Final Study Report

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Real-World Observational Study to Assess Drug Utilisation Patterns in the US Among Migraine Patients Treated with Lasmiditan

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PASS Information

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Country(-ies) of study	United States
Author	Lilly Global Patient Safety Pharmacoepidemiologist
Signature of principal investigator	Lilly Global Patient Safety Pharmacoepidemiologist

Abbreviations: EU PAS = European Union Post-Authorisation Studies; N/A = not applicable.

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1. Abstract

Title: Real-World Observational Study to Assess Drug Utilisation Patterns in the US Among Migraine Patients Treated with Lasmiditan.

Keywords: Lasmiditan, adult migraine, paediatric migraine, utilization, acute migraine treatment

Rationale and background: Drug abuse/misuse is an important potential risk based on drug-liking data observed in recreational drug users treated with lasmiditan. Real-world use of lasmiditan was studied by accessing a healthcare database to evaluate use patterns (abuse/misuse) after approval, as well as the length of therapy.

Research question and objectives: The purpose of this study was to

- assess drug utilization patterns for lasmiditan prescriptions over a period of up to 3 years after market availability to identify potential patterns of drug misuse or abuse
- identify patients treated for longer than 1 year and describe treatment patterns
- assess off-label treatment with lasmiditan among paediatric and adolescent patients with migraine, and
- describe characteristics of lasmiditan-treated patients, including patients treated beyond 1 year.

Study design: A cohort study using a US electronic claims database to assess drug utilization patterns. The potential for abuse and misuse was assessed by evaluating prescription refill behaviours during the study period from January 2020 through December 2022. Treatment patterns were described and, where possible, diagnosis information was used to confirm indication for use.

Setting: Subjects and study size, including dropouts: The available number of lasmiditan-exposed patients was determined by uptake of lasmiditan in the US. No minimum sample size is described, because this study consists solely of summaries of use in the US.

Subjects and study size, including dropouts

This analysis identified 8 patients age 15 to 17 years and 941 adults age 18 to 81 years. This population was identified using the IBM® MarketScan® database from 01 January 2020 through 30 June 2022.

Variables and data sources: Demographic characteristics including age, gender, and geographic region. Clinical characteristics including migraine diagnosis and comorbid conditions at baseline and during the follow-up period, concomitant medications at baseline and during the follow-up period, lasmiditan prescription frequency, dose, and prescriber and pharmacy information. The IBM MarketScan databases capture longitudinal, individual-level administrative claims data from the US. Patients in the databases are active employees, dependents, retirees, Consolidated Omnibus Budget Reconciliation Act (COBRA) recipients, and Medicare or Medicaid enrolees. Data were drawn from large employers, health plans, and public organizations in the US.

Results

This analysis identified 8 patients younger than 18 years old and 941 adult patients aged 18 years and older with at least 1 filled prescription for lasmiditan from 01 January 2020 through 30 June 2022. The majority of patients were female gender (88%), and the mean length of therapy was approximately 200 days for the paediatric population and approximately 290 days among adults. Over 25% of patients had concomitant prescriptions for other migraine medications. In addition, the majority of adult patients with migraine diagnosis codes had codes for chronic migraine. Approximately 20% (189) of adults had an instance of 2 or more filled prescriptions of lasmiditan in a 30-day period and 129 (68%) of these patients have a diagnosis of chronic migraine during the study period.

Discussion

The findings from this study show that among approximately 950 patients, lasmiditan prescriptions are filled on a monthly basis rather than 1 to 2 per 6 months. This pattern alone does not indicate misuse, as individuals who have multiple migraine headache attacks per month (for example, many patients with episodic migraine experience 4 to 14 migraine headache days per month, and those with chronic migraine, by definition, experience 15 or more migraine headache days per month) may choose to use lasmiditan to treat those attacks accordingly. A large portion of adult patients treated with lasmiditan are managing chronic migraine (n=537), which results in a need for more frequent use of lasmiditan to treat acute migraine headache attacks in those patients.

