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

RAYVOW 50 mg film-coated tablets
RAYVOW 100 mg film-coated tablets
RAYVOW 200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

RAYVOW 50 mg film-coated tablets

Each film-coated tablet contains 50 mg lasmiditan (as succinate).

RAYVOW 100 mg film-coated tablets

Each film-coated tablet contains 100 mg lasmiditan (as succinate).

RAYVOW 200 mg film-coated tablets

Each film-coated tablet contains 200 mg lasmiditan (as succinate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

RAYVOW 50 mg film-coated tablets

Light grey, oval tablet of 8.9 x 4.9 mm, debossed with “4312” on one side and “L-50” on the other.

RAYVOW 100 mg film-coated tablets

Light purple, oval tablet of 11.2 x 6.15 mm, debossed with “4491” on one side and “L-100” on the other.

RAYVOW 200 mg film-coated tablets

Grey, oval tablet of 14.1 x 7.75 mm, debossed with “4736” on one side and “L-200” on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RAYVOW is indicated for the acute treatment of the headache phase of migraine attacks, with or without aura in adults.

4.2 Posology and method of administration

Posology

In general, recommended initial dose in adults is 100 mg lasmiditan for acute treatment of migraine attacks. If necessary, the dose can be increased to 200 mg for greater efficacy or can be decreased to 50 mg for greater tolerability.

If the migraine headache recurs within 24 hours of an initial response after taking 50 mg or 100 mg lasmiditan, a second dose of the same strength may be taken. The second dose should not be taken within 2 hours of the initial dose.

No more than 200 mg should be taken in 24 hours.

If a patient does not respond to the first dose, it is unlikely that a second dose will be of benefit in the same attack.

Lasmiditan may be taken with or without food.

Elderly (> 65 years)
No dose adjustment is required for elderly patients (see section 5.2).

Renal impairment
No dose adjustment is necessary in patients with mild, moderate, or severe renal impairment (see section 5.2).

Hepatic impairment
No dose adjustment is necessary in patients with mild or moderate hepatic impairment. The use of lasmiditan has not been studied in subjects with severe hepatic impairment and therefore is not recommended for this population (see section 5.2).

Paediatric population
The safety and efficacy of lasmiditan in children and adolescents aged 6 to <18 years have not yet been established. No data are available.

There is no relevant use of lasmiditan in children below the age of 6 years for the treatment of migraine.

Method of administration

Oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Central nervous system (CNS) effects and driving impairment

Lasmiditan is associated with CNS adverse reactions. In a simulated driving study in healthy subjects, lasmiditan significantly impaired the ability to drive (see section 4.7). Patients should be advised not to drive or engage in other activities requiring heightened attention until at least 8 hours after taking each dose of lasmiditan, even if they feel well enough to do so. Patients who cannot follow this advice should not take lasmiditan.

Serotonin syndrome

Serotonin syndrome has been reported and may occur with lasmiditan or when administered with other serotonergic medicinal products [e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase (MAO) inhibitors]. Clinical experience for the use of lasmiditan and triptans in temporal proximity is limited. The risks of developing serotonin syndrome may be additive. Serotonin syndrome symptoms may include mental status changes (e.g. agitation, hallucinations, coma), autonomic instability (e.g. tachycardia, labile blood pressure, hyperthermia), neuromuscular signs (e.g. hyperreflexia, incoordination), and/or gastrointestinal signs and symptoms (e.g. nausea, vomiting, diarrhoea). These reactions can be severe. The onset of symptoms usually occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medicinal product. If concomitant treatment with other serotonergic medicinal products is clinically warranted, appropriate observation of the patient is advised, particularly during treatment initiation, and with dose increases. Lasmiditan should be discontinued if serotonin syndrome is suspected.

CNS depressants

Because of the potential of lasmiditan to cause sedation, as well as other cognitive and/or neuropsychiatric adverse reactions, lasmiditan should be used with caution if used in combination with alcohol or other CNS depressants.

Medicinal products misuse or abuse potential

In a human abuse potential study with recreational drug users, single lasmiditan doses of 100 or 200 mg were associated with greater drug-liking than placebo. In a separate study, there was no evidence of physical withdrawal in healthy subjects following abrupt cessation after 7 days of dosing. Patients should be evaluated for risk of drug abuse and observed for signs of lasmiditan misuse or abuse.

Medication overuse headache (MOH)

Overuse of any type of medicinal products for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained, and treatment should be discontinued. The diagnosis of MOH should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medicinal products.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

Heart rate lowering medicinal products

Lasmiditan has been associated with a lowering of heart rate (HR). Propranolol and lasmiditan together decreased HR by a mean maximum of 19.3 beats per minute (bpm), i.e., an additional lowering of 5.1 bpm compared to propranolol alone. This should be taken into consideration for patients in whom these magnitudes of HR decrease may pose a concern, including patients taking medicinal products that lower heart rate.

Serotonergic medicinal products

Concomitant administration of lasmiditan and medicinal products (e.g., SSRIs, SNRIs, TCAs) that increase serotonin may increase the risk of serotonin syndrome. Clinical experience for the use of

lasmiditan and triptans in temporal proximity is limited. The risks of developing serotonin syndrome may be additive. Caution is advised (see section 4.4).

