ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 10 mg tablets
AQUIPTA 60 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

AQUIPTA 10 mg tablets

Each tablet contains 10 mg of atogepant.

AQUIPTA 60 mg tablets

Each tablet contains 60 mg of atogepant.

Excipient with known effect

Each 60 mg tablet contains 31.5 mg sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

AQUIPTA 10 mg tablets

White to off-white, round biconvex tablet, diameter 6 mm, and debossed with “A” and “10” on one side.

AQUIPTA 60 mg tablets

White to off-white, oval biconvex tablet, 16 mm x 9 mm, and debossed with “A60” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AQUIPTA is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month.

4.2 Posology and method of administration

Posology

The recommended dose is 60 mg atogepant once daily.

The tablets can be taken with or without meals.

Missed dose

A missed dose should be taken as soon as it is remembered. If it is forgotten for an entire day, the missed dose should be skipped and the next dose taken as scheduled.

Dose modifications

Dosing modifications for concomitant use of specific medicinal products are provided in Table 1 (see section 4.5).

Table 1: Dose modifications for interactions

Dose modifications	Recommended once daily dose
Strong CYP3A4 inhibitors	10 mg
Strong OATP inhibitors	10 mg

Special populations

Elderly

Population pharmacokinetic modelling suggests no clinically significant pharmacokinetic differences between elderly and younger subjects. No dose adjustment is needed in elderly patients.

Renal impairment

No dose adjustment is recommended for patients with mild or moderate renal impairment (see section 5.2). In patients with severe renal impairment (creatinine clearance [CLcr] 15-29 mL/min), and in patients with end-stage renal disease (ESRD) (CLcr < 15 mL/min), the recommended dose is 10 mg once daily. For patients with ESRD undergoing intermittent dialysis, AQUIPTA should preferably be taken after dialysis.

Hepatic impairment

No dose adjustment is recommended for patients with mild or moderate hepatic impairment (see section 5.2). Atogepant should be avoided in patients with severe hepatic impairment.

Paediatric population

The safety and efficacy of atogepant in children (< 18 years of age) have not yet been established. No data are available.

Method of administration

AQUIPTA is for oral use. Tablets should be swallowed whole and should not be split, crushed, or chewed.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 (see section 4.4).

4.4 Special warnings and precautions for use

Serious hypersensitivity reactions

Serious hypersensitivity reactions, including anaphylaxis, dyspnoea, rash, pruritus, urticaria, and facial oedema, have been reported with use of AQUIPTA (see section 4.8). Most serious reactions have

occurred within 24 hours of first use, however, some hypersensitivity reactions can occur days after administration. Patients should be warned about the symptoms associated with hypersensitivity. If a hypersensitivity reaction occurs, discontinue AQUIPTA and institute appropriate therapy.

Hepatic impairment

Atogepant is not recommended in patients with severe hepatic impairment (see section 4.2).

Excipients with known effect

AQUIPTA 10 mg tablets contain less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

AQUIPTA 60 mg tablets contain 31.5 mg sodium per tablet, equivalent to 1.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

CYP3A4 inhibitors

Strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, ritonavir) can significantly increase systemic exposure to atogepant. Co-administration of atogepant with itraconazole resulted in increased exposure (C_{max} by 2.15-fold and AUC by 5.5-fold) of atogepant in healthy subjects (see section 4.2). Changes in atogepant exposure when co-administered with weak or moderate CYP3A4 inhibitors are not expected to be clinically significant.

Transporter inhibitors

Organic anion transporting polypeptide (OATP) inhibitors (e.g., rifampicin, ciclosporin, ritonavir) can significantly increase systemic exposure to atogepant. Co-administration of atogepant with single dose rifampicin resulted in increased exposure (C_{max} by 2.23-fold and AUC by 2.85-fold) of atogepant in healthy subjects (see section 4.2).