Conclusion

This claims-based, retrospective, observational study summarizes data available on the real-world use patterns among patients treated with lasmiditan, including identification of potential patterns of lasmiditan misuse or abuse. The results describe utilization patterns in the US for patients treated with lasmiditan in routine clinical practice using IBM MarketScan commercial administrative claims data. Utilization of lasmiditan to treat patients with migraine is low (N=941 adults, N=8 adolescents). One of the study objectives was to apply a misuse algorithm adopted from opioid abuse models. Although approximately 20% of patients met the criteria for possible misuse based on the algorithm applied, upon further investigation it was discovered that the type of patient using lasmiditan and the treatment use pattern differed from what was initially assumed. The assumption was that patients would be treated with lasmiditan on a periodic (and infrequent) basis, where in fact patients, whom the majority have a diagnosis of chronic migraine, are being treated on a routine basis. Additional analyses were conducted to understand treatment patterns among the lasmiditan-treated cohort by identifying the frequency of lasmiditan prescription fills in a 30-day period. This additional analysis shows that the majority of patients with 2 or more prescription fills in a 30-day period have a diagnosis of chronic migraine. Chronic migraine patients experience migraine 15 or more days within a 30-day period and, therefore, a lasmiditan prescription that contains 8 tablets (the package quantity) would require a refill to meet migraine management needs. The data do not suggest misuse among

patients treated with lasmiditan, as patients with monthly filled prescriptions also show routine visits with healthcare professionals and the majority also have a diagnosis of chronic migraine.

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2. List of Abbreviations

Term	Definition
CCAE	Commercial Claims and Encounters
CGRP	calcitonin gene-related peptide
COBRA	Consolidated Omnibus Budget Reconciliation Act
ICD-10-CM	International Classification of Disease, 10th revision
ICHD-3	International Classification of Headache Disorders 3
MDCR	Medicare Supplemental and Coordination of Benefits
NDC	National Drug Code
SAE	serious adverse event
SAR	serious adverse reaction

3. Investigators

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4. Other Responsible Parties

Not applicable.

5. Milestones

Milestone	Planned Date	Actual Date	Comments
Start of data collection*	31December 2021	22 May 2023	None
End of data collection	31 December 2022	20 June 2023	None
Registration in the EU PAS register	28 January 2022	16 March 2023	None
Final report of study results	31 December 2023	See Page 1	None

Abbreviation: EU PAS = European Union Post-Authorisation Studies.

* Date data was first extracted.

6. Rationale and Background

Migraine is the second leading cause of disability in the world, with an estimated 1.04 billion individuals with the disease in 2016 (Stovner et al. 2018). It is a recurrent neurological headache disorder characterized by painful attacks lasting 4 to 72 hours often accompanied by other symptoms, including nausea, vomiting, sensitivity to light and sound, and changes in vision (Katsarava et al. 2012). The clinical symptoms and headache attack frequency vary along a continuum from episodic migraine to chronic migraine. Migraine occurs more frequently in females (18%) than in males (6%) (Chandler et al. 2021).

Episodic migraine is characterized by no more than 14 headache days per month. In recently conducted clinical trials investigating the use of CGRP-targeted monoclonal antibodies and small molecule CGRP antagonists (gepants) for the preventive treatment of migraine, episodic migraine was defined as patients with 4 to 14 migraine headache days per month.

Chronic migraine is characterized by 15 or more headache days per month for 3 or more months, of which 8 or more days meet the criteria for migraine without aura and/or respond to migraine specific treatment (Oleson 2018, Katsarava et al. 2012) and is much less common than episodic migraine (Lipton et al. 2007; Buse et al. 2012). Migraine is 2 to 3 times more prevalent in women than in men (Vetvik and McGregor 2017), and its prevalence peaks in the middle of life in both sexes (Stovner et al. 2018). Migraine has been consistently associated with increased risk of ischemic stroke and myocardial infarction, with a significantly higher risk among patients who had migraine with aura versus without and among women compared with men (Schurks et al. 2009; Mahmoud et al. 2018). The majority of patients with migraine use acute treatments such as triptans or nonsteroidal anti-inflammatory drugs for migraine attacks.

Results from a human abuse potential study showed statistically significantly higher drug liking among patients using lasmiditan compared with placebo (Lasmiditan package insert, 2021). However, lasmiditan has not been found to produce physical dependence based on results of studies in healthy subjects showing a lack of withdrawal symptom observed in healthy subjects (Lasmiditan package insert, 2021). In addition, treatment with lasmiditan in the paediatric population was not studied in clinical trials.

Administrative claims data contain information on millions of patients, including patients with migraine, and reflect routine clinical practice with diagnoses and procedures, outpatient prescription drug use, outpatient laboratory test result data, as well as health care utilization. These data include patients who may not be referred to or choose to participate in clinical trials and can be readily used to investigate potential safety signals. To fill the knowledge gap of the clinical trials, this observational study using claims data to evaluate the drug utilization prescription patterns of patients treated with lasmiditan in real-world routine practice in the US.

Lasmiditan was approved in the US in October 2019 by the FDA for the acute treatment of migraine with or without aura in adults. There is limited information on the real-world use of lasmiditan for the acute treatment of migraine. This is a claims-based, retrospective, observational study to assess real-world drug utilization patterns, including identification of potential patterns of lasmiditan misuse or abuse.