Potential for lasmiditan to affect other medicinal products

Daily dosing of lasmiditan did not alter the PK of midazolam, caffeine, or tolbutamide, which are substrates of CYP3A, CYP1A2, and CYP2C9, respectively. Coadministration of lasmiditan with sumatriptan (MAO-A and OCT1 substrate) or propranolol (CYP2D6 substrate) resulted in no clinically meaningful changes in exposure of these medicinal products. Following a single dose of lasmiditan, creatinine renal clearance over 24 hours decreased slightly (11 %) compared with placebo, without changes in glomerular filtration rate (GFR).

Lasmiditan is an *in vitro* inhibitor of P-glycoprotein (P-gp) and breast cancer resistant protein (BCRP). In a drug interaction study, lasmiditan increased the systemic exposure of coadministered dabigatran (P-gp substrate) by approximately 25%. Therefore, when RAYVOW is administered with P-gp substrates that have a narrow therapeutic index (such as digoxin), increases in the systemic exposure of the coadministered medication may be clinically meaningful (see section 5.2). In the same study, no significant change in rosuvastatin (BCRP substrate) PK was observed when it was coadministered with lasmiditan.

Potential for other medicinal products to affect lasmiditan

No change in lasmiditan PK was observed when coadministered with dabigatran etexilate, rosuvastatin, sumatriptan, or propranolol. Based on its metabolism clearance pathways, CYP inhibitors or inducers are unlikely to affect lasmiditan exposure and no change in lasmiditan PK was observed when coadministered with topiramate (CYP3A4 inducer and CYP2C19 inhibitor).

4.6 Fertility, pregnancy and lactation

Pregnancy

There is a limited amount of data from the use of lasmiditan in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). The effects of lasmiditan on human foetal development are not known. RAYVOW is not recommended during pregnancy.

Breast-feeding

Lasmiditan and/or its metabolites were excreted into the milk of lactating rats (see section 5.3). There are no data on the presence of lasmiditan in human milk, the effects of lasmiditan on the breastfed infant, or the effects of lasmiditan on milk production.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from RAYVOW therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Exposure of the newborn can be minimised by avoiding breast-feeding for 24 hours after treatment.

Fertility

It is unknown whether lasmiditan affects human reproductive potential. Animal studies do not indicate any effect on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Lasmiditan has major influence on the ability to drive and use machines. Driving performance was evaluated using a computer-based driving simulation. The primary outcome measure was the difference from placebo in the Standard Deviation of Lateral Position (SDLP), a measure of driving performance. Administration of single 50 mg, 100 mg, or 200 mg doses of lasmiditan significantly

impaired subjects' ability to drive 90 minutes after dosing. In another study of lasmiditan 100 mg or 200 mg, driving performance did not reach the threshold for driving impairment at 8 hours or later after administration of RAYVOW at either dose.

Patients should be advised not to engage in activities requiring heightened attention, such as operating machinery or driving, for at least 8 hours after taking each dose of lasmiditan, even if they feel well enough to do so. Patients who cannot follow this advice should not take lasmiditan (see section 4.4).

4.8 Undesirable effects

Summary of the safety profile

The most commonly occurring adverse reactions are dizziness (19.9 %), somnolence (7.8 %), fatigue (7.7 %), paraesthesia (6.8 %), nausea (4.9 %), vertigo (2.6 %), hypoaesthesia (2.5 %), and muscular weakness (2.3 %). Most of the adverse events showed a dose response.

Tabulated list of adverse reactions

In the following table, adverse reactions are listed in order of MedDRA body system organ class and frequency. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequency gradings are: 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).

Table 1. Adverse reactions

System organ class	Very common	Common	Uncommon	Rare
Immune system disorders			Hypersensitivity	
Psychiatric disorders		Sleep abnormalities	Confusion Hallucinations Euphoric mood Anxiety Restlessness	
Nervous system disorders	Dizziness	Incoordination Paraesthesia Hypoaesthesia Somnolence	Lethargy Disturbance in attention Cognitive disorder Mental impairment Tremor Speech abnormalities	Serotonin syndrome
Eye disorders		Visual impairment		
Ear and labyrinth disorders		Vertigo		
Cardiac disorders		Palpitations		
Respiratory, thoracic and mediastinal disorders			Dyspnoea	
Gastrointestinal disorders		Vomiting Nausea		

Musculoskeletal and connective tissue disorders		Muscular weakness	Muscle spasm Limb discomfort	
General disorders and administration site conditions		Feeling abnormal Fatigue Malaise	Chest discomfort Feeling hot or feeling cold	

Description of selected adverse reactions

Heart rate decrease
In clinical pharmacology studies, lasmiditan was associated with decreases in heart rate of 5 to 10 bpm compared to a decrease of 2-5 bpm for placebo. Incidence of bradycardia (< 50 bpm and a decrease from baseline ≥ 15 bpm) observed in lasmiditan-treated subjects was 7 % for 50 mg, 3 % for 100 mg, 4 % for 200 mg, and 1 % for placebo.

Blood pressure increase
Single dose administration of lasmiditan may lead to a transient increase in blood pressure. In non-elderly healthy volunteers a mean increase from baseline in ambulatory systolic and diastolic blood pressure of approximately 2 to 3 mm Hg one hour after administration of 200 mg lasmiditan was observed, compared to an increase of about 1 mm Hg for placebo. In healthy volunteers over 65 years of age, the mean increase from baseline in ambulatory systolic blood pressure was 7 mm Hg one hour after administration of 200 mg lasmiditan compared to a mean increase of 4 mm Hg for placebo. By 2 hours, there were no increases in mean blood pressure with lasmiditan compared to placebo. Clinical data for the use of lasmiditan in patients with ischemic heart disease is limited.