Frequently co-administered medicinal products

Co-administration of atogepant with oral contraceptive components ethinyl estradiol and levonorgestrel, paracetamol, naproxen, sumatriptan, or ubrogepant did not result in significant pharmacokinetic interactions for either atogepant or co-administered medicinal products. Co-administration with famotidine or esomeprazole did not result in clinically relevant changes of atogepant exposure.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of atogepant in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Atogepant is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

Pharmacokinetic data after single-dose administration showed minimal transfer of atogepant into breast milk (see section 5.2).

There are no data on the effects of atogepant on the breastfed infant or the effects of atogepant on milk production.

The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for atogepant and any potential adverse effects on the breastfed infant from atogepant or from the underlying maternal condition.

Fertility

No human data on the effect of atogepant on fertility are available. Animal studies showed no impact on female and male fertility with atogepant treatment (see section 5.3).

4.7 Effects on ability to drive and use machines

Atogepant has no or negligible influence on the ability to drive and use machines. However, it may cause somnolence in some patients. Patients should exercise caution before driving or using machinery until they are reasonably certain that atogepant does not adversely affect performance.

4.8 Undesirable effects

Summary of the safety profile

Safety was evaluated in 2 657 patients with migraine who received at least one dose of atogepant in clinical studies. Of these, 1 225 patients were exposed to atogepant for at least 6 months and 826 patients were exposed for 12 months.

In 12-week, placebo-controlled clinical studies, 678 patients received at least one dose of atogepant 60 mg once daily, and 663 patients received placebo.

The most commonly reported adverse drug reactions were nausea (9%), constipation (8%), and fatigue/somnolence (5%). Most of the reactions were mild or moderate in severity. The adverse reaction that most commonly led to discontinuation was nausea (0.4%).

Tabulated list of adverse reactions

Adverse reactions reported in clinical trials and from post-marketing experience are listed below by system organ class and frequency, most frequent reactions first. Frequencies are defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 2. Adverse reactions identified with atogepant

System organ class	Frequency	Adverse reaction
Immune system disorders	Not known	Hypersensitivity (e.g., anaphylaxis, dyspnoea, rash, pruritus, urticaria, facial oedema)
Metabolism and nutrition disorders	Common	Decreased appetite
Gastrointestinal disorders	Common	Nausea, Constipation
General disorders and administration site conditions	Common	Fatigue/somnolence
Investigations	Common	Weight decreased*
	Uncommon	ALT/AST increased**

* Defined in clinical trials as weight decrease of at least 7% at any point.

** Cases of ALT/AST elevations (defined as ≥ 3× upper limit of normal) temporally associated with atogepant were observed in clinical trials, including cases with a potential positive dechallenge history that resolved within 8 weeks of discontinuation. However, the overall frequency of liver enzyme elevations was similar in the atogepant and placebo groups.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In clinical studies, atogepant was administered as single doses up to 300 mg and as multiple doses up to 170 mg once daily. Adverse reactions were comparable to those seen at lower doses, and no specific toxicities were identified. There is no known antidote for atogepant. Treatment of an overdose should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, calcitonin gene-related peptide (CGRP) antagonists, ATC code: N02CD07

Mechanism of action

Non-clinical receptor binding studies and *in vitro* functional studies point to an involvement of more than one receptor type in the pharmacological effects of atogepant. Atogepant shows affinity to several receptors of the calcitonin/CGRP-receptor family. In view of the clinically relevant free plasma concentrations of atogepant (C_{max} > 20 nM for a 60 mg dose) and the fact that CGRP and amylin-1 receptors are considered to be involved in the pathophysiology of migraine, inhibitory effects of atogepant at these receptors (K_i-value 26 pM and 2.4 nM, respectively) could be of clinical relevance. However, the precise mechanism of action of atogepant in the prophylaxis of migraine remains to be established.

Clinical efficacy and safety

Atogepant was evaluated for the prophylaxis of migraine in two pivotal studies across the migraine spectrum in chronic and episodic migraine. The episodic migraine study (ADVANCE) enrolled patients who met International Classification of Headache Disorders (ICHD) criteria for a diagnosis of migraine with or without aura. The chronic migraine study (PROGRESS) enrolled patients who also met ICHD criteria for chronic migraine. Both studies excluded patients with myocardial infarction, stroke, or transient ischemic attacks within six months prior to screening.