7. Research Question and Objectives

This study aimed to describe utilization patterns in the US for patients treated with lasmiditan in routine clinical practice using administrative claims data.

The primary objectives of this study are to:

- describe real-world utilization of lasmiditan using prescription data over a period of 3 years after market availability to identify potential patterns of drug misuse or abuse
- identify patients treated for longer than 1 year and describe treatment patterns
- assess off-label treatment with lasmiditan among paediatric and adolescent patients with migraine, and
- describe characteristics of lasmiditan-treated patients, including patients treated beyond 1year.

8. Amendments and Updates

Not applicable.

9. Research Methods

9.1. Study Design

This is a retrospective cohort database study evaluating real-world utilization patterns among patients treated with lasmiditan in the US using IBM MarketScan commercial administrative claims. This study describes real-world utilization patterns for patients treated with lasmiditan and patient characteristics including demographics, comorbidities, and concomitant medication use.

9.2. Setting

The study was conducted using US administrative claims data from the IBM MarketScan database over a period of 36 months, from 01 January 2020 through 31 December 2022. Filled prescriptions patterns were described for patients treated with lasmiditan identified over a period of 30 months in the US from 01 January 2020 through 30 June 2022. Data for patients with at least 1 filled prescription of lasmiditan were eligible for inclusion and indexed on the first prescription date.

9.3. Subjects

9.3.1. Lasmiditan Cohort

The study population includes all available patients who met the following criteria.

Inclusion criteria

- at least 1 NDC claim for lasmiditan, between 31 January 2020 and 30 June 2022
- continuous medical and pharmacy coverage for at least 365 days before the index date (baseline period) to assess preindex migraine characteristics and comorbidities
- at least 180 days continuous medical and pharmacy coverage after the index date, and
- a diagnosis of migraine, within 365 days prior to index.

Exclusion criteria

None.

9.3.2. Special Populations of Interest

Lasmiditan is a serotonin 5-hydroxytryptamine 1F receptor agonist indicated for the acute treatment of migraine with or without aura in adults. This study also describes real-world utilization among patients younger than 18 years old. This paediatric cohort was defined as patients younger than 18 years of age for at least 90 days after the index date.

Limited information is available for patients treated long-term with lasmiditan for longer than 1 year. This study describes demographics, clinical characteristics, and prescription patterns for patients with refills beyond 12 months after the index date.

9.4. Variables

9.4.1. Demographics

Patient demographic characteristics were assessed at index and include age, gender, and geographic region (using US census regions) (Table B005.9.1).

Table B005.9.1. Demographic Characteristics

Age (years)	Age at first prescription represented in age categories: <18 18-29 30-49 50 and older
Gender	Male, female, unknown
US geographic region	Northeast, Southeast, West, Southwest, Midwest
Date	Month and year of lasmiditan claims

9.4.2. Drug Exposure

Patients who met the eligibility criteria were indexed on the date of the first prescription claim for lasmiditan. Prescriptions were identified using the NDC codes as listed in Table B005.9.2. The lasmiditan cohort of patients were identified using a 30-month window from January 2020 through 30 June 2022. Prescription fill patterns are described, including the date of claim, tablet count, and strength. Prescriber specialty for each lasmiditan prescription have been identified and described. Refill patterns are described, including time between prescription fills, tablet count, and strength for each claim. For misuse, a utilization-based misuse indicator has been calculated.

Table B005.9.2. Lasmiditan National Drug Code List

Code	Strength	Route	Marketed Date
0002-4312-61	50 mg	Tablet	03 March 2021
0002-4312-08	50 mg	Tablet	31 January 2020
0002-4491-08	100 mg	Tablet	31 January 2020
0002-4491-61	100 mg	Tablet	31 January 2020

9.4.3. Baseline Variables

All available data within 12 months prior to the index date were defined as the baseline period and used to identify clinical characteristics. Clinical characteristics identified during the baseline period have been described.

Clinical characteristics listed in Table B005.9.3 are described in Sections 10.2.3, 10.2.4, 10.4.1, and 10.4.2.

Table B005.9.3. Clinical Characteristics Identified during the Baseline Period

Variable	Description
Migraine diagnosis	Migraine with and without aura
Baseline comorbid conditions	All diagnoses occurring during the 12-month baseline period. The most common are reported.
Baseline concomitant medication (nonmigraine)	Concomitant medication during the observation period
Baseline concomitant medication (migraine)	Acute (triptans, gepants, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, non-NSAIDs, nonopioid analgesics, and ergotamines) and preventive (CGRP antagonists, anticonvulsants, antidepressants, antihypertensives, and botulinum toxins) medication

Abbreviation: CGRP = calcitonin gene-related peptide

9.4.4. Follow-Up Variables

The descriptive statistics include measures of the number and type of treatments identified, as well as any comorbid diagnoses during the follow-up period. These variables are outlined in Table B005.9.4.