Hypersensitivity
Events of hypersensitivity, including angioedema, rash, and photosensitivity reaction, occurred in patients treated with lasmiditan. In clinical trials, hypersensitivity was reported in 0.1 % of patients treated with lasmiditan compared to no patients in the placebo group; all events were mild to moderate in severity and occurred within minutes to a day after dosing with lasmiditan. If a serious or severe hypersensitivity reaction occurs, appropriate therapy should be initiated and administration of lasmiditan should be discontinued.

Dizziness
In clinical trials, dizziness was the most common adverse reaction, reported in 19.9 % of patients. It was generally mild to moderate in severity (severe dizziness 1.2 %) and self-limiting with a median time to onset of 0.7 hours and a median duration of 2 hours. No accidents or injuries were reported in patients reporting dizziness. The frequency of patients reporting dizziness, and other common adverse events, typically decreases with repeat dosing.

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

There is limited clinical trial experience with lasmiditan overdose. In cases reported as overdose, adverse events were similar to those seen at lower doses, including dizziness, somnolence, fatigue, paraesthesia, and hypoaesthesia but have not been associated with increase in severity or frequency. However, because adverse reactions are possible in case of an overdose, patients should be monitored

for any signs or symptoms of adverse reactions and appropriate symptomatic treatment initiated. There is no known antidote to lasmiditan overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, antimigraine preparations, ATC code: N02CC08

Mechanism of action

Lasmiditan is a high affinity, centrally-penetrant, 5-hydroxytriptamine 1F (5-HT_{1F}) receptor agonist. The precise mechanism of action is unknown, however, the therapeutic effects of lasmiditan in the treatment of migraine presumably involve agonistic effects at the 5-HT_{1F} receptor, a decrease of neuropeptide release and an inhibition of pain pathways, including the trigeminal nerve.

Pharmacodynamic effects

In *in vitro* binding studies, lasmiditan showed a > 440-fold selectivity for the 5-HT_{1F} receptor versus the 5-HT_{1B} and 5-HT_{1D} receptors. Lasmiditan does not constrict, *ex-vivo* human coronary arteries, *ex-vivo* human internal mammary arteries, or *ex-vivo* human middle meningeal arteries, likely due to its low affinity at the vasoconstrictive 5-HT_{1B} receptor.

Cardiac electrophysiology

In a thorough QT study, lasmiditan was associated with a heart rate decrease of 6 bpm when compared to placebo, and administration of a supra-therapeutic dose of 400 mg suggested a prolongation of the QTc in females. Subgroup analyses suggested gender-related differences, since a more pronounced QTc prolongation was observed in the female subset. However, as the maximum recommended dose is limited to 200 mg, no clinically relevant effect is expected.

Clinical efficacy and safety

The efficacy and safety of lasmiditan has been studied in three phase 3, randomized, placebo-controlled, double-blind studies in adult patients (N = 5910). The studies enrolled patients aged 18 and older with 3 - 8 migraine attacks per month, and at least moderately disabling migraine (Migraine Disability Assessment (MIDAS) score ≥ 11).

Single attack studies
The population enrolled in the single attack studies (SAMURAI and SPARTAN) was predominantly female (84 %) with a mean age of 42.3 years. Patients had an average of 5.2 migraine attacks per month in the 3 months prior to enrolment and a mean MIDAS total score of 31.7. SAMURAI, but not SPARTAN, excluded patients with known coronary artery disease, clinically significant arrhythmia, or uncontrolled hypertension. 78.3 % of patients had ≥ 1 cardiovascular risk factor, including age > 40 (54.2 %), low HDL-cholesterol (31.1 %), high blood pressure/hypertension (21.3 %), current smoker (14.3 %), high total cholesterol (10.9 %), and history of diabetes (5.9 %), in addition to migraine. 21.7 % of patients were prescribed preventive medicinal products for migraine, and 37 % had taken a triptan within 3 months of entering the study. The most bothersome symptom (MBS) was photophobia (50.3 %), followed by nausea (22.2 %), and phonophobia (20.6 %). In these studies, a second dose of study drug or other medicinal product was allowed 2 to 24 hours after the initial treatment for persistent or recurrent migraine.

