

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

<sup>PR</sup>**QULIPTA™**

atogepant tablets

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

Calcitonin gene-related peptide (CGRP) receptor antagonist

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Date of Initial Authorization:  
December 21, 2022

Submission Control Number: 253186

**RECENT MAJOR LABEL CHANGES**


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## **PART I: HEALTH PROFESSIONAL INFORMATION**

### **1 INDICATIONS**

QULIPTA (atogepant tablets) is indicated for:

- the prevention of episodic migraine (< 15 migraine days per month) in adults.

#### **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=66) 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](#).

### **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**

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

**Table 1 Dose Modifications for Special Populations and for Drug Interactions**

Special Populations/Drug Interactions	Recommended Daily Dose
<b>Patients with Hepatic Impairment. See <a href="#">7 WARNINGS AND PRECAUTIONS, 8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data</a>, and <a href="#">10.3 Pharmacokinetics, Special Populations and Conditions</a>.</b>	
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
<b>Patients with Renal Impairment. See <a href="#">10.3 Pharmacokinetics, Special Populations and Conditions</a></b>	
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
<b>Concomitant Drug. See <a href="#">9 Drug Interactions</a></b>	
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.

QULIPTA 10, 30 and 60 mg are supplied in bottles of 30’s and in blister packs of 4’s (physician sample).

## 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 QULIPTA 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 trials, 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](#).

## 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, clinical studies of QULIPTA did not include adequate number of patients aged 65 years and over (N=66) 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 1970 patients were exposed to QULIPTA who received at least one dose, representing 1121 patient-years of exposure. Of these, 997 were exposed to QULIPTA once daily for at least 6 months and 670 patients received QULIPTA for 12 months.

In pooled placebo-controlled trials (Studies 1 and 2), 1727 patients with episodic migraine received various doses of QULIPTA (N=1319) and Placebo (N=408). In these studies, 56.7% of patients treated with QULIPTA and 53.4% of patients treated with placebo experienced adverse events.

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

In these studies, 4.1%, 3.4%, and 2.9% of the patients receiving atogepant 10 mg, 30 mg, and 60 mg, respectively, discontinued the trial (placebo: 2.7%). Adverse events that led to discontinuation in QULIPTA arms of placebo-controlled studies included constipation (0.5%), nausea (0.5%), fatigue/somnolence (0.5%), ALT increased (0.2%), and decreased appetite (0.2%). The most common adverse reaction resulting in discontinuation in the long-term safety study was nausea (0.6%). Other adverse events that led to discontinuation in the long-term safety study included fatigue (0.4%), dizziness (0.4%), rash (0.4%), constipation (0.2%), ALT increased (0.2%), and decreased appetite (0.2%).

## 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 clinical studies (Study 1 and Study 2) of the 1727 patients, approximately 88% were female, 80% were White, 17% were Black, and 12% were of Hispanic or Latino ethnicity.

In the two pivotal 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  $\geq 2\%$  in any treatment group in the Placebo Controlled Studies 1 and 2**

	Placebo (N= 408) %	QULIPTA 10 mg (N=314) %	QULIPTA 30 mg (N=411) %	QULIPTA 60 mg (N=417) %
<b>Gastrointestinal disorders</b>				
Nausea	3	5	6	9
Constipation	1	6	6	6
Diarrhoea	1	1	1	2
Vomiting	2	1	<1	2
<b>General disorders and administration site conditions</b>				
Fatigue	2	1	2	3
<b>Infections and infestations</b>				
Upper respiratory tract infection	6	5	7	5
Nasopharyngitis	3	2	5	5
Urinary tract infection	3	2	5	3
Sinusitis	1	3	1	2



	Placebo (N= 408) %	QULIPTA 10 mg (N=314) %	QULIPTA 30 mg (N=411) %	QULIPTA 60 mg (N=417) %
Gastroenteritis	1	1	2	2
<b>Investigations</b>				
Blood creatine phosphokinase increased	1	3	1	2
Alanine aminotransferase increased	2	2	1	1
Aspartate aminotransferase increased	2	1	1	1
<b>Metabolism and nutrition disorders</b>				
Decreased appetite	<1	2	1	2
<b>Nervous system disorders</b>				
Somnolence	1	3	2	2

The overall safety profile in the open-label, long-term, 52-week safety study was consistent with the placebo-controlled Studies 1 and 2.

