For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

LASMIRAY

1. Generic Name

Lasmiditan Tablets 50 mg and 100 mg

2. Qualitative and quantitative composition

LASMIRAY 50

Each Film coated tablet contains:

Lasmiditan Hemisuccinate……..57.824 mg

Eq. to Lasmiditan …….50 mg

Colour: Titanium Dioxide I.P.

LASMIRAY 100

Each Film coated tablet contains:

Lasmiditan Hemisuccinate……..115.65 mg

Eq. to Lasmiditan ……..…..100 mg

Colour: Titanium Dioxide I.P.

The Excipients used are Microcrystalline cellouse, Sodium lauryl Sulphate, Pregelatinized starch, Croscrmellose Sodium, Colloidal silicon dioxide, Magnesium Stearate, and Opadry II White.

3. Dosage form and strength

Dosage form: Film coated tablet

Strength: 50 mg and 100 mg

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the acute treatment of migraine with or without aura in adult.

4.2 Posology and method of administration

Posology

The recommended dose is 1 tablet, to be given once daily depending upon severity of Pain or as directed by the Physician. Do not exceed Stated dose.

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.

Renal impairment

No dose adjustment is necessary in patients with mild, moderate, or severe renal impairment

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.

Paediatric population

The safety and efficacy of lasmiditan in children and adolescents aged 6 to <18 years have not yet been estabslished. 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

Orally and As directed by the Physician.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Polyvinyl alcohol Titanium dioxide

Macrogol

Talc Iron oxide black

Iron oxide red

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.Central Nervous System Depression

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 Drugs interactions

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 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

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 GFR.

Potential for other medicinal products to affect lasmiditan

No change in lasmiditan PK was observed when coadministered with 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).-vitro.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

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

Breast-feeding

Lasmiditan and/or its metabolites were excreted into the milk of lactating rats. 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 LASMIRAY 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

4.7 Effects on ability to drive and use machines

Not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle or operating machinery for at least 8 hours after taking each dose of LASMIRAY

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).

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	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 beats per minute (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

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

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 Mechanism of Action

Lasmiditan is a high affinity, centrally-penetrant, 5-hydroxytriptamine 1F (5-HT1F) 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-HT1F receptor, a decrease of neuropeptide release and an inhibition of pain pathways, including the trigeminal nerve.

5.2 Pharmacodynamic Properties

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 (Study 1and Study 2) 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. Study 1, but not Study 2, 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.

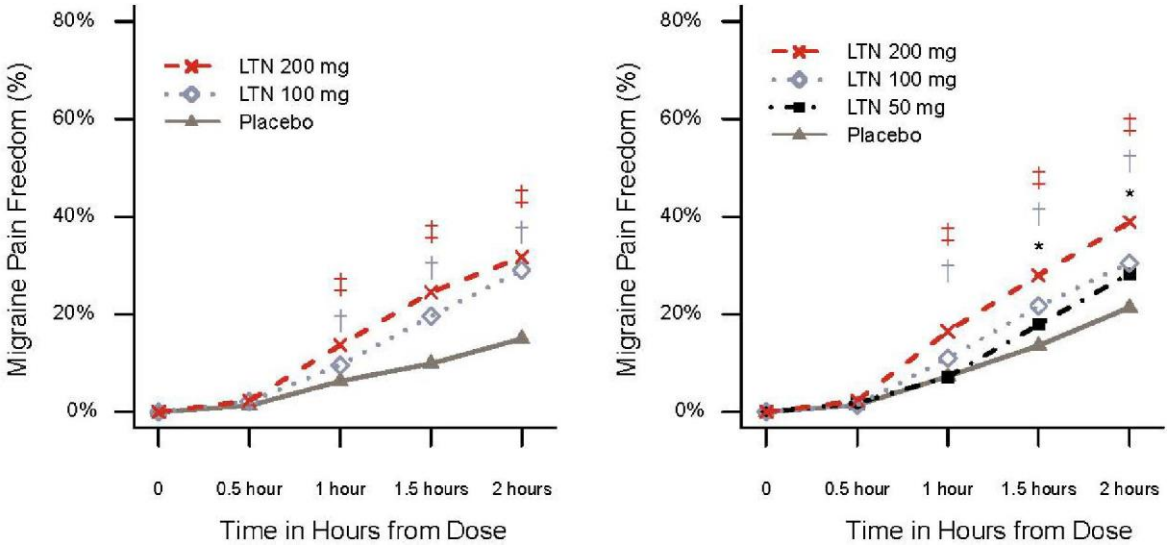
The primary and key secondary endpoints in both studies were the proportion of patients free from pain, and the proportion of patients free from their MBS, compared to placebo at 2 hours after treatment.

