values ranging from 1.0 to 2 hours. Atogepant displays dose-proportional pharmacokinetics through 300 mg single dose with little to no accumulation upon once daily dosing.

Effect of Food

When QULIPTA was administered with a high-fat meal, AUC and C_{max} were reduced by approximately 18% and 22%, respectively with no effect on median time to maximum atogepant plasma concentration. QULIPTA was administered without regard to food in clinical efficacy studies.

Distribution

Plasma protein binding of atogepant was not concentration-dependent in the range of 0.1 to 10 µM; the unbound fraction of atogepant was 4.7% in human plasma. Following oral administration, the mean apparent volume of distribution of atogepant (Vz/F) is approximately 292 L.

Metabolism

Atogepant is eliminated mainly through metabolism, primarily by CYP3A4. The parent compound (atogepant), and a metabolite tentatively characterized as dioxygenated methylated glucuronide of atogepant, metabolite M23, (approximately 15% of radioactivity exposure and not a long-lasting metabolite) were the most prevalent circulating components in human plasma. Metabolite M23 is a glucuronide conjugate, and therefore unlikely to be pharmacologically active. It is found at low levels in human plasma below the threshold that would indicate concern for drug-drug interactions.

Elimination

The elimination half-life of atogepant is approximately 11 hours. The mean apparent oral clearance (CL/F) of atogepant for healthy volunteers and patients with episodic migraine were approximately 19 L/h and 17.4 L/h, respectively. Atogepant is excreted mostly via the biliary/fecal route, while the renal route is a minor route of elimination. Following single oral dose of 50 mg ^{14}C-atogepant dose to healthy male subjects, 42% and 5% of the dose was recovered as unchanged atogepant in feces and urine, respectively.

Special Populations and Conditions

Based on a population pharmacokinetic analysis, age, sex, race, and body weight did not have a significant effect on the pharmacokinetics (C_{max} and AUC) of atogepant. Therefore, no dose adjustments are warranted based on these factors.

- **Pediatrics**

Safety and efficacy of QULIPTA in pediatric patients have not been studied.

- **Geriatrics**

Clinical studies of QULIPTA included only 80 elderly patients, which is insufficient to determine whether the elderly respond differently to QULIPTA compared to younger individuals. Population pharmacokinetic modeling suggests no clinically significant pharmacokinetic differences between elderly and younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and maintained at the lowest effective dose. See **1.2 Geriatrics**.

- **Hepatic Insufficiency**

In patients with pre-existing mild (Child-Pugh Class A), moderate (Child-Pugh Class B), or severe (Child-Pugh Class C) hepatic impairment, atogepant exposure was increased by 24%, 15% and 38%, respectively. No dose adjustment of QULIPTA is recommended for patients with mild or moderate hepatic impairment. QULIPTA is not recommended for patients with severe hepatic impairment. See **8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data** and **4.2 Recommended Dose and Dosage Adjustment**.

- **Renal Insufficiency**

Population pharmacokinetic analysis based on pooled data from clinical studies was used to evaluate the effect of renal impairment. Atogepant pharmacokinetics were similar between patients with normal renal function (CLcr >90 mL/min) and those with mild (CLcr 60-89 mL/min) or moderate (CLcr 30-59 mL/min) renal impairment. Patients with severe renal impairment (CLcr 15-29 mL/min) or End Stage Renal Disease (ESRD; CLcr <15 mL/min) have not been studied. A Physiologically-Based Pharmacokinetic model predicted that atogepant exposures increase by about 2.3-fold in patients with severe renal impairment. Based on ADME information, in patients with ESRD, atogepant exposure is unlikely to increase beyond 6-fold. Therefore, the maximum recommended daily dose of atogepant in patients with severe renal impairment and ESRD is 10 mg. For patients with ESRD undergoing intermittent dialysis, QULIPTA should be taken after dialysis. No dose adjustment is recommended for patients with mild or moderate renal impairment. See **4 DOSAGE AND ADMINISTRATION**.