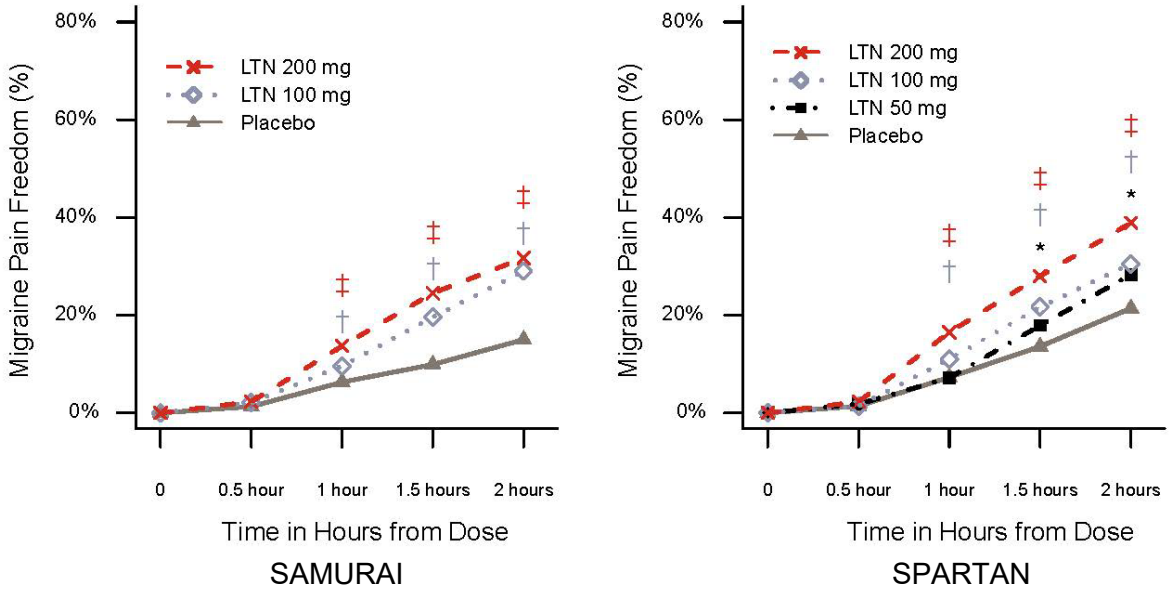
The primary and key secondary endpoints in both studies were the proportion of patients free from pain, and the proportion of patients free from their MBS, compared to placebo at 2 hours after treatment.

Both studies met the primary and key secondary endpoints. All doses of lasmiditan demonstrated statistically significant and clinically meaningful improvement in the percentage of patients achieving pain freedom, MBS freedom, and pain relief (defined as a reduction in pain severity from moderate or severe at baseline to mild or none or from mild to none) 2 hours after treatment (see Table 2). The timing of onset of pain freedom is demonstrated in Figure 1; onset of pain relief followed the same pattern as pain freedom at 50 mg and 100 mg, with additional separation from placebo seen at the earlier time of 30 mins for the 200 mg dose (17.7 % for 200 mg vs 11.6 % for placebo, p = 0.004 in SAMURAI, 18.6 % for 200 mg vs 14.7 % for placebo, p = 0.014 in SPARTAN).

Table 2. SAMURAI and SPARTAN: Summary of efficacy data

	SAMURAI lasmiditan			SPARTAN lasmiditan			
	100 mg	**200 mg**	**Placebo**	**50 mg**	**100 mg**	**200 mg**	**Placebo**
Pain free at 2 hours							
N	503	518	524	556	532	528	540
Responders (%)	28.2	32.2	15.3	28.6	31.4	38.8	21.3
p-value	< 0.001	< 0.001		0.006	< 0.001	< 0.001	
MBS free at 2 hours							
N	469	481	488	512	500	483	514
Responders (%)	40.9	40.7	29.5	40.8	44.2	48.7	33.5
p-value	< 0.001	< 0.001		0.018	< 0.001	< 0.001	
Pain relief at 2 hours							
N	562	555	554	598	571	565	576
Responders (%)	54.1	54.6	39.2	55.5	59.7	60.7	44.9
p-value	< 0.001	< 0.001		< 0.001	< 0.001	< 0.001	

Figure 1. Percentage of patients achieving migraine pain freedom within 2 hours in SAMURAI and SPARTAN.



‡ Statistical significance for 200 mg LTN vs placebo; † Statistical significance for 100 mg LTN vs placebo; * Statistical significance for 50 mg LTN vs placebo
Abbreviations: LTN = lasmiditan

Consistency of effect study
In a study assessing the consistency of effect, patients were treated with lasmiditan 100 mg, 200 mg, or control for 4 migraine attacks (CENTURION). In the control group, patients received a single dose of lasmiditan 50 mg to treat either their third or fourth attack and placebo for the remaining attacks. The population enrolled was predominantly female (84 %) with a mean age of 41.4 years. Patients had an average of 4.9 migraine attacks per month in the 3 months prior to enrolment and a mean MIDAS total score of 31.9. The study did not exclude patients with cardiovascular diseases, and 58.5 % of patients had ≥ 1 cardiovascular risk factor, including age > 40 **(**52.8 %), high total cholesterol (10.8 %), high blood pressure/hypertension (16.9 %), and history of diabetes (3.1 %), in addition to migraine. 28.8 % of patients were currently prescribed preventive medicinal products for migraine, and 65.0 % had previously taken a triptan. The MBS was photophobia (39.7 %), followed by nausea (31.9 %), and phonophobia (19.3 %).

The co-primary endpoints were the proportion of patients at 2 hours post dose that were free from pain after the first attack, and those that were free from pain in at least 2 out of 3 attacks, compared to placebo.

The study met its primary and all key secondary endpoints. Both doses of 100 mg and 200 mg of lasmiditan demonstrated statistically significant and clinically meaningful improvement in the percentage of patients achieving pain freedom, pain relief (a reduction in pain severity from moderate or severe at baseline to mild or none or from mild to none), MBS freedom, 2 hours after treatment, and sustained pain freedom after 24 hours (see Table 3). The timing of onset of pain freedom is demonstrated in Figure 2. Pain relief followed the same pattern as pain freedom at 50 mg and 100 mg, and was observed at the earlier time of 30 minutes with the 200 mg dose (22.4 % for 200 mg vs 14.0 % for placebo, p = 0.001).