### 8.3 Less Common Clinical Trial Adverse Reactions

Adverse events reported by <2% of patients in controlled clinical trials of QULIPTA in adult patients with episodic 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

**Ear and labyrinth disorders:** vertigo

**Gastrointestinal disorders:** toothache, abdominal pain upper, dyspepsia, food poisoning, gastroesophageal reflux disease

**General disorders and administration site conditions:** non-cardiac chest pain

**Infections and infestations:** viral upper respiratory tract infection, cellulitis, gastroenteritis viral, pharyngitis streptococcal

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

**Musculoskeletal and connective tissue disorders:** arthralgia, neck pain, tendonitis

**Nervous system disorders:** dizziness, mental impairment

**Psychiatric disorders:** insomnia, abnormal dreams, irritability

**Renal and urinary disorders:** proteinuria

**Skin and subcutaneous tissue disorders:** pruritus generalized, 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 clinical trials, similar proportion of patients in atogepant (1%) and placebo (1.8%) 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 controlled clinical trials of atogepant was constipation, reported by 6% (70/1142) of patients (Placebo: 1% [5/408]). Constipation also led to the discontinuation in 0.5% (6/1142) of patients in the combined atogepant arms (Placebo: 0%). These events were not dose-dependent. Approximately 4% of patients had previous history of constipation. In the 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. One patient receiving atogepant discontinued the study. Among the placebo-controlled trials and long-term safety study, there were no serious cases. 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 Studies 1 and 2, patients had a mean weight of 83.6 kg and mean BMI of 30.34 kg/m<sup>2</sup>. 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 (-0.81 kg). Patients receiving placebo gained a mean body weight of 0.32 kg during the course of these studies. The proportion of patients with a weight decrease  $\geq 7\%$  at any point during the studies was 2.8% for placebo, 3.8% for QULIPTA 10 mg, 3.2% for QULIPTA 30 mg, and 4.9% for QULIPTA 60 mg. No patients in Studies 1 and 2 discontinued treatment due to an adverse event of decreased weight.

In the 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<sup>2</sup>. 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  $\geq 7\%$  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 group. Maximum weight loss of approximately 1.7 kg was also reported at 6 and 9 months. In this study, no patients discontinued either standard of care or atogepant treatment group due to an adverse event of decreased or increased weight.

## 8.5 Post-Market Adverse Reactions

Not applicable.

## 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. 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. 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. 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.

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Atogepant Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C <sub>max</sub>	AUC	
Moderate CYP3A4 inhibitors	PBPK Modeling <sup>a</sup>	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 <sup>a</sup>	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	<b>(multiple doses)</b> 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.
Rifampicin (strong OATP inhibitor)	CT	<b>(single dose)</b> 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 <a href="#">9.2</a> .
BCRP inhibitors	PBPK Modeling <sup>a</sup>	NA	single 60 mg dose	Increased 1.29-fold	Increased 1.18-fold	No atogepant dose adjustment is anticipated.
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.

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Atogepant Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C <sub>max</sub>	AUC	
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 <sup>a</sup>	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, OCT2, or MATE1)	In vitro <sup>a</sup>	N/A	N/A	Atogepant is a substrate of P-gp, BCRP, OATP1B1, OATP1B3, and OAT1 and inhibitors of these may increase atogepant exposure. Atogepant was not a substrate of OAT3, OCT2, or MATE1.		Maximum 30 mg atogepant dose when coadministered with strong OATP inhibitors. No atogepant dose 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 <sub>max</sub>	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.
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.
(Induction of) CYP isoforms	In vitro <sup>a</sup>	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		No dose adjustment of coadministered CYP substrates is anticipated.