Table B005.9.4. Variables Identified during the Follow-Up Period

Variable	Description
Prescription frequency	The number of prescription fills during the study period
Total treatment dose	Sum of the lasmiditan doses for all claims (note: excluding the last purchase)
Follow up period comorbid diagnosis	All diagnoses occurring during the follow-up period
Follow up period concomitant prescription medication	Medication claims during the follow-up period
Other acute prescription migraine treatment	Triptans, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, non-NSAIDs, nonopioid analgesics, and ergotamines
Follow up period preventive prescription treatments	Anticonvulsants, antidepressants, antihypertensives, botulinum toxins, calcitonin gene-related peptide (CGRP) monoclonal antibodies
Prescriber information	Prescribing physician
Pharmacy use	Description of the count of different pharmacies used to fill lasmiditan prescriptions
Length of therapy	Date of dispensing plus 180 days
Discontinuation	Length of therapy plus a 30-day allowable gap without a refill

Variable	Description
Treatment episode	180 days for each prescription, with an allowable 30-day gap including any prescription refills
Persistence	Length of therapy plus 30 days
Chronic use	Greater than 2 filled prescriptions within a 6-month period

9.5. Data Sources

The IBM MarketScan databases capture longitudinal, individual-level administrative claims data from the US. Patients in the databases are active employees, dependents, retirees, COBRA gap insurance recipients, and Medicare or Medicaid enrolees. Data were drawn from large employers, health plans, and public organizations in the US. The data included 3 components of MarketScan:

- Commercial Claims and Encounters (CCAE) database
- Medicare Supplemental and Coordination of Benefits (MDCR) database, and
- Medicaid Database.

The CCAE database includes over 200 million enrolees annually who are covered by employer-sponsored private health insurance. The MDCR database includes health insurance programs for people aged 65 years or older, people aged under 65 years with certain disabilities, and people of all ages with end stage renal disease (CMS 2023). This database includes the Medicare Advantage Plan and supplemental plans. The Medicaid database includes data from multiple states for medical, surgical procedures, and prescription drugs. This includes data on approximately 50 million patients (IBM [WWW]).

9.6. Bias

Not applicable for this descriptive study design.

9.7. Study Size

The available number of lasmiditan-exposed patients depends on the uptake of lasmiditan in the US. No minimum sample size is described, because this study consists solely of summaries of use in the US.

9.8. Data Transformation

Not applicable.

9.9. Statistical Methods

9.9.1. Main Summary Measures

All data are summarized using descriptive statistics. Categorical variables are presented using percentages and frequencies. Continuous variables are presented as means and medians with associated standard deviations.

9.9.2. Main Statistical Methods

Patient exposures

To understand real-world utilization, the length of therapy and prescribed dose are described where available. The count of tablets included in each dispensing of lasmiditan are described.

Any patient not receiving a refill within 180 days of the first dispensing of lasmiditan was considered discontinued. When a patient discontinued or reinitiated therapy, they were considered compliant during the period of up to 180 days. The length of therapy was estimated to include a minimum of 180 days for each prescription. If a refill occurred within the 180-day period, the end of therapy is assumed to be 180 days after the last prescription date. Findings are reported in aggregate and stratified by age group for pediatric patients (less than 18 years) and adult patients (18 years and older).

Misuse has been characterized using utilization-based misuse indicators that are commonly applied to opioids (Cochran 2017). The utilization-based misuse indicator has been calculated by coding the number of prescribers, pharmacies used, and days supplied over 6-month periods (Parente et al. 2004). The total scores for 12-month periods were calculated and patients has been placed in the following categories:

- no suspected misuse
- possible misuse, and
- probable misuse.

The utilization-based misuse indicator calculation was calculated for lasmiditan treated patients by coding number of prescribers (≤2 prescribers = 0, 3 to 4 prescribers = 1, ≥5 prescribers = 2), number of pharmacies used for medication filling (≤2 pharmacies = 0, 3 to 4 pharmacies = 1, ≥5 pharmacies = 2), days supplied (≤185 days = 0, 186 to 240 days = 1, >240 days = 2) over 6-month periods. Six-month periods were summated into 1-year periods. Total scores were divided into 3 categories: no suspected misuse (0 to 1), possible misuse (2 to 4), and probable misuse (≥5).