11 STORAGE, STABILITY AND DISPOSAL

Store between 15°– 30°C.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

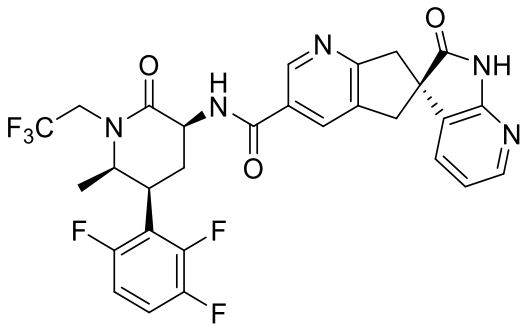
Proper/Common name: atogepant

Chemical name: (3'*S*)-*N*-[(3*S*,5*S*,6*R*)-6-methyl-2-oxo-1-(2,2,2-trifluoroethyl)-5-(2,3,6-trifluorophenyl)piperidin-3-yl]-2'-oxo-1',2',5,7-tetrahydrospiro[cyclopenta[*b*]pyridine-6,3'-pyrrolo[2,3-*b*]pyridine]-3-carboxamide

Molecular formula and molecular mass:

$C_{29}H_{23}F_6N_5O_3$ and molecular weight is 603.5 g/mol.

Structural formula:



Physicochemical properties: Atogepant (as atogepant monohydrate) is a white to off-white powder. It is freely soluble in ethanol, soluble in methanol, sparingly soluble in acetone, slightly soluble in acetonitrile and practically insoluble in water.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Episodic Migraine

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. In both studies, patients were allowed to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, acetaminophen, and opioids) as needed. The studies excluded patients with clinically significant liver disease at screening and myocardial infarction, stroke, or transient ischemic attacks within six months prior to screening.

In Study 1, after a 28-day baseline period, a total of 910 patients were randomized 1:1:1:1 to receive either QULIPTA 10 mg (N = 222), QULIPTA 30 mg (N = 230), QULIPTA 60 mg (N = 235) or placebo (N = 223) once daily for 12 weeks. In Study 2, after a 28-day baseline period, a total of 652 patients were randomized 1:2:2:2 to receive either QULIPTA 10 mg (N = 94), QULIPTA 30 mg (N = 185), QULIPTA 60 mg (N = 187), or placebo (N = 186) once daily for 12 weeks.

The primary efficacy endpoint in Study 1 was the change from baseline in mean monthly migraine days across the 12-week treatment period. Secondary endpoints included the change from baseline in mean monthly headache days, change from baseline in mean monthly acute medication use days, and proportion of patients achieving a ≥ 50% reduction from baseline in mean monthly migraine days (average over 12 weeks).

Likewise, in Study 2, the primary efficacy endpoint was the change from baseline in mean monthly migraine days across the 12-week treatment period. Secondary endpoints were monthly headache days, ≥ 50% reduction from baseline in mean monthly migraine days across the 12-week treatment period, and change from baseline in mean monthly acute medication use days.

In Study 1, nearly 83% of the patients were White, 14% were Black and 9% were of Hispanic or Latino ethnicity. The mean migraine frequency at baseline was approximately 8 migraine days per month (range: 4-16) and was similar across treatment groups. In Study 2, nearly 76% of the patients were White, 20% were Black, and 16% were of Hispanic of Latino ethnicity. The mean migraine frequency at baseline was approximately 8 migraine days per month (range: 4-16) and was similar across treatment groups.

A total of 88% (604/687) of patients randomized to once-daily atogepant doses in Study 1 completed the 12-week double-blind study (placebo: 90% or 201/223 patients). In Study 2, a total of 84% (393/466) of patients randomized to once-daily atogepant doses completed the 12-week double-blind study (placebo: 80% or 148/186 patients).

Table 6 Summary of Patient Demographics in Studies 1 and 2

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
1	Phase 3, randomized, double-blind, placebo-controlled	QULIPTA 10 mg, 30 mg, or 60 mg orally once daily for 12 weeks	QULIPTA 10 mg (N = 222) 30 mg (N = 230) 60 mg (N = 235) Placebo (N = 223)	42 years (18-73)	89% Female 11% Male
2	Phase 2/3, randomized, double-blind, placebo-controlled	QULIPTA 10 mg, 30 mg, or 60 mg orally once daily for 12 weeks	QULIPTA 10 mg (N = 94) 30 mg (N = 185) 60 mg (N = 187) Placebo (N = 186)	40 years (18-74)	86% Female 14% Male

Study Results

QULIPTA treatment demonstrated clinically meaningful and statistically significant improvements for the primary and secondary efficacy endpoints compared to placebo (Table 7). The results of most other efficacy endpoints were also supportive.