Episodic migraine

Atogepant was evaluated for the prophylaxis of episodic migraine (4 to 14 migraine days per month) in a randomised, multicentre, double-blind, placebo-controlled study (ADVANCE). Patients were randomised to AQUIPTA 60 mg (N = 235) or placebo (N = 223) once daily for 12 weeks. Patients were allowed to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, paracetamol and opioids) as needed. The use of a concomitant medicinal product that acts on the CGRP pathway was not permitted for either acute or preventive treatment of migraine.

A total of 88% patients completed the 12-week double-blind study period. Patients had a mean age of 42 years (range: 18 to 73 years), 4% were 65 years or older, 89% were female, and 83% were white. The mean migraine frequency at baseline was approximately 8 migraine days per month and was similar across treatment groups.

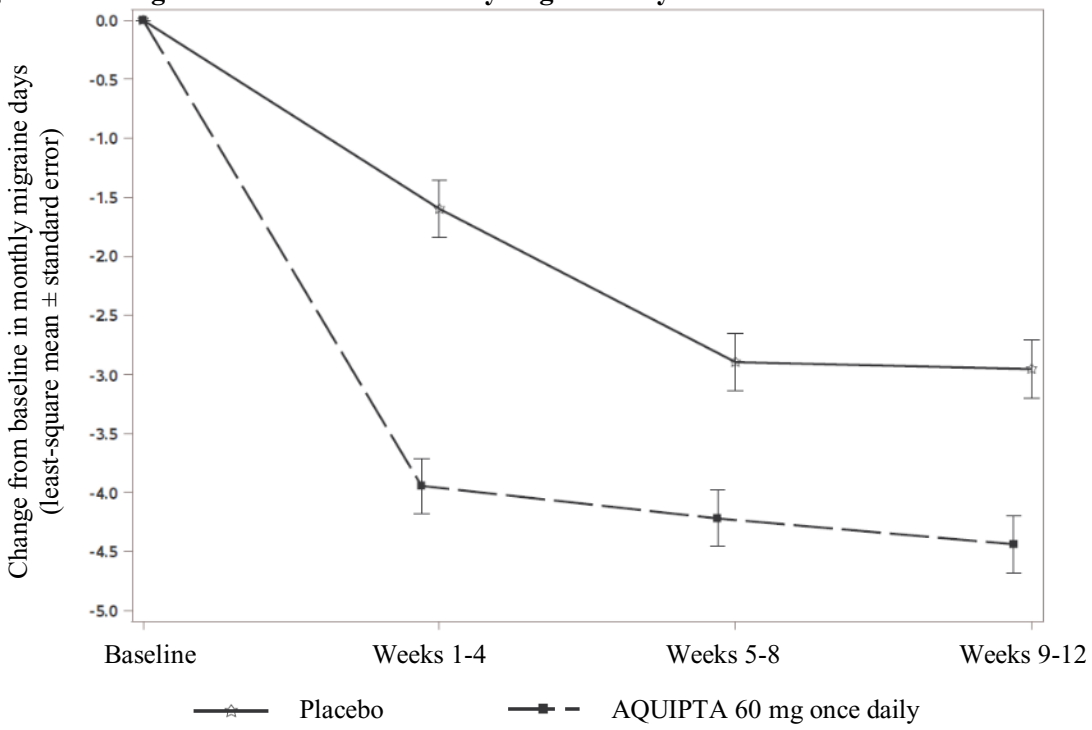
The primary efficacy endpoint was the change from baseline in mean monthly migraine days (MMD) across the 12-week treatment period. Secondary endpoints controlled for multiplicity included the change from baseline in mean monthly headache days, the change from baseline in mean monthly acute medication use days, the proportion of patients achieving at least a 50% reduction from baseline in mean MMD (3 month average), and several patient-reported outcome measures assessing functioning. Statistically significant findings were demonstrated for AQUIPTA versus placebo for the primary and secondary efficacy endpoints in ADVANCE, as summarized in Table 3.