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 Study 1, 18.6 % for 200 mg vs 14.7 % for placebo, p = 0.014 in Study 2).

Table 2. Study 1 and Study 2: Summary of efficacy data

	Study 1 lasmiditan			**Study 2 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 Study 1 and Study 2.



‡ 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. 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.

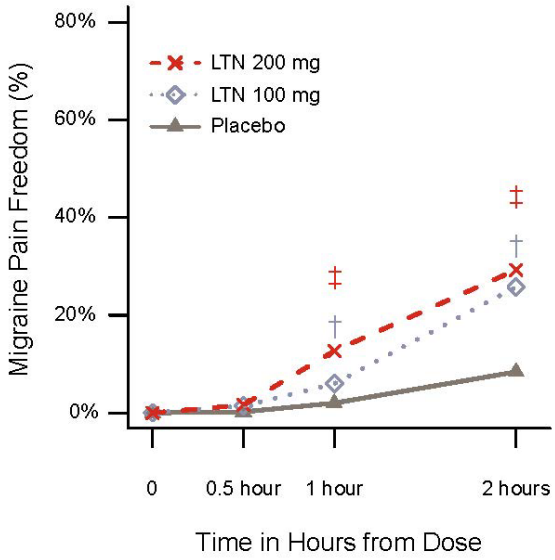
The study met its primary and all key secondary endpoints. Both doses of 100 mg and 200 mg of lasmiditan demonstrated statistically significant and clinically meaningful improvement in the percentage of patients achieving pain freedom, pain relief (a reduction in pain severity from moderate or severe 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 2). 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

Table 3. Study 3: 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	

Figure 2. Percentage of patients achieving migraine pain freedom within 2 hours in Study 3



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

Abbreviations: LTN = lasmiditan

5.3 Pharmacokinetic properties

Absorption

Following oral administration, lasmiditan is rapidly absorbed with a median tmax 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 Cmax and AUC values by 22 % and 19 %, respectively, and delayed the median tmax 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.

Elimination

Lasmiditan was eliminated with a geometric mean t½ 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.

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*.

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 Cmax (~ 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.

Geriatric Use

In a clinical pharmacology study, administration of lasmiditan to subjects 65 years of age or older demonstrated 26% greater exposure in AUC(0-∞) and 21% higher C , compared to subjects 45 years of age or less. This difference in exposure is not expected to be clinically significant.

Renal impairment

Administration of lasmiditan to subjects with severe renal impairment (eGFR <30 mL/min/1.73 m2) demonstrated 18 % greater exposure in AUC(0-∞) and 13 % higher Cmax, 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 Cmax 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.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Carcinogenesis

No drug-related tumors were observed following oral administration of lasmiditan to TgRasH2 mice at doses of up to 150 (males) or 250 (females) mg/kg/day for 26 weeks or to rats at doses of up to 75 mg/kg/day for 2 years. Plasma exposures (AUC) at the highest dose tested in rats were approximately 15 times that in humans at the maximum recommended human dose (MRHD) of 200 mg/day.

