Report RAYVOW® - lasmiditan

Product & Mechanism of action

Substance: lasmiditan

Brand Name: Rayvow

Originator/licensee: Eli Lilly Nederland B.V.

Classification: NCE

ATC code: N02CC

Orphan Status:
Eu: No
Us: No

Mechanism of action: The precise mechanism is unknown.
Lasmiditan is a high-affinity, highly selective 5-HT_{1F} receptor agonist and a first in class ditan. It is presumed that lasmiditan acts effecting a decrease of neuropeptide release and an inhibition of pain pathways [1,2].

Authorized indications Licensing status

Authorized Indication:
EMA: lasmiditan is indicated for the acute treatment of the headache phase of migraine attacks, with or without aura in adults [1].

Route of administration: OS

Licensing status
EU CHMP P.O. date: 23/06/2022
EU M.A. date:
FDA M.A. date: 03/06/2022

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: No

ABBREVIATIONS:
AE: adverse event
Hrs: hours
ICHD: International Classification of Headache Disorders
LTN: lasmiditan
MBS: most-bothersome symptom
MIDAS: Migraine Disability Assessment Score
NSAID: non steroidal anti-inflammatory drug
OS: oral somministration
PBO: placebo
Pts: patients
SAE: serious adverse event
TEAEs: Treatment emergent adverse event
Yrs: years
5-HT1F: 5-hydroxytryptamine 1F

Essential therapeutic features

Summary of clinical EFFICACY:
SAMURAI (NCT02439320) and SPARTAN (NCT02605174) were phase III, randomized, double-blind, placebo-controlled studies to evaluate the efficacy of LTN vs PBO in treating migraine-related headache pain and MBS. Patients aged ≥18 yrs with a diagnosis of episodic migraine, with or without aura, fulfilling the ICHD-II diagnostic criteria. Inclusion criteria included MIDAS* ≥11 (moderate disability) and 3-8 migraine attacks per month. 18% of pts used migraine preventive treatment.
Pts (SAMURAI n=2232; SPARTAN n=3005) were randomized to a first oral dose of treatment (SAMURAI, 1:1:1 ratio of LTN 200/100 mg or PBO, SPARTAN, 1:1:1:1 ratio of LTN 200/100/50 mg or placebo) which was taken within four hours of migraine onset (moderate severity or worse and not improving).
Primary outcome were:
- percentage of participants headache pain free at 2 hrs post dose
- percentage of pts who are MBS free 2 hrs post dose

At 2 hrs post-first dose, a significantly greater proportion of pts were headache pain-free and MBS-free with LTN 200 mg compared with PBO. For both endpoints, significance was also reported for other LTN dose groups (100 mg, 50 mg) compared to PBO. The efficacy outcomes were not significantly different between pts using or not using migraine preventives treatments [2-4].
*where MIDAS score 0-5 means little or no disability and 21+ means severe disability

SAMURAI	100 mg	200 mg	PBO
% of pts with 2-hrs pain freedom	28% vs PBO p<0.001	32% vs PBO p<0.001	15%
% of pts with freedom from most bothersome symptom at 2-hrs	41% vs PBO p<0.001	41% vs PBO p<0.001	30%

SPARTAN	50 mg	100 mg	200 mg	PBO
% of pts with 2-hrs pain freedom	29% vs PBO p=0.003	31% vs PBO p<0.001	39% vs PBO p<0.001	21%
% of pts with freedom from most bothersome symptom at 2-hrs	41% vs PBO p=0.009	44% vs PBO p<0.001	49% vs PBO p<0.001	34%

Summary of clinical SAFETY:
Rates of AEs, SAEs and TEAEs were similar for pts using and not using preventive medications. Pts using preventive drugs experienced SAEs at rates of 0% with PBO vs. 0.2% with LTN , whereas pts not using preventive treatments experienced SAEs at rates of 0.3% with PBO vs. 0.3% with lasmiditan .
No deaths in either group were repoerted. The most frequent TEAEs were mild-to-moderate in severity and were, respectively in PBO and ALL LTN*: dizziness (3% vs 15%), paresthesia (15% vs 1-2%), somnolence (2% vs 4-6%), fatigue (1% vs 3-4%) and nausea (1-2% vs 4-3%) [2-4].
*ALL LTN: population receiving lasmidan (LTN) 50 mg, 100 mg or 200 mg.

Ongoing studies:
- ***For the same indication:*** Yes [6].
- ***For other indications:*** No

Discontinued studies (for the same indication): Yes [6].

References:

[1]. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/rayvow
[2]. https://www.io.nihr.ac.uk/wp-content/uploads/2022/01/6824-Lasmiditan-for-Migraine-V1.0-JAN2020-NON-CONF.pdf
[3]. https://n.neurology.org/content/90/15_Supplement/S50.008
[4]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6734212/pdf/10194_2019_Article_1032.pdf
[5]. https://www.iss.it/documents/20126/0/Emicrania-una-patologia-di-genere.pdf/d5c39e7f-bf71-1d3a-91ef-6d71efc87a6e?t=1576061517293
[6]. https://adisinsight.springer.com/drugs/800028519
[7]. https://www.clinicaltrials.gov/

NHS impact

Cost of therapy:
Price not available yet.

Epidemiology:
Studies conducted on the Italian population have shown a prevalence of migraine equal to 24.7%, corresponding to 32.9% of women and 13% of men [5].

POSSIBLE PLACE IN THERAPY
For adults with migraine (with or without aura) NICE recommends:
- combination therapy with an oral triptan and a NSAID, or an oral triptan and paracetamol;
- for people who prefer to take only one drug, monotherapy with an oral triptan NSAID, aspirin (900 mg) or paracetamol* has to be considered;
- for people in whom oral formulations are ineffective or not tolerated, a non-oral preparation of metoclopramide or prochlorperazine has to be considered, adding a non-oral NSAID or triptan if these have not been tried* [2].

* taking into account the person's preference, comorbidities and risk of AE;

OTHER INDICATIONS IN DEVELOPMENT: No

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: No

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: Anisodine Hydrobromide, Dihydroergotamine [7].

*Service reorganization No
*Possible off label use Yes