Table 7 Results of Primary and Secondary Efficacy Endpoints in Studies 1 and 2

	Placebo **N=214**	**QULIPTA** **10 mg/day** **N=214**	**QULIPTA** **30 mg/day** **N=223**	**QULIPTA** **60 mg/day** **N=222**
Study 1				
Monthly Migraine Days (MMD) across 12 weeks				
Baseline	7.5	7.5	7.9	7.8
Mean change from baseline	-2.5	-3.7	-3.9	-4.2
Placebo-subtracted change	--	-1.2	-1.4	-1.7
p-value		<0.001	<0.001	<0.001
Monthly Headache Days across 12 weeks				
Baseline	8.4	8.4	8.8	9.0
Mean change from baseline	-2.5	-3.9	-4.0	-4.2
Placebo-subtracted change	--	-1.4	-1.5	-1.7
p-value		<0.001	<0.001	<0.001
Monthly Acute Medication Use Days across 12 weeks				
Baseline	6.5	6.6	6.7	6.9
Mean change from baseline	-2.4	-3.7	-3.7	-3.9
Placebo-subtracted change	--	-1.3	-1.3	-1.5
p-value		<0.001	<0.001	<0.001
≥ 50% MMD Responders across 12 weeks				
% Responders	29	56	59	61
Placebo-subtracted change	--	27	30	32
p-value		<0.001	<0.001	<0.001

	Placebo N= 178	QULIPTA 10 mg/day N= 92	QULIPTA 30 mg/day N= 182	QULIPTA 60 mg/day N= 177
Study 2				
Monthly Migraine Days (MMD) across 12 weeks				
Baseline	7.8	7.6	7.6	7.7
Mean change from baseline	-2.8	-4.0	-3.8	-3.6
Placebo-subtracted change	--	-1.1	-0.9	-0.7
p-value		0.024	0.039	0.039
Monthly Headache Days across 12 weeks				
Baseline	9.1	8.9	8.7	8.9
Mean change from baseline	-2.9	-4.3	-4.2	-3.9
Placebo-subtracted change	--	-1.4	-1.2	-0.9
p-value		0.024	0.039	0.039
≥ 50% MMD Responders across 12 weeks				
% Responders	40	58	53	52
Placebo-subtracted change		17	13	12
p-value		NS	NS	NS
Monthly Acute Medication Use Days across 12 weeks				
Baseline	6.6	6.2	6.6	6.8
Mean change from baseline	-2.4	-3.7	-3.9	-3.5
Placebo-subtracted change	--	-1.3	-1.4	-1.1
p-value		NS	NS	NS

Legend: NS = not statistically significant

The least square mean change from baseline in moderate or severe headache days for each of the treatment groups was -2.42 in the placebo group, -3.48 in QULIPTA 10mg, -3.50 in QULIPTA 30mg, and -3.98 in QULIPTA 60mg. The least square mean change from baseline in severe headache days for

each of the treatment groups was -1.21 in the placebo group, -1.50 in QULIPTA 10mg, -1.58 in QULIPTA 30mg, and -1.77 in QULIPTA 60mg.

In Study 1, across the 12-week treatment period, the proportions of patients with ≥ 50% reduction in monthly migraine days were 29% with placebo and between 56% and 61% across QULIPTA treatment arms. The proportions of patients with ≥ 75% reduction were 11% with placebo and between 30% and 38% across QULIPTA treatment arms. The proportions of patients with 100% reduction were 1% with placebo and between 5% and 8% across QULIPTA treatment arms.

In Study 2, across the 12-week treatment period, the proportions of patients with ≥ 50% reduction in monthly migraine days were 40% with placebo and between 52% and 58% across QULIPTA treatment arms. The proportions of patients with ≥ 75% reduction were 18% with placebo and between 29% and 36% across QULIPTA treatment arms. The proportions of patients with 100% reduction were 3% with placebo and approximately 11% across QULIPTA treatment arms.

Chronic Migraine

The efficacy of QULIPTA for the preventive treatment of chronic migraine in adults was demonstrated in a randomized, multicenter, double-blind, placebo-controlled study (Study 3). The study enrolled patients with at least a 1-year history of chronic migraine, according to the ICHD-3 diagnostic criteria (2018).

Study 3 randomized patients to QULIPTA 60 mg once daily (N = 262) or placebo (N = 259) for 12 weeks. Approximately 11% of the patients continued to use one concomitant migraine preventive medication (e.g., amitriptyline, propranolol, topiramate) when entering the study. However, concomitant use of other CGRP receptor antagonists was not permitted for either acute or preventive treatment of migraine. Patients were allowed to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, acetaminophen, and opioids), as needed. The study excluded patients with myocardial infarction, stroke, or transient ischemic attacks, as well as any significant liver disease, within six months prior to screening.