Mutagenesis

Lasmiditan was negative in in vitro (bacterial reverse mutation, chromosomal aberration

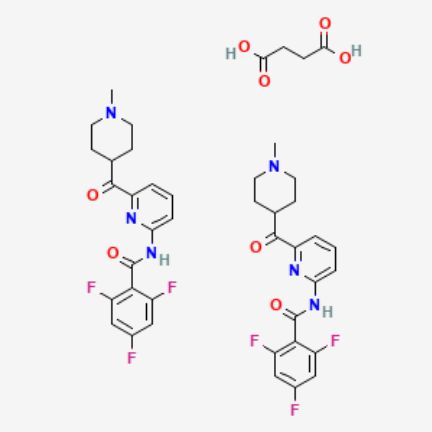
Impairment of Fertility

Oral administration of lasmiditan to male (0, 100, 175, or 200 mg/kg/day) or female (0, 100, 150, or 200 mg/kg/day) 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) at the highest dose tested (200 mg/kg/day) were approximately 26 times that in humans at the MRHD.

7. Description

Lasmiditan Hemisuccinate:

Lasmiditan Hemisuccinate is butanedioic acid;2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)pyridin-2-yl]benzamid. The empirical formula is $C_{42}H_{42}F_6N_6O_8$ and its molecular weight is 872.8 g/mol. The chemical structural formula is:



LASMIRAY

Lasmiditan Tablets are white to off white colored, round, biconvex, plain on both side, film coated tablets. The Excipients used are Microcrystalline cellouse, Sodium lauryl Sulphate, Pregelatinized starch, Croscrmellose Sodium, Colloidal silicon dioxide, Magnesium Stearate and Opadry II White.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

LASMIRAY is available in pack of 4 tablets.

8.4 Storage and handing instructions

Store at a temperature not exceeding 25^0C.

Keep the medicines out of reach of children.

9. Patient Counselling information

Package leaflet: information for the patient

LASMIRAY

Lasmiditan Tablets 50 mg and 100 mg

- 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.

What is in this leaflet?

9.1 What LASMIRAY is and what it is used for

LASMIRAY contains Lasmiditan Tablets 50 mg and 100 mg film coated tablet.

It is indicated for the acute treatment of migraine with or without aura in adult.

9.2 What you need to know before you take LASMIRAY

Before you take LASMIRAY, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- have high blood pressure
- have a low heart rate
- are allergic to lasmiditan
- are pregnant or plan to become pregnant. It is not known if LASMIRAY will harm your unborn baby.

Warnings and precautions

Driving Impairment

LASMIRAY may cause significant driving impairment. In a driving study, administration of single 50 mg, 100 mg, or 200 mg doses of LASMIRAY significantly impaired subjects' ability to drive additionally, more sleepiness was reported at 8 hours following a single dose of LASMIRAY compared to placebo. Advise patients not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle or operating machinery, for at least 8 hours after each dose of LASMIRAY. Patients who cannot follow this advice should not take LASMIRAY. Prescribers and patients should be aware that patients may not be able to assess their own driving competence and the degree of impairment caused by LASMIRAY.

Central Nervous System Depression

LASMIRAY may cause central nervous system (CNS) depression, including dizziness and sedation Because of the potential for LASMIRAY to cause sedation, other cognitive and/or neuropsychiatric adverse reactions, and driving impairment, LASMIRAY should be used with caution if used in combination with alcohol or other CNS depressants Patients should be warned against driving and other activities requiring complete mental alertness for at least 8 hours after LASMIRAY is taken.

Serotonin Syndrome

In clinical trials, reactions consistent with serotonin syndrome were reported in patients treated with LASMIRAY who were not taking any other drugs associated with serotonin syndrome. Serotonin syndrome may also occur with LASMIRAY during coadministration with serotonergic drugs [e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase (MAO) inhibitors]. 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, diarrhea). The onset of symptoms usually occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. Discontinue LASMIRAY if serotonin syndrome is suspected

Medication Overuse Headache

Overuse of acute migraine drugs (e.g., ergotamines, triptans, opioids, or a combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (i.e., medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients including withdrawal of the overused drugs and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

Other medicines and LASMIRAY

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

CNS Depressants

Concomitant administration of LASMIRAY and alcohol or other CNS depressant drugs has not been evaluated in clinical studies. Because of the potential of LASMIRAY to cause sedation, as well as other cognitive and/or neuropsychiatric adverse reactions, LASMIRAY should be used with caution if used in combination with alcohol or other CNS depressants.