Treatment patterns

Persistence curves showing the percentages of patients remaining on, discontinuing, or restarting therapy in 6-month intervals. A 30-day gap (grace period) has been used when determining persistence. The persistence curves show the patients who discontinued lasmiditan, the patients that reinitiated therapy, the gap in between treatment episodes, and the duration.

Treatment episodes during the follow-up period for each patient have been reported by aggregating all prescriptions refilled with a 30-day allowable gap after a 180-day length of therapy, assumed in 180 days, in the prior prescription. The percentages of patients and number of treatment episodes are reported by age group. The mean, standard deviation, and median length of therapy for each treatment episode stratified by age group are provided. The length of therapy has been calculated by assuming a 30-day supply for each prescription in a given treatment episode. The mean, standard deviation, and median length of therapy has been reported

and stratified by age group. A distribution has been estimated with the percentage of patients with 1 or more treatment episodes over the 36-month observation period. The percentage of patients who discontinued lasmiditan and then reinitiated therapy, the gap in between, and length of therapy are described.

Patients have been excluded from the analysis if information on strength, package size, or package count is incomplete.

Descriptive analysis

Descriptive statistics, including frequencies and proportions of patient count, and demographics, such as age and gender, have been provided for each calendar year as well as for the total sample. Frequencies and proportions have been provided for population characteristics, such as common comorbidities and concomitant medication.

Utilization of lasmiditan is characterized using the following variables:

- multiple prescribers within treatment episodes
- multiple pharmacy use
- overlap of prescription fills, and
- chronic use.

9.9.3. Missing Values

Missing values have been treated as unknown.

9.9.4. Sensitivity Analyses

Not applicable.

9.9.5. Amendments to the Statistical Analysis Plan

Evaluation of treatment patterns among patients treated with lasmiditan show that the assumed treatment patterns were not correct. The initial assumption during the design of the study was that patients treated with lasmiditan would require 2 to 3 prescription fills annually and that patients would infrequently use lasmiditan to treat migraine headaches. The data, however, show that a proportion of patients are treated for frequent migraines, including patients with chronic migraine. To further understand this observation, additional analyses were conducted. Patients who filled 2 or more prescriptions in a 30-day period were identified and described. Additional stratifications for these patients included 2, 3 to 4, and 5 or more prescription fills in a 30-day period. Among these patients, the analysis identified patients with a diagnosis code for chronic migraine during the study period. In addition, dose information was described to understand the quantity of lasmiditan patients have access to.

9.10. Quality Control

All data gathering and analyses have been overseen by 2 pharmacoepidemiologists experienced in the field of register-based research. Programming for this project has been conducted by an experienced primary analyst and validated by a separate analyst (validation analyst). For all data

processing steps, the validation analyst has reviewed the program along with input and output datasets. For the analysis steps of the project, double-programming techniques to reduce the potential for programming errors have been employed.

10. Results

10.1. Participants

This study evaluated multiple characteristics among patients treated with lasmiditan using administrative claims data. Among adults with a prescription for lasmiditan in the MarketScan database from 01 January 2020 through 30 June 2022, a total of 941 adult patients were identified. Among patients younger than 18 years old, 8 patients were identified, meeting inclusion and exclusion criteria. These patients have at least 1 filled prescription for lasmiditan during the study period, were continuously enrolled for at least 1 year before the index date, and had a recorded migraine diagnosis prior to the index date.

10.2. Descriptive Data

10.2.1. Demographics Summary

Table B005.10.1. Demographic Characteristics among Lasmiditan Treated Patients Age <18 and Adults during the Period of 01 January 2020 through 31 June 2022

Variable	Categories	Age: 0-17 (N=8)	Age: 18+ (N=941)
Age at Index (years)	Mean (Std dev)	16.38 (0.7)	44.23 (11.6)
	Min-Max	15-17	18-81
Age Categories (years)	0-17, n (%)	8 (100%)	-
	18-29, n (%)	-	106 (11.3%)
	30-49, n (%)	-	504 (53.6%)
	50+, n (%)	-	331 (35.2%)
Region	Northeast Region, n (%)	1 (12.5%)	90 (9.6%)
	South Region, n (%)	4 (50%)	356 (37.8%)
	West Region, n (%)	2 (25%)	122 (13%)
	Unknown, n (%)	1 (12.5%)	157 (16.7%)
	North Central Region, n (%)	-	216 (23%)
Gender	Male, n (%)	1 (12.5%)	110 (11.7%)
	Female, n (%)	7 (87.5%)	831 (88.3%)

Abbreviations: Max = maximum; Min = minimum; N = count of patients in specified category; n = subpopulation; Std dev = standard deviation.