Both doses demonstrated consistency of effect with a statistically significant and clinically meaningful improvement in the percentage of patients achieving pain freedom and pain relief in at least 2 out of 3 attacks (see Table 3).

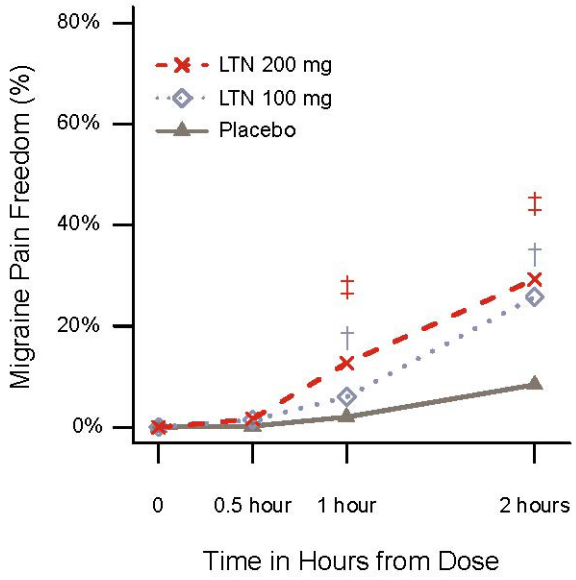
Table 3. CENTURION: Summary of efficacy data

	lasmiditan		
	100 mg	**200 mg**	**Placebo**
Single attack endpoints (ITT)	**N = 419**	**N = 434**	**N = 443**
Pain freedom at 2 hours post-dose during first attack			
Responders (%)	25.8	29.3	8.4
p-value versus placebo	< 0.001	< 0.001	
Pain relief at 2 hours post-dose during first attack			
Responders (%)	65.4	65.2	41.3
p-value versus placebo	< 0.001	< 0.001	
Sustained pain freedom up to 24 hours post-dose during first attack			
Responders (%)	13.6	17.3	4.3
p-value versus placebo	< 0.001	< 0.001	
MBS freedom at 2 hours post-dose during first attack	**N = 376**	**N = 395**	**N = 396**
Responders (%)	40.4	39.0	28.0
p-value versus placebo	< 0.001	0.001	
Consistency endpoints (ITT Consistency)			
Pain freedom at 2 hours post-dose in at least 2 out of 3 attacks	**N = 340**	**N = 336**	**N = 373**
Responders (%)	14.4	24.4	4.3
p-value versus placebo	< 0.001	< 0.001	

Pain relief at 2 hours post-dose in at least 2 out of 3 attacks	N = 332	N = 333	N = 320
Responders (%)	62.3	66.7	36.9
p-value versus placebo	< 0.001	< 0.001	

Abbreviations: ITT = intent to treat

Figure 2. Percentage of patients achieving migraine pain freedom within 2 hours in CENTURION.



‡ Statistical significance for 200 mg LTN vs placebo; † Statistical significance for 100 mg LTN vs placebo

Abbreviations: LTN = lasmiditan

Paediatric population

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

5.2 Pharmacokinetic properties

Absorption

Following oral administration, lasmiditan is rapidly absorbed with a median t_{max} of 1.8 hours. In patients with migraine, the pharmacokinetics of lasmiditan was not different during a migraine attack versus during the interictal period. Over the clinical dose range of 50 to 200 mg, the absolute bioavailability is predicted to be 50 % to 58 % based on results from the population PK analysis. Coadministration of lasmiditan with a high-fat meal increased the mean lasmiditan C_{max} and AUC values by 22 % and 19 %, respectively, and delayed the median t_{max} by 1 hour. This difference in exposure is not expected to be clinically meaningful. Lasmiditan was administered without regard to food in clinical efficacy studies.

Distribution

The human plasma protein binding of lasmiditan is approximately 55 % to 60 % and independent of concentration between 15 and 500 ng/mL. The estimated mean volume of distribution was 304 L.

Biotransformation

Lasmiditan undergoes hepatic and extrahepatic metabolism primarily by non-CYP enzymes, with ketone reduction to S-M8 as the major pathway. The following enzymes were not involved in metabolism of lasmiditan: MAO-A, MAO-B, flavin monooxygenase 3, CYP450 reductase, xanthine oxidase, alcohol dehydrogenase, aldehyde dehydrogenase, and aldo-keto reductases.

Lasmiditan is also oxidized on the piperidine ring to M7. Relative to lasmiditan, the metabolites are pharmacologically inactive. Lasmiditan is a substrate of P-gp *in vitro*.

Lasmiditan and its major metabolites are *in vitro* inducers of CYP enzymes. Lasmiditan inhibits CYP2D6 *in vitro*. Lasmiditan and its major metabolite are not inhibitors of MAO-A. Lasmiditan inhibits P-gp, BCRP, and OCT1 efflux transporters *in vitro*. Lasmiditan inhibits OCT2, MATE1, and MATE2-K renal transporters *in vitro*.

A clinical drug interaction study indicates that lasmiditan is a weak inhibitor of P-gp (see section 4.5).