The primary efficacy 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, and the proportion of patients achieving at least a 50% reduction from baseline in mean MMD (3-month average).

In Study 3, 60% of the patients were White, 3% were Black, 36% were Asian, and 4% were of Hispanic or Latino ethnicity. The mean migraine frequency at baseline was approximately 19 migraine days per month and was similar across treatment groups. A total of 89% (233/262) of patients randomized to atogepant in Study 3 completed the 12-week double-blind study (placebo: 89% or 230/259 patients).

Table 8 Summary of Patient Demographics in Study 3

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
3	Phase 3, randomized, multicenter, double-blind, placebo-controlled study	QULIPTA 60 mg orally once daily for 12 weeks	QULIPTA 60 mg QD (N = 262) Placebo (N = 259)	42 years (18-74)	87% Female 13% Male

Study Results

Key efficacy results of Study 3 are summarized in Table 9.

Table 9 Results of Primary and Key Secondary Efficacy Endpoints in Study 3

	QULIPTA 60 mg QD N=256	Placebo N=246
Monthly Migraine Days (MMD) across 12 weeks		
Baseline	19.2	19.0
Mean change from baseline	-6.9	-5.1
Difference from placebo	-1.8	
p-value	<0.001	
Monthly Headache Days across 12 weeks		
Baseline	21.5	21.4
Mean change from baseline	-7.0	-5.1
Difference from placebo	-1.9	
p-value	<0.001	
Monthly Acute Medication Use Days across 12 weeks		
Baseline	15.5	15.4
Mean change from baseline	-6.2	-4.1
Difference from placebo	-2.1	
p-value	<0.001	
≥ 50% MMD Responders across 12 weeks		
% Responders	41	26

	QULIPTA 60 mg QD N=256	Placebo N=246
Difference from placebo (%)	15	
p-value	<0.001	

Patients treated with QULIPTA 60 mg QD had greater mean decreases from baseline in MMD across the 12-week treatment period compared to patients who received placebo.

Across the 12-week treatment period, the proportions of patients with ≥ 75% reduction were 6% with placebo and 19% with QULIPTA (2 arms, 30 mg BID and 60 mg QD). Approximately 1% of QULIPTA-treated patients became migraine-free (Placebo: 0%). The results of most other efficacy endpoints were also supportive.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: The toxicity studies conducted to date have demonstrated margins of approximately 2 to 33 times that in human at the maximum recommended human dose (MRHD) of 60 mg/day. The NOAEL of 100 mg/kg/day in the 6-month rat chronic study represents an exposure multiple of approximately 33-fold. The NOAEL of 300 mg/kg/day for 9-month dosing in the monkey represents a 12-fold margin.

Genotoxicity: Atogepant was negative in *in vitro* (Ames, chromosomal aberration test in Chinese Hamster Ovary cells) and in vivo (rat bone marrow micronucleus) assays.

Carcinogenicity: Two-year oral carcinogenicity studies of atogepant were conducted in mice (0, 5, 20, or 75 mg/kg/day in males; 0, 5, 30, 160 mg/kg/day in females) and rats (0, 10, 20, or 100 mg/kg in males; 0, 25, 65, or 200 mg/kg in females). There was no evidence of drug-related tumors in either species. Plasma exposure (AUC) at the highest dose tested in mice was approximately 9 times that in humans at the MRHD of 60 mg/day. Similarly, in rats it was at least 23 times that in humans at the MRHD of 60 mg/day.

Reproductive and Developmental Toxicology: Oral administration of atogepant (0, 5, 20, or 125 mg/kg/day) to male and female rats (mated with drug-naïve females and males, respectively) resulted in no adverse effects on fertility or reproductive performance at doses corresponding to approximately 20 times the human equivalent therapeutic dose.

Oral administration of atogepant (0, 5, 15, 125, or 750 mg/kg/day) to pregnant rats during the period of organogenesis resulted in decreased fetal body weight and an increased incidence of fetal skeletal variations at 125 and 750 mg/kg which were not associated with maternal toxicity. AUC at the no-effect dose (15 mg/kg/day) for adverse effects on embryofetal development was approximately 5 times that in humans at the MRHD of 60 mg/day. Slight maternal toxicity was noted at the highest dose of atogepant administered to pregnant rabbits (130 mg/kg/day), with fetal visceral and skeletal variations. No adverse effects were observed in pregnant rabbits at oral doses of atogepant up to 90 mg/kg/day (AUC approximately 3 times that in humans at the MRHD).