Table 3: Efficacy endpoints in ADVANCE

	AQUIPTA 60 mg N=226	**Placebo N=216**
Monthly migraine days (MMD) across 12 weeks		
Baseline	7.8	7.5
Mean change from baseline	-4.1	-2.5
Difference from placebo	-1.7	
p-value	<0.001	
Monthly headache days across 12 weeks		
Baseline	9.0	8.5
Mean change from baseline	-4.2	-2.5
Difference from placebo	-1.7	
p-value	<0.001	
Monthly acute medication use days across 12 weeks		
Baseline	6.9	6.5
Mean change from baseline	-3.8	-2.3
Difference from placebo	-1.4	
p-value	<0.001	
≥ 50% MMD responders across 12 weeks		
% Responders	59	29
Odds ratio (95% CI)	3.55 (2.39, 5.28)	
p-value	<0.001	

Figure 1 shows the mean change from baseline in MMD in ADVANCE. Patients treated with AQUIPTA 60 mg once daily had greater mean decreases from baseline in MMD across the 12-week treatment period compared to patients who received placebo. AQUIPTA 60 mg once daily resulted in significant decreases from baseline in mean monthly migraine days within the first 4-week interval compared to placebo-treated patients.

Figure 1: Change from baseline in monthly migraine days in ADVANCE



Long-term efficacy

Efficacy was sustained for up to one year in an open-label study in which 546 patients with episodic migraine were randomised to receive AQUIPTA 60 mg once daily. 68% (373/546) of patients completed the treatment period. The reduction in the least-squares mean number of monthly migraine days in the first month (weeks 1-4) was -3.8 days and improved to a least-squares mean reduction of -5.2 days in the last month (weeks 49-52). Approximately 84%, 70%, and 48% of patients reported ≥ 50%, ≥ 75%, and 100% reduction in monthly migraine days at weeks 49-52, respectively.

Patients with previous failure to 2 to 4 classes of oral prophylactic treatments

In the ELEVATE study, 315 adult patients with episodic migraine who previously failed 2 to 4 classes of oral prophylactic treatments (e.g., topiramate, tricyclic antidepressants, beta-blockers) based on efficacy and/or tolerability were randomised 1:1 to receive either atogepant 60 mg (N = 157) or placebo (N = 158) for 12 weeks. Results in this study were consistent with the main findings of previous episodic migraine efficacy studies and statistically significant for primary and secondary efficacy endpoints including several patient-reported outcome measures assessing functioning. Atogepant treatment led to a reduction of 4.2 days in mean MMD compared to 1.9 days in the placebo group ($p<0.001$). 50.6% (78/154) of patients in the atogepant group achieved at least a 50% reduction from baseline in MMD compared to 18.1% (28/155) in the placebo group (odds ratio [95% CI]: 4.82 [2.85, 8.14], $p<0.001$).

Chronic migraine

Atogepant was evaluated for the prophylaxis of chronic migraine (15 or more headache days per month with at least 8 migraine days) in a randomised, multicentre, double-blind, placebo-controlled study (PROGRESS). Patients were randomised to AQUIPTA 60 mg (N = 262) or placebo (N = 259) once daily for 12 weeks. A subset of patients (11%) was allowed to use one concomitant migraine prophylaxis medicinal product (e.g., amitriptyline, propranolol, topiramate). Patients were allowed to use acute headache treatments (i.e., triptans, ergotamine derivatives, NSAIDs, paracetamol and opioids) as needed. Patients with acute medication overuse and medication overuse headache also were enrolled. The use of a concomitant medicinal product that acts on the CGRP pathway was not permitted for either acute or preventive treatment of migraine.

A total of 463 (89%) patients completed the 12-week double-blind study. Patients had a mean age of 42 years (range: 18 to 74 years), 3% were 65 years or older, 87% were female, and 59% were white. The mean migraine frequency at baseline was approximately 19 migraine days per month and was similar across treatment groups.