Co-administered Drug	Reference	Dose Schedule Clinical comment		Effect on Co-administered Drug Pharmacokinetics		Recommendation
		Co-administered Drug	Atogepant	C <sub>max</sub>	AUC	
				pharmacokinetics of CYP3A4 substrates.		
(Inhibition of) CYP isoforms, MAO-A, and UGT1A1	In vitro <sup>a</sup>	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, OATP1B3, OCT1 and MATE1	In vitro <sup>a</sup>	N/A	N/A	Atogepant inhibited OATP1B1, OATP1B3, OCT1 and MATE1 but is not anticipated to interact significantly with concomitant medications that are substrates.		No dose adjustment of coadministered OATP1B1, OATP1B3, OCT1 and MATE1 substrates is anticipated.
(Inhibition of) efflux transporters P-gp, BCRP, BSEP and MRPs	In vitro <sup>a</sup>	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 CYP3A4 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 suprathreshold 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  $\mu$ M; the unbound fraction of atogepant was 4.7% in human plasma. Following oral administration, the mean apparent volume of distribution of atogepant ( $V_z/F$ ) 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 <sup>14</sup>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 66 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 hepatic impairment (Child-Pugh Class C), 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 (CL<sub>cr</sub> >90 mL/min) and those with mild (CL<sub>cr</sub> 60-89 mL/min) or moderate (CL<sub>cr</sub> 30-59 mL/min) renal impairment. Patients with severe renal impairment (CL<sub>cr</sub> 15-29 mL/min) or End Stage Renal Disease (ESRD; CL<sub>cr</sub> <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. 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

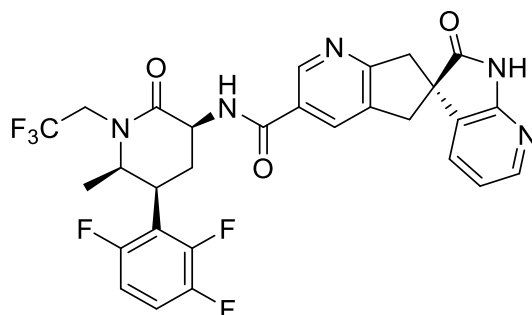
Proper/Common name: atogepant

Chemical name: (3'S)-N-[(3S,5S,6R)-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<sub>29</sub>H<sub>23</sub>F<sub>6</sub>N<sub>5</sub>O<sub>3</sub> 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 Trial Design and Study Demographics 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  $\geq 50\%$  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,  $\geq 50\%$  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 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.

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
<b>Study 1</b>				
<b>Monthly Migraine Days (MMD) across 12 weeks</b>				
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
<i>p</i> -value		<0.001	<0.001	<0.001
<b>Monthly Headache Days across 12 weeks</b>				
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
<i>p</i> -value		<0.001	<0.001	<0.001
<b>Monthly Acute Medication Use Days across 12 weeks</b>				
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
<i>p</i> -value		<0.001	<0.001	<0.001
<b>≥ 50% MMD Responders across 12 weeks</b>				
% Responders	29	56	59	61
Placebo-subtracted change	--	27	30	32
<i>p</i> -value		<0.001	<0.001	<0.001

	<b>Placebo</b> N= 178	<b>QULIPTA</b> <b>10 mg/day</b> N= 92	<b>QULIPTA</b> <b>30 mg/day</b> N= 182	<b>QULIPTA</b> <b>60 mg/day</b> N= 177
<b>Study 2</b>				
<b>Monthly Migraine Days (MMD) across 12 weeks</b>				
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
<i>p</i> -value		0.024	0.039	0.039
<b>Monthly Headache Days across 12 weeks</b>				
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
<i>p</i> -value		0.024	0.039	0.039
<b>≥ 50% MMD Responders across 12 weeks</b>				
% Responders	40	58	53	52
Placebo-subtracted change		17	13	12
<i>p</i> -value		NS	NS	NS
<b>Monthly Acute Medication Use Days across 12 weeks</b>				
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
<i>p</i> -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  $\geq 50\%$  reduction in monthly migraine days were 29% with placebo and between 56% and 61% across QULIPTA treatment arms. The proportions of patients with  $\geq 75\%$  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  $\geq 50\%$  reduction in monthly migraine days were 40% with placebo and between 52% and 58% across QULIPTA treatment arms. The proportions of patients with  $\geq 75\%$  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.

## 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**

**Pr**QULIPTA™

#### **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 less than 15 migraine days per month (i.e., episodic migraine).

#### **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;
- 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;
- fatigue;
- 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);
- nausea;
- rash;
- vomiting.

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](http://www.abbvie.ca), or by calling 1-888-704-8271.

This leaflet was prepared by AbbVie Corporation.

Last Revised December 21, 2022

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