Elimination

Lasmiditan was eliminated with a geometric mean $t_{½}$ value of approximately 5.7 hours. No accumulation of lasmiditan was observed with daily dosing. The estimated mean total body clearance was 66.2 L/h. Lasmiditan generally exhibits linear PK over the clinical dose range of 50 to 200 mg. Lasmiditan is primarily eliminated via metabolism. Renal excretion is a minor route of lasmiditan clearance with approximately 3 % of the dose recovered as unchanged lasmiditan in urine. Metabolite S-M8 represented approximately 66% of the dose in urine, with the majority of recovery within 48 hours post-dose.

Special populations

Age, gender, race, ethnicity and body weight
Age, gender, race, ethnicity, and body weight did not have a significant effect on the exposure in a population pharmacokinetic analysis of lasmiditan. In a study, gender had an effect on PK of lasmiditan with higher C_{max} (~ 20 - 30 %) and AUC (~ 30 %) in women compared to men, irrespective whether lasmiditan was administered in fed or fasted conditions. No dose adjustment is necessary based on age, gender, race, ethnicity or body weight.

Renal impairment
Administration of lasmiditan to subjects with severe renal impairment (eGFR <30 mL/min/1.73 m^2) demonstrated 18 % greater exposure in AUC(0-∞) and 13 % higher C_{max}, compared to subjects with normal renal function. This difference in exposure is not expected to be clinically significant. No dose adjustment is necessary in patients with mild, moderate, or severe renal impairment.

Hepatic impairment
In subjects with mild and moderate hepatic impairment (Child-Pugh Class A and B, respectively) lasmiditan exposure was 11 % and 35 %, respectively, higher [AUC(0-∞)] than that in subjects with normal hepatic function. The C_{max} were higher by 19 % and 33 %, respectively, for subjects with mild and moderate hepatic impairment. This difference in exposure is not expected to be clinically significant. No dose adjustment is necessary in patients with mild or moderate hepatic impairment. The use of lasmiditan has not been studied in subjects with severe hepatic impairment and therefore is not recommended for this population.

5.3 Preclinical safety data

Carcinogenicity was assessed in a two-year rat study and a six-month transgenic mouse study. In rats, an increase in pituitary tumour-related deaths in male rats was seen. The relevance of these findings in terms of human risk is unknown. No evidence of carcinogenicity was seen in mice.

Lasmiditan was not genotoxic based on results from the Ames assay in bacteria, a chromosome aberration study in Chinese hamster ovary cells, and micronucleus tests in mice.

Developmental and reproductive toxicity

In studies with rats, there were no effects on male or female fertility.

In embryofoetal development studies with rats and rabbits, decreased foetal body weights and skeletal variations occurred; in rabbits, there was a slight increase in post-implantation loss (embryofoetal mortality), and foetal cardiovascular defects (malformations) occurred at a low incidence. Exposure at the no-observed-adverse effect doses of 175 mg/kg/day (rats) and 75 mg/kg/day (rabbits) were approximately 37 and 1.5-fold, respectively, higher than in humans at 200 mg.

In a rat pre- and postnatal study, prolonged gestation and parturition and an increased number of stillborn pups and frequency of postnatal death occurred at the highest dose tested of 225 mg/kg/day. At this high exposure, a decrease in F1 pup mean body weights observed during the preweaning phase in both genders was maintained throughout the F1 maturation phase with no recovery. Exposure at the no-observed effect dose of 150 mg/kg/day was estimated to be > 19 fold higher than that in humans at 200 mg.

All effects occurred at maternally toxic exposures which exceeded human exposure at a clinical dose of 200 mg.

Studies in animals have shown that lasmiditan and/or its metabolites were excreted into the milk of lactating rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate
Pregelatinized starch
Sodium laurilsulfate

Film coating (50 mg and 200 mg)

Polyvinyl alcohol
Titanium dioxide (E171)
Macrogol 3350
Talc
Iron oxide black (E172)

Film coating (100 mg)

Polyvinyl alcohol
Titanium dioxide (E171)
Macrogol 3350
Talc
Iron oxide black (E172)
Iron oxide red (E172)

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

Polychlorotrifluoroethylene/polyvinyl chloride (PCTFE/PVC) perforated unit dose blisters sealed with an aluminium foil lid in packs of 2 x 1, 4 x 1, 6 x 1, 12 x 1 and 16 x 1 film-coated tablets.
Polyvinyl chloride (PVC) perforated unit dose blisters sealed with an aluminium foil lid in packs of 2 x 1, 4 x 1, 6 x 1, 12 x 1 and 16 x 1 film-coated 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

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

RAYVOW 50 mg film-coated tablets

EU/1/21/1587/001
EU/1/21/1587/002
EU/1/21/1587/003
EU/1/21/1587/004
EU/1/21/1587/005
EU/1/21/1587/006
EU/1/21/1587/007
EU/1/21/1587/008
EU/1/21/1587/009
EU/1/21/1587/010

RAYVOW 100 mg film-coated tablets

EU/1/21/1587/011
EU/1/21/1587/012
EU/1/21/1587/013
EU/1/21/1587/014
EU/1/21/1587/015
EU/1/21/1587/016
EU/1/21/1587/017
EU/1/21/1587/018
EU/1/21/1587/019
EU/1/21/1587/020