No adverse effects on development were observed in rats at oral atogepant doses throughout gestation and lactation of up to 125 mg/kg/day (AUC approximately 5 times that in humans at the MRHD). Maternal transfer to the pups via lactation was demonstrated by a milk to plasma ratio of 2 to 3-fold.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrQULIPTA™

Atogepant Tablets

Read this carefully before you start taking **QULIPTA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **QULIPTA**.

What is QULIPTA used for?

QULIPTA is used to prevent migraine headaches in adults who have at least 4 migraine days per month.

How does QULIPTA work?

QULIPTA belongs to a group of medicines known as calcitonin gene-related peptide (CGRP) receptor antagonists. It works by blocking the action of a chemical in the body called CGRP that is linked to migraine headaches.

What are the ingredients in QULIPTA?

Medicinal ingredient: atogepant.

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, mannitol, microcrystalline cellulose, polyvinylpyrrolidone/vinyl acetate copolymer, sodium chloride, sodium stearyl fumarate, and vitamin E polyethylene glycol succinate.

QULIPTA comes in the following dosage forms:

Tablets; 10 mg, 30 mg and 60 mg of atogepant.

Do not use QULIPTA if:

- you are allergic to atogepant, or any of the other ingredients in QULIPTA.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take QULIPTA. Talk about any health conditions or problems you may have, including if you:

- have kidney problems or are on dialysis;
- have heart problems;
- have liver problems;
- are pregnant or plan to become pregnant. It is not known if QULIPTA will harm your unborn baby;

- are breastfeeding or plan to breastfeed. It is not known if QULIPTA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while using QULIPTA;
- are 65 years of age or older.

Other warnings you should know about:

Driving and using machines: QULIPTA can cause fatigue and drowsiness. Do not drive, operate machinery, or do tasks that require special attention until you are certain that QULIPTA does not affect you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with QULIPTA:

- medicines used to treat bacterial infections (e.g., clarithromycin and rifampicin);
- medicines used to treat fungal infections (e.g., itraconazole and ketoconazole);
- medicines used to treat HIV (e.g., efavirenz and etravirine);
- medicines used to treat seizures and epilepsy (e.g., carbamazepine and phenytoin);
- cyclosporine, a medicine used to suppress the immune system following organ transplant;
- ubrogepant, a medicine used to treat migraines;
- St. John's wort, a herbal medicine commonly used to treat depression and mood disorders.

How to take QULIPTA:

Take QULIPTA tablets by mouth exactly as your healthcare professional tells you to. QULIPTA must be taken one time each day and can be taken with or without food.

Do not use QULIPTA for a condition for which it was not prescribed. Do not give QULIPTA to anyone else, even if they have the same symptoms you have. It may harm them. You can ask your healthcare professional for information about QULIPTA.

Usual dose:

Your healthcare professional will determine the right dose of QULIPTA for you and how long you should take it. Do not stop taking QULIPTA without first speaking to your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have taken too much QULIPTA, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of your medication, you can take the missed dose as soon as you remember. If it is almost time for your next dose, skip your missed dose and take the next dose of your medication at your regularly scheduled time. Do not take 2 doses at the same time to make up for a missed dose.

What are possible side effects from using QULIPTA?

These are not all the possible side effects you may have when taking QULIPTA. If you experience any side effects not listed here, tell your healthcare professional.

Side effects of QULIPTA may include:

- common cold;
- constipation;
- decreased appetite;
- decrease in body weight;
- diarrhea;
- dizziness;
- drowsiness;
- facial swelling;
- fatigue;
- hives;
- infection of the kidneys, ureters, bladder or urethra (urinary tract infection);
- infection of the sinuses and throat (upper respiratory tract infection);
- inflammation of the sinuses (sinusitis) or stomach and intestines (gastroenteritis);
- life threatening allergic reaction;
- itching;
- nausea;
- rash;
- shortness of breath.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store QULIPTA tablets between 15°C to 30°C.

Keep out of reach and sight of children.

If you want more information about QULIPTA:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.abbvie.ca, or by calling 1-888-704-8271.

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