Among the population of patients in MarketScan with migraine, 941 adult patients were treated with lasmiditan, and 8 patients younger than 18 years old were treated with lasmiditan from 01 January 2020 through 31 June 2022. Among these patients, the mean age for the adult

population was 44 years with age range from 18 to 81 years. Among the population younger than 18 years, the mean age was 16 years with a range from 15 to 17 years old as a result, these patients will be described as adolescents rather than pediatric patients. The majority of patients treated are female gender (approximately 88%) and live in the southern US.

10.2.2. Utilization Information

Table B005.10.2. Prescription Patterns for Lasmiditan Treated Patients Age <18 and Adults during the Period of 01 January 2020 through 31 June 2022 Information

Variable	Categories	Age: 0-17 (N=8)	Age: 18+ (N=941)
Prescriptions Filled	Mean (Std dev)	1.25 (0.46)	3.36 (4.03)
	Median [25%,75%]	1 [1,1.5]	2 [1,4]
	Min-Max	1-2	1-32
Total Dosage	Mean (Std dev)	800 (523.7)	2320.51 (2914)
	Median [25%,75%]	600 [400,1200]	800 [800,2800]
	Min-Max	400-1600	400-25,600
Dosage Frequency – 50 mg	% population	50%	34%
Dosage Frequency – 100 mg	% population	50%	73%

Abbreviations: Max = maximum; Min = minimum; N = count of patients in specified category;; Std dev = standard deviation.

Among the adolescent patients treated with lasmiditan, patients filled approximately 1 prescription on average during the January 2020 through June 2022. The mean summed dosage during the study period was 800 mg (see Table B005.10.2). Half of all prescriptions among the adolescent population were for the 50-mg dose, and half were for the 100-mg dose. Among the adult population, patients filled 3 prescriptions on average with a maximum fill of 32 prescriptions. Among adults, 73% of the filled prescriptions were for the 100-mg dose and 34% were for the 50-mg dose.

Table B005.10.3. Treatment Duration for Lasmiditan Treated Patients Age <18 and Adults during the Period of 01 January 2020 through 31 June 2022 Information

Variable	Categories	Age: 0-17 (N=8)	Age: 18+ (N=941)
Length of Therapy (in days)	Mean (Std dev)	198.6 (39.9)	290.52 (165.1)
	Median [25%,75%)	180 [180,198.5)	208 [180,351)
	Min-Max	180-292	180-1041
Tablet Count at Index	Mean (Std dev)	8 (0.00)	8 (0.0)

Variable	Categories	Age: 0-17 (N=8)	Age: 18+ (N=941)
	Min-Max	8-8	8-8
# of Treatment Episodes	Mean (Std dev)	1 (0.0)	1 (0.0)
	Median [25%,75%]	1 [1,1]	1 [1,1]
	Min-Max	1-1	1-1
# of Treatment Episodes (Age: 0-17)	Mean (Std dev)	1 (0.0)	-
	Median [25%,75%]	1 [1,1]	-
	Min-Max	1-1	-
# of Treatment Episodes (Age: 18-29)	Mean (Std dev)	-	1 (0.0)
	Median [25%,75%]	-	1 [1,1]
	Min-Max	-	1-1
# of Treatment Episodes (Age: 30-49)	Mean (Std dev)	-	1 (0.0)
	Median [25%,75%]	-	1 [1,1]
	Min-Max	-	1-1
# of Treatment Episodes (Age: 50+)	Mean (Std dev)	-	1 (0.0)
	Median [25%,75%]	-	1 [1,1]
	Min-Max	-	1-1
Average Days between Prescriptions Filled	Mean (Std dev)	36.33 (67.71)	32.76 (42.67)
	Median [25%,75%]	0 [0,65.5]	26.11 [0,48.8]
	Min-Max	0-159.67	0-311
Chronic Use (>2 Prescriptions filled in a 6 month)	Yes	0 (0.0%)	314 (33.4%)
	Mean (Std dev)	1.25 (0.46)	2.4 (1.9)
	Median [25%,75%]	1 [1,1.5]	2 [1,3]
	Min-Max	1-2	1-13
Length of Therapy >365 days	No	8 (100%)	726 (77.2%)
	Yes	-	215 (22.9%)

Abbreviations: Max = maximum; Min = minimum; N = count of patients in specified category; Std dev = standard deviation.

Among adolescent patients treated with lasmiditan, (n=8), the average length of therapy was 198.6 days, approximately 7 months. In that time, adolescents patients filled an average of 1 prescription translating to 1 treatment episode per patient. Given the low number of prescription fills for the adolescent population, none of the adolescent patients were considered chronic users of lasmiditan, and none of these patients were treated for longer than 1 year.