RAYVOW 200 mg film-coated tablets

EU/1/21/1587/021
EU/1/21/1587/022
EU/1/21/1587/023
EU/1/21/1587/024
EU/1/21/1587/025
EU/1/21/1587/026
EU/1/21/1587/027
EU/1/21/1587/028
EU/1/21/1587/029
EU/1/21/1587/030

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 August 2022

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(S) 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(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Lilly S.A.
Avda. de la Industria 30
Alcobendas
Madrid
28108
Spain

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

CARTON FOR 50 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 50 mg film-coated tablets
lasmiditan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 50 mg lasmiditan (as succinate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet

2 x 1 film-coated tablets
4 x 1 film-coated tablets
6 x 1 film-coated tablets
12 x 1 film-coated tablets
16 x 1 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral 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

Do not drive or operate machinery for at least 8 hours after each dose

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

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1587/001 (2 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/002 (4 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/003 (6 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/004 (12 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/005 (16 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/006 (2 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/007 (4 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/008 (6 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/009 (12 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/010 (16 x 1 film-coated tablets PVC/alu blister)

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

RAYVOW 50 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR 50 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 50 mg tablets
lasmiditan

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Lilly

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 100 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 100 mg film-coated tablets
lasmiditan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 100 mg lasmiditan (as succinate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet

2 x 1 film-coated tablets
4 x 1 film-coated tablets
6 x 1 film-coated tablets
12 x 1 film-coated tablets
16 x 1 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral 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

Do not drive or operate machinery for at least 8 hours after each dose

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

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1587/011 (2 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/012 (4 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/013 (6 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/014 (12 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/015 (16 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/016 (2 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/017 (4 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/018 (6 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/019 (12 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/020 (16 x 1 film-coated tablets PVC/alu blister)

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

RAYVOW 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR 100 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 100 mg tablets
lasmiditan

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Lilly

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 200 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 200 mg film-coated tablets
lasmiditan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 200 mg lasmiditan (as succinate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet

2 x 1 film-coated tablets
4 x 1 film-coated tablets
6 x 1 film-coated tablets
12 x 1 film-coated tablets
16 x 1 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral 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

Do not drive or operate machinery for at least 8 hours after each dose

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

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1587/021 (2 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/022 (4 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/023 (6 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/024 (12 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/025 (16 x 1 film-coated tablets PCTFE/PVC/alu blister)
EU/1/21/1587/026 (2 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/027 (4 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/028 (6 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/029 (12 x 1 film-coated tablets PVC/alu blister)
EU/1/21/1587/030 (16 x 1 film-coated tablets PVC/alu blister)

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

RAYVOW 200 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR 200 MG FILM-COATED TABLETS

1. NAME OF THE MEDICINAL PRODUCT

RAYVOW 200 mg tablets
lasmiditan

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Lilly

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

RAYVOW 50 mg film-coated tablets
RAYVOW 100 mg film-coated tablets
RAYVOW 200 mg film-coated tablets
lasmiditan

▼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 RAYVOW is and what it is used for

RAYVOW contains the active substance lasmiditan, which is used to treat the headache phase of migraine attacks with or without aura in adults.

RAYVOW helps to reduce or get rid of the pain and other symptoms associated with a migraine headache. Pain relief may be felt from as early as 30 minutes after taking RAYVOW.

2. What you need to know before you take RAYVOW

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

Warnings and precautions
Do not take part in activities requiring your full attention, such as driving or operating machinery, within 8 hours of taking each dose of RAYVOW, even if you feel well enough to do so, because it can affect your ability to drive or operate machinery safely. If you cannot do this, you should not take RAYVOW.

Talk to your doctor or pharmacist before taking RAYVOW if you:
- are taking medicines that increase the level of serotonin (see ‘Other medicines and RAYVOW’). These medicines increase the risk of side effects such as serotonin syndrome (a rare reaction which may cause mental changes, such as seeing things that are not there (hallucinations),

agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; trouble walking; nausea, vomiting, or diarrhoea).
- are taking other medicines or substances that cause sleepiness such as sleeping pills, medicines for psychiatric conditions, or alcohol
- have ever been addicted to prescription medicines, alcohol, or other drugs.

If you repeatedly use any medicines for the treatment of migraine over several days or weeks, this can cause long-term daily headaches. Tell your doctor if you experience this as you might need to stop treatment for a while.

Children and adolescents
RAYVOW should not be given to patients under the age of 18 years because there is not enough information about how it works in this age group.

Other medicines and RAYVOW
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist before taking RAYVOW if you are taking:
- medicines that lower heart rate, such as propranolol
- medicines that increase the level of serotonin (including SSRIs, SNRIs, tricyclic antidepressants, monoamine oxidase inhibitors [MAOIs], or triptans)
- digoxin (used to treat heart disorders)

RAYVOW with alcohol
Care should be taken if you drink alcohol while taking RAYVOW.

Pregnancy, breast-feeding and fertility
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. It is not known if RAYVOW will harm your unborn baby. RAYVOW is not recommended during pregnancy.

If you are breast-feeding, ask your doctor for advice before taking this medicine. It is not known if lasmiditan passes into your breastmilk. It is recommended to avoid breast-feeding for 24 hours after treatment in order to minimise the amount of lasmiditan that is passed onto your baby.

It is not known whether RAYVOW affects your fertility.