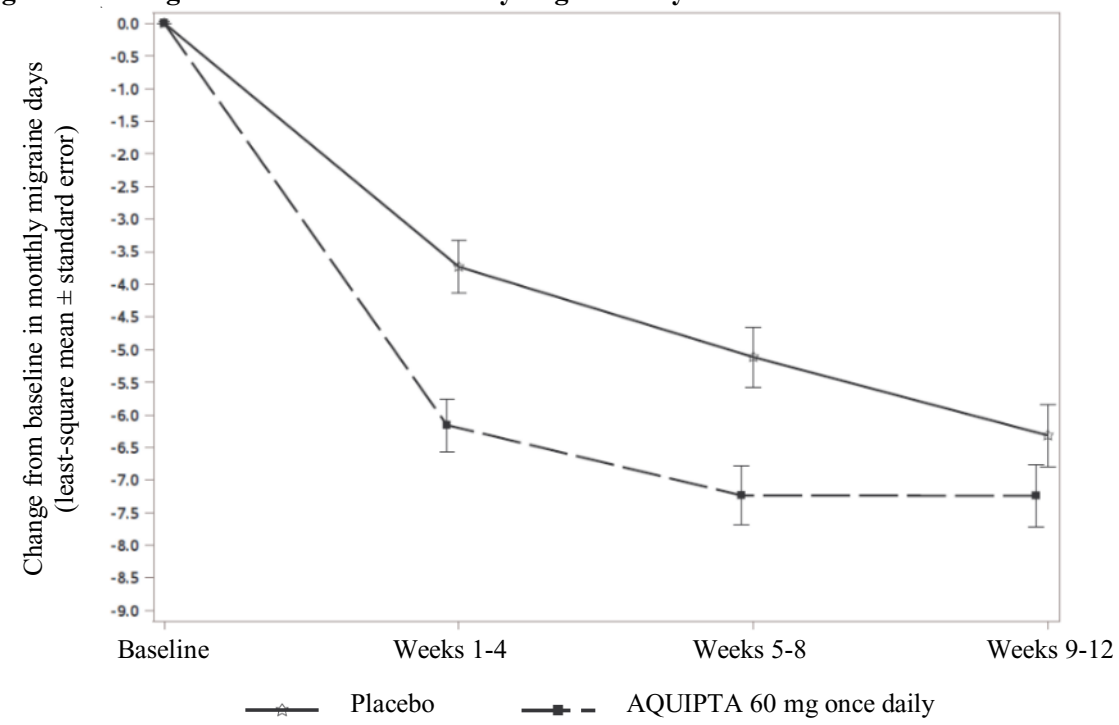
The primary efficacy endpoint was the change from baseline in mean MMD across the 12-week treatment period. Secondary endpoints controlled for multiplicity included the change from baseline in mean monthly headache days, the change from baseline in mean monthly acute medication use days, the proportion of patients achieving at least a 50% reduction from baseline in mean MMD (3-month average), and several patient-reported outcome measures assessing functioning. Statistically significant findings were demonstrated for AQUIPTA versus placebo for the primary and secondary efficacy endpoints for PROGRESS, as summarized in Table 4.

Table 4: Efficacy endpoints in PROGRESS

	AQUIPTA 60 mg N=257	**Placebo N=249**
Monthly migraine days (MMD) across 12 weeks		
Baseline	19.2	19.0
Mean change from baseline	-6.8	-5.1
Difference from placebo	-1.7	
p-value	0.002	
Monthly headache days across 12 weeks		
Baseline	21.5	21.4
Mean change from baseline	-6.9	-5.2
Difference from placebo	-1.7	
p-value	0.002	
Monthly acute medication use days across 12 weeks		
Baseline	15.5	15.3
Mean change from baseline	-6.2	-4.1
Difference from placebo	-2.1	
p-value	0.002	
≥ 50% MMD responders across 12 weeks		
% Responders	40	27
Odds ratio (95% CI)	1.90 (1.29, 2.79)	
p-value	0.002	

Figure 2 shows the mean change from baseline in MMD in PROGRESS. Patients treated with AQUIPTA 60 mg once daily had a greater mean decrease from baseline in MMD across the 12-week treatment period compared to patients who received placebo.