Among adult patients treated with lasmiditan (n=941), the average length of therapy was 290.5 days, approximately 10 months. The average number of treatment episodes for adults was 1. The treatment episodes were estimated using a 6-month window. For every filled prescription, the assumed treatment duration was 6 months. If a patient filled greater than 1 prescription in the initial 6-month window, the treatment episode would be extended. Among the adults, these patients were either treated in one 6-month window or routinely filled prescriptions without a maximum 30-day gap. As a result, patients ongoing routine treatment, had 1 long treatment episode. A chronic user was defined as more that 2 prescriptions filled in a 6-month period. Approximately 33% of adult patients met criteria for a chronic user within the study period. Long term intermittent use was identified among 22% of adult patients.

10.2.3. Migraine Diagnoses

Table B005.10.3. Migraine and Headache Diagnoses for Lasmiditan Treated Patients Age <18 During the Period of 01 January 2020 through 31 June 2022 Information

Diagnosis Code	Description of Diagnoses Code	Baseline N = 8 n (%)	Follow-up N = 8 n (%)
G43.909	Migraine, unspecified, not intractable, without status migrainosus; Migraine NOS	6 (75%)	-
G43.009	Migraine without aura, not intractable, without status migrainosus; Migraine without aura NOS	4 (50%)	-
R51.9	Headache		4 (50%)
G43.109	Migraine with aura, not intractable, without status migrainosus; Migraine with aura NOS	3 (38%)	-
G43.709	Chronic migraine without aura, not intractable, without status migrainosus	-	2 (25%)
G43.019	Chronic migraine without aura, intractable, without status migrainosus	3 (38%)	3 (38%)

Abbreviations: N = count of patients in specified category; n = subpopulation; NOS = not otherwise specified.

Among the adolescent population, patients had a diagnosis of migraine and/or headache during the baseline period with varying frequency. Within the G43 classification, 3 codes were used to diagnose migraine: G43.909, G43.009, and G43.109. In addition, a portion of the adolescent patients had a diagnosis of chronic migraine, 3 (38%) during the baseline period and 5 (63%) during the follow up period.

Table B005.10.4. Migraine and Headache Diagnoses for Lasmiditan Treated Adult Patients during the Period of 01 January 2020 through 31 June 2022

Diagnosis Code	Description of Diagnoses Code	Baseline N = 941 n (%)	Follow-up N = 941 n (%)
G43.909	Migraine, unspecified, not intractable, without status migrainosus; Migraine NOS	464 (49%)	332 (35%)
G43.009	Migraine without aura, not intractable, without status migrainosus; Migraine without aura NOS	408 (43%)	
G43.709	Chronic migraine without aura, not intractable, without status migrainosus; Chronic migraine without aura NOS	371 (39%)	333 (35%)
G43.109	Migraine with aura, not intractable, without status migrainosus; Migraine with aura NOS	346 (37%)	-
R51.9	Headache, unspecified	-	279 (30%)
G43.719	Chronic migraine without aura, intractable, without status migrainosus	-	276 (29%)

Abbreviations: N = count of patients in specified category; n = subpopulation; NOS = not otherwise specified.

Among the adult population, similar to the adolescent patients, diagnosis codes for migraine were used with varying frequency during the baseline and follow up period. Adult patients treated with lasmiditan were also diagnosed with chronic migraine (G43.709) during the baseline (39%) and follow-up period (35%), and chronic migraine (G43.719) during the follow-up period (29%). Headache was diagnosed during the follow up period (30%).

10.2.4. Comorbid Conditions

Table B005.10.5. Nonmigraine Comorbid Conditions for Lasmiditan Treated Patients Age <18 during the Period of 01 January 2020 through 31 June 2022

Diagnosis Code	Description of Diagnoses Code	Total population N=8	
		Baseline n (%)	Follow-up n (%)
F41.9	Anxiety disorder, unspecified; Anxiety NOS	5 (63%)	-

Diagnosis Code	Description of Diagnoses Code	Total population N=8	
		Baseline n (%)	Follow-up n (%)
F32.9	Major depressive disorder, single episode, unspecified; Major depression NOS	4 (50%)	-
K59.00	Constipation, unspecified	4 (50%)	-
M25.50	M25.50 Pain in unspecified joint	3 (38%)	-
F41.1	Generalized anxiety disorder	-	3 (38%)
Z23	Encounter for immunization	-	3 (38%)
B07.8	Other viral warts	-	2 (25%)
E61.1	Iron deficiency	-	2 (25%)
F45.1	Undifferentiated somatoform disorder	-	2 (25%)

Abbreviations: N = count of patients in specified category; n = subpopulation; NOS = not otherwise specified.