Serotonergic Drugs

Concomitant administration of LASMIRAY and drugs (e.g., SSRIs, SNRIs, TCAs, MAO inhibitors, trazodone, etc.), over-the counter medications (e.g., dextromethorphan), or herbal supplements (e.g., St. John's Wort) that increase serotonin may increase the risk of serotonin syndrome LASMIRAY with caution in patients taking medications that increase serotonin.

Heart Rate Lowering Drugs

LASMIRAY has been associated with a lowering of heart. In a drug interaction study, addition of a single 200 mg dose of LASMIRAY to propranolol decreased heart rate by an additional 5 beats per minute compared to propranolol alone, for a mean maximum of 19 beats per minute. Use LASMIRAY with caution in patients taking concomitant medications that lower heart rate if this magnitude of heart rate decrease may pose a concern.

P-glycoprotein (P-gp) Transporter Substrates

Coadministration of LASMIRAY with P-gp substrates where a small change in substrate plasma concentration may lead to serious toxicities (e.g., digoxin) is not recommended.

Driving and using machines

Do not drive or operate machinery for at least 8 hours after taking LASMIRAY.

9.3 How to take LASMIRAY

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

You can take LASMIRAY with or without food.

Your doctor may prescribe LASMIRAY together with another oral anti-diabetic medicine. Remember to take all medicines as directed by your doctor to achieve the best results for your health.

If you take more LASMIRAY than you should, talk to a doctor immediately.

If you forget to take LASMIRAY

- If you forget to take a dose of LASMIRAY, take it as soon as you remember it. However, if it is nearly time for the next dose, skip the missed dose.
- Do not take a double dose to make up for a forgotten dose. Never take two doses on the same day.

9.4 Possible side effects

Serotonin syndrome. Serotonin syndrome is a rare but serious problem that can happen in people using LASMIRAY, especially if LASMIRAY is used with antidepressant medicines called SSRIs or SNRIs. Call your healthcare provider right away if you have any of the following symptoms of serotonin syndrome:

- 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 diarrhea

Medication overuse headache. Some people who take medicines like LASMIRAY for the acute treatment of migraine attacks for 10 or more days each month may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with LASMIRAY.

The most common side effects of LASMIRAY include:

- dizziness
- sleepiness
- numbness
- feeling tired
- tingling

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store LASMIRAY

Store at a temperature not exceeding 25^0C.

Keep all the medicines out of reach of children.

9.6 Contents of the pack and other information

LASMIRAY consists of Lasmiditan tablets as active ingredient.

Lasmiditan Tablets are white to off white colored, round, biconvex, plain on both side, film coated tablets. The Excipients used are Microcrystalline cellouse, Sodium lauryl Sulphate, Pregelatinized starch, Croscrmellose Sodium, Colloidal silicon dioxide, Magnesium Stearate and Opadry II White.

LASMIRAY is available in pack of 4 tablets.

10. Details of manufacturer

Pure & Cure Healthcare Pvt. Ltd.

(A subsidiary of Akums Drugs & Pharmaceuticals Ltd.)

Plot No. 26A, 27-30, Sector-8A, I.I.E., SIDCUL,

Ranipur, Haridwar- 249 403, Uttarakhand.

11. Details of permission or licence number with date

Mfg. Licence. No.: 31/UA/2013 Issued on: 05.12.2023

12. Date of revision

Not applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/LASMIRAY 50, 100 mg/Jan-24/01/PI