Figure 2: Change from baseline in monthly migraine days in PROGRESS



Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with AQUIPTA in one or more subsets of the paediatric population in prophylaxis of migraine headaches (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Following oral administration, atogepant is absorbed with peak plasma concentrations at approximately 1 to 2 hours. Following once daily dosing, atogepant displays dose-proportional pharmacokinetics up to 170 mg (approximately 3 times the highest recommended dose), with no accumulation.

Effect of food

When atogepant 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. Atogepant 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 approximately 4.7% in human plasma. The mean apparent volume of distribution of atogepant (V_z/F) after oral administration is approximately 292 L.

Biotransformation

Atogepant is eliminated mainly through metabolism, primarily by CYP3A4. The parent compound (atogepant), and a glucuronide conjugate metabolite (M23) were the most prevalent circulating components in human plasma.

CYP3A4 inducers

Co-administration of atogepant with steady state rifampicin, a strong CYP3A4 inducer, resulted in a significant decrease in exposure (Cmax by 30% and AUC by 60%) of atogepant in healthy subjects.

Co-administration of atogepant with steady-state topiramate, a mild CYP3A4 inducer, resulted in a decrease in exposure (Cmax by 24% and AUC by 25%) of atogepant.

In vitro, atogepant is not an inhibitor for CYP3A4, 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, MAO-A, or UGT1A1 at clinically relevant concentrations. Atogepant also is not an inducer of CYP1A2, CYP2B6, or CYP3A4 at clinically relevant concentrations.

Elimination

The elimination half-life of atogepant is approximately 11 hours. The mean apparent oral clearance (CL/F) of atogepant is approximately 19 L/h. Following single oral dose of 50 mg ^{14}C-atogepant to healthy male subjects, 42% and 5% of the dose was recovered as unchanged atogepant in faeces and urine, respectively.

Transporters

Atogepant is a substrate of P-gp, BCRP, OATP1B1, OATP1B3, and OAT1. Dose adjustment for concomitant use with strong inhibitors of OATP is recommended based on a clinical interaction study with a strong OATP inhibitor. Atogepant is not a substrate of OAT3, OCT2, or MATE1.

Atogepant is not an inhibitor of P-gp, BCRP, OAT1, OAT3, NTCP, BSEP, MRP3, or MRP4 at clinically relevant concentrations. Atogepant is a weak inhibitor of OATP1B1, OATP1B3, OCT1, and MATE1, but no clinically relevant interactions are expected.

Special populations

Renal impairment

The renal route of elimination plays a minor role in the clearance of atogepant. Based on population pharmacokinetic analysis, there is no significant difference in the pharmacokinetics of atogepant in patients with mild or moderate renal impairment (CLcr 30-89 mL/min) relative to those with normal renal function (CLcr ≥ 90 mL/min). As patients with severe renal impairment or end-stage renal disease (ESRD; CLcr < 30 mL/min) have not been studied, use of atogepant 10 mg is recommended in those patients.

Hepatic impairment

In patients with pre-existing mild (Child-Pugh Class A), moderate (Child-Pugh Class B), or severe hepatic impairment (Child-Pugh Class C), total atogepant exposure was increased by 24%, 15% and 38%, respectively. However, unbound atogepant exposure was approximately 3-fold higher in patients with severe hepatic impairment. The use of AQUIPTA in patients with severe hepatic impairment should be avoided.

Transfer into breast milk

In a study of 12 healthy lactating women administered a single oral dose of atogepant 60 mg between 1 to 6 months postpartum, peak levels of atogepant in breast milk occurred between 1 to 3 hours after administration. The C_{max} and AUC of atogepant in breast milk were significantly lower by approximately 93% compared to women's plasma. The mean relative infant dose was approximately 0.19% (range 0.06 to 0.33%) of the maternal weight-adjusted dose with a mean milk-to-plasma ratio of 0.08 (0.02 to 0.10). The cumulative amount of atogepant excreted in breast milk over 24 hours was minimal, at less than 0.01 mg.