Driving and using machines
RAYVOW affects your ability to drive and use machines. Do not take part in activities requiring your full attention, such as driving or operating machinery, for at least 8 hours after taking each dose of lasmiditan, even if you feel well enough to do so. If you cannot do this, you should not take RAYVOW.

RAYVOW contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially “sodium-free”.

3. How to take RAYVOW

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

- The recommended starting dose is 100 mg lasmiditan. Your doctor will decide which dose of lasmiditan is appropriate for you.
- If you do not become pain free after the first tablet, do not take a second tablet for the same attack as it is unlikely to be effective.
- If after a first tablet of 50 mg or 100 mg your migraine is completely resolved and then comes back, you may take a second tablet of the same strength no sooner than 2 hours after the first dose.
- You should not take more than 200 mg within 24 hours.
- If your dose of 100 mg does not relieve your migraine or causes side effects, talk to your doctor, who may recommend a higher (200 mg) or lower (50 mg) dose.

Use in children and adolescents and patients with liver impairment
RAYVOW is not recommended in children and adolescents (under 18 years of age), or in patients with severe liver problems.

Route of administration
RAYVOW is for oral use. You should swallow your tablet with a drink of water during the headache phase of your migraine attack. You can take the tablet either with or without food.

If you take more RAYVOW than you should
If you take more RAYVOW than you should, immediately contact your doctor. You may get some of the side effects described in section 4.

If you forget to take RAYVOW
RAYVOW is indicated for the acute treatment of migraine headaches and should only be taken when necessary.

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.

Tell your doctor immediately if you experience any of the following serious side effects after taking this medicine:
- allergic reactions including rashes and swelling of eyelids, face, or lips (frequency uncommon)
- signs and symptoms of serotonin syndrome, a rare reaction which may cause mental changes, such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; trouble walking; gastrointestinal signs such as nausea, vomiting, or diarrhoea.

Other side effects may include:

Very common (may affect more than 1 in 10 people):
- Dizziness

Common (may affect up to 1 in 10 people):
- Feeling sleepy
- Feeling tired
- Prickling or tingling of the skin
- Feeling sick
- Numbness
- Feeling of general discomfort

- Feeling of spinning and loss of balance
- Muscle weakness
- Difficulty controlling movement e.g. lack of coordination
- Feeling abnormal
- Vomiting
- Poor quality sleep
- Feeling the heart pumping in the chest, e.g. palpitations
- Vision problems, e.g. blurred vision

Uncommon (may affect up to 1 in 100 people):
- Sensation of restlessness or an inability to sit or stand still
- Shaking or tremor
- Feeling anxious
- Feeling hot or cold
- Muscle cramp
- Feeling sluggish
- Arm or leg discomfort
- Difficulty in concentrating
- Thinking changes such as memory loss or foggy thinking
- Feeling of mind not working properly
- Speech problems, e.g. slurred speech
- Feeling confused
- Chest discomfort
- Extremely happy or excited mood
- Seeing or hearing things that are not there
- Shortness of breath or difficulty breathing

Lasmiditan has been associated with a lowering of heart rate (on average about 5 to 10 beats per minute), and a small increase in blood pressure, in the hours after dosing.

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 listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store RAYVOW

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 blister and carton 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. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What RAYVOW contains

- The **active** substance is lasmiditan.
  - RAYVOW 50 mg film coated tablets
    Each film coated tablet contains 50 mg lasmiditan (as succinate).
  - RAYVOW 100 mg film coated tablets
    Each film coated tablet contains 100 mg lasmiditan (as succinate).
  - RAYVOW 200 mg film coated tablets
    Each film coated tablet contains 200 mg lasmiditan (as succinate).
- The **other** ingredients are: croscarmellose sodium, magnesium stearate, microcrystalline cellulose, sodium laurilsulfate, pregelatinized starch
  - For 50 mg and 200 mg colour mixture grey: polyvinyl alcohol, titanium dioxide (E171), macrogol 3350, talc, iron oxide black (E172)
  - For 100 mg colour mixture purple: polyvinyl alcohol, titanium dioxide (E171), macrogol 3350, talc, iron oxide black (E172), iron oxide red (E172)

What RAYVOW looks like and contents of the pack

RAYVOW is available in 3 strengths: 50 mg, 100 mg and 200 mg

- The 50 mg film-coated tablets are light grey, oval tablet with “4312” on one side and “L-50” on the other.
- The 100 mg film-coated tablets are light purple, oval tablet with “4491” on one side and “L-100” on the other.
- The 200 mg film-coated tablets are grey, oval tablet with “4736” on one side and “L-200” on the other.

RAYVOW is available in polychlorotrifluoroethylene/polyvinyl chloride (PCTFE/PVC) and polyvinyl chloride (PVC) perforated unit dose blisters sealed with an aluminium foil lid in packs of 2 x 1, 4 x 1, 6 x 1, 12 x 1 and 16 x 1 film-coated tablets. Not all the pack sizes may be marketed.

Marketing Authorisation Holder

Eli Lilly Nederland B.V.,
Papendorpseweg 83,
3528 BJ Utrecht,
The Netherlands

Manufacturer

Lilly S.A.,
Avda. de la Industria, 30,
28108 Alcobendas,
Madrid,
Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Eli Lilly Benelux S.A./N.V.
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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