Other special populations

Based on a population pharmacokinetic analysis, 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.

5.3 Preclinical safety data

Notwithstanding marked interspecies differences in CGRP-receptor affinity of atogepant, non-clinical data reveal no special hazard for atogepant in humans based on conventional studies of safety pharmacology, repeat dose toxicity, genotoxicity, phototoxicity or carcinogenic potential.

Impairment of fertility

Oral administration of atogepant to male and female rats prior to and during mating and continuing in females to gestation day 7 resulted in no adverse effects on fertility or reproductive performance. Plasma exposures (AUC) are up to approximately 15 times that in humans at the maximum recommended human dose (MRHD).

Reproductive and developmental toxicology

Oral administration of atogepant to pregnant rats and rabbits during the period of organogenesis resulted in decreased foetal body weight in rats and an increased incidence of foetal visceral and skeletal variations at doses associated with minimal maternal toxicity. At the no-effect dose for adverse effects on embryofoetal development, plasma exposure (AUC) was approximately 4 times in rats and 3 times in rabbits that in humans at the MRHD of 60 mg/day.

Oral administration of atogepant to rats throughout gestation and lactation resulted in non-adverse significant decreased pup body weight which persisted into adulthood. Plasma exposure (AUC) at the no-effect dose for pre- and postnatal development were approximately 5-times that in humans at the MRHD. In lactating rats, oral dosing with atogepant resulted in levels of atogepant in milk approximately 2-fold higher than those in maternal plasma.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyvinylpyrrolidone/Vinyl acetate copolymer
Vitamin E polyethylene glycol succinate
Mannitol
Microcrystalline cellulose
Sodium chloride
Croscarmellose sodium
Colloidal silicon dioxide
Sodium stearyl fumarate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

AQUIPTA 10 mg tablets

Aluminium foil and PVC/PE/PCTFE blisters, each containing 7 tablets.
Packs containing 28 or 98 tablets.

AQUIPTA 60 mg tablets

Aluminium foil and PVC/PE/PCTFE blisters, each containing 7 tablets.
Packs containing 28 or 98 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1750/001
EU/1/23/1750/002
EU/1/23/1750/003
EU/1/23/1750/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 August 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

AbbVie S.r.l
S.R. 148 Pontina Km 52 Snc
Campoverde di Aprilia, Latina 04011
Italy

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 10 mg tablets
atogepant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of atogepant.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet
28 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1750/001
EU/1/23/1750/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

aquipta 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Inner carton of 49 tablets (for the 98 pack)

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 10 mg tablets
atogepant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of atogepant.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet
49 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1750/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

aquipta 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 10 mg tablets
atogepant

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 60 mg tablets
atogepant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 60 mg of atogepant.

3. LIST OF EXCIPIENTS

Contains sodium.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet
28 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1750/003
EU/1/23/1750/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

aquipta 60 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Inner carton of 49 tablets (for the 98 pack)

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 60 mg tablets
atogepant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 60 mg of atogepant.

3. LIST OF EXCIPIENTS

Contains sodium.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet
49 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1750/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

aquipta 60 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

AQUIPTA 60 mg tablets
atogepant

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

AQUIPTA 10 mg tablets
AQUIPTA 60 mg tablets
atogepant

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What AQUIPTA is and what it is used for

AQUIPTA contains the active substance atogepant. AQUIPTA is used to prevent migraine in adult patients who have at least 4 migraine days per month.

AQUIPTA is thought to block the activity of the calcitonin/calcitonin gene related peptide (CGRP)-receptor family, which have been linked to migraine.

2. What you need to know before you take AQUIPTA

Do not take AQUIPTA
- if you are allergic to atogepant or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Stop taking AQUIPTA and tell your doctor immediately if you experience any symptoms of an allergic reaction such as:
- difficulty breathing
- swelling of the face
- rash, itching, or hives

Some of these symptoms can occur within 24 hours of first use. Sometimes they can happen several days after you take AQUIPTA.

Talk to your doctor, pharmacist, or nurse before taking AQUIPTA if you have severe liver problems.

Children and adolescents
Do not give this medicine to children or adolescents under 18 years old because the use of AQUIPTA has not been studied in this age group.

Other medicines and AQUIPTA
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines may increase the risk of getting side effects (see section 4).

The following is a list of examples of medicines that may require your doctor to lower the dose of AQUIPTA:
- ketoconazole, itraconazole, clarithromycin, rifampicin (medicines used to treat fungal or bacterial infections)
- ritonavir (medicine used to treat HIV)
- ciclosporin (medicine that affects your immune system)

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

If you are pregnant, you should not take AQUIPTA. If you are a woman who could become pregnant, you should use adequate contraception during treatment with AQUIPTA.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine. You and your doctor should decide if you will use AQUIPTA while breast-feeding.

Driving and using machines
AQUIPTA may make you feel sleepy. Do not drive or use machines if you are affected.

AQUIPTA contains sodium

AQUIPTA 10 mg tablets
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

AQUIPTA 60 mg tablets
This medicine contains 31.5 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 1.6% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to take AQUIPTA

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
The recommended dose is 60 mg atogepant once a day. Your doctor may tell you to take a lower dose if:
- you are taking other medicines (listed in section 2)
- you have severe kidney problems or you are undergoing dialysis.

How to take
AQUIPTA is for oral use. Do not split, crush, chew or break the tablet before swallowing. The tablets may be taken with or without food.

If you take more AQUIPTA than you should
If you have taken more tablets than you should, tell your doctor. You may get some of the side effects listed in section 4.

If you forget to take AQUIPTA
- If you miss a dose, take it as soon as you remember.
- If you forget your dose for an entire day, just skip the missed dose and take a single dose as usual the following day.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking AQUIPTA
Do not stop taking AQUIPTA without talking to your doctor first. Your symptoms may return if you stop the treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop taking AQUIPTA and contact your doctor immediately if you have any of the following symptoms, which may be part of a serious allergic reaction:
- difficulty breathing
- swelling of the face
- rash, itching, or hives

Other side effects
Tell your doctor if you notice any of the following side effects:

Common (may affect up to 1 in 10 people):
- nausea (feeling sick in your stomach)
- constipation
- fatigue (tiredness)
- somnolence (sleepiness)
- decreased appetite
- weight loss

Uncommon (may affect up to 1 in 100 people)
- increased levels of liver enzymes

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listing in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store AQUIPTA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What AQUIPTA contains

AQUIPTA 10 mg tablets
- The active substance is atogepant. Each tablet contains 10 mg of atogepant.
- The other ingredients are: Polyvinylpyrrolidone/Vinyl acetate copolymer, vitamin E polyethylene glycol succinate, mannitol, microcrystalline cellulose, sodium chloride, croscarmellose sodium, colloidal silicon dioxide and sodium stearyl fumarate (see section 2).

AQUIPTA 60 mg tablets
- The active substance is atogepant. Each tablet contains 60 mg of atogepant.
- The other ingredients are: Polyvinylpyrrolidone/Vinyl acetate copolymer, vitamin E polyethylene glycol succinate, mannitol, microcrystalline cellulose, sodium chloride, croscarmellose sodium, colloidal silicon dioxide and sodium stearyl fumarate (see section 2).

What AQUIPTA looks like and contents of the pack

AQUIPTA 10 mg tablets
AQUIPTA 10 mg tablet is a white to off-white, round biconvex tablet debossed with “A” and “10” on one side. It is available in packs containing 28 or 98 tablets.

AQUIPTA 60 mg tablets
AQUIPTA 60 mg tablet is a white to off-white, oval biconvex tablet debossed with “A60” on one side. It is available in packs containing 28 or 98 tablets.

Not all pack sizes may be marketed.

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/.

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.