The majority of adolescent patients treated with lasmiditan had a diagnosis of anxiety disorder, unspecified or anxiety disorder NOS (63%), and major depressive disorder (50%) during the baseline period. During the follow up period, 38% of patients had a diagnosis of generalized anxiety disorder, and 38% were immunized. During the follow up period, 25% of patients were diagnosed with iron deficiency, somatoform disorder, and viral warts.

Table B005.10.6. Nonmigraine Comorbid Conditions for Lasmiditan Treated Adult Patients during the Period of 01 January 2020 through 31 June 2022

Diagnosis Code	Description of Diagnoses Code	Total population N=941	
		Baseline n (%)	Follow-up n (%)
M54.2	Cervicalgia	376 (40%)	309 (33%)
Z79.899	Other long term (current) drug therapy	350 (37%)	299 (32%)
F41.9	Anxiety disorder, unspecified; Anxiety NOS	344 (37%)	265 (28%)
Z23	Encounter for immunization	322 (34%)	267 (28%)
Z00.00	Encounter for general adult medical examination without abnormal findings; Encounter for adult health check-up NOS	316 (34%)	-
Z20.822	Contact with and (suspected) exposure to COVID-19	-	288 (31%)
I10	Essential (primary) hypertension	305 (32%)	293 (31%)

Abbreviations: N = count of patients in specified category; n = subpopulation; NOS = not otherwise specified.

Approximately 37% of adults at baseline and 28% during the follow up period had a diagnosis of anxiety disorder, unspecified or anxiety disorder NOS. Approximately 30% had a diagnosis of hypertension during the baseline and follow up period. During the follow up period, approximately 30% recorded exposure to COVID-19 and approximately 30% recorded an encounter for immunization which could be related to COVID-19.

10.3. Outcome Data

Not applicable.

10.4. Main Results

Additional findings characterizing patients with a migraine diagnosis treated with lasmiditan are summarized in the tables below.

10.4.1. Concomitant Nonmigraine Medication use

Table B005.10.7. Concomitant Nonmigraine Medications among Lasmiditan Treated Patients Age <18 during the Period of 01 January 2020 through 31 June 2022

	Total population N=8	
Generic Drug Name	**Baseline n (%)**	**Follow-up n (%)**
Ondansetron	3 (38%)	4 (50%)
Buspirone Hydrochloride	-	2 (25%)
Midodrine Hydrochloride	-	2 (25%)
Tramadol Hydrochloride	-	2 (25%)
Acetazolamide	-	1 (13%)
Azithromycin	-	1 (13%)
Baclofen	-	1 (13%)
Bupropion Hydrochloride	-	1 (13%)
Omeprazole	4 (50%)	-
Prednisone	4 (50%)	-
Amoxicillin/Clavulanate Potassium	2 (25%)	-
Clindamycin Hydrochloride	2 (25%)	-
Cyclobenzaprine Hydrochloride	2 (25%)	-
Dapsone	2 (25%)	-

Generic Drug Name	Total population N=8	
	Baseline n (%)	Follow-up n (%)
Dicyclomine Hydrochloride	2 (25%)	-
Fluoxetine Hydrochloride	2 (25%)	-
Desvenlafaxine Succinate	1 (13%)	1 (13%)

Abbreviations: N = count of patients in specified category; n = subpopulation.

During the baseline period, 50% of adolescent patients were treated with omeprazole and prednisone, and approximately 38% were treated with ondansetron. The remaining treatments identified were found among 1 to 2 patients resulting in a frequency of 25% and 13%.

Table B005.10.8. Concomitant Nonmigraine Medications among Lasmiditan Treated Adult Patients during the Period of 01 January 2020 through 31 June 2022

Generic Drug Name	Adult Population N=941	
	Baseline n (%)	Follow-up n (%)
Ondansetron	382 (41%)	223 (24%)
Prednisone	343 (36%)	217 (23%)
Promethazine Hydrochloride	245 (26%)	207 (22%)
Tizanidine Hydrochloride	-	185 (20%)
Albuterol Sulfate	-	176 (19%)
Methylprednisolone	-	176 (19%)
Cyclobenzaprine Hydrochloride	234 (25%)	175 (19%)
Ondansetron Hydrochloride		175(19%)
Fluconazole	189 (20%)	161 (17%)
Venlafaxine Hydrochloride	-	102 (11%)
Albuterol Sulfate	225 (24%)	-
Tizanidine Hydrochloride	196 (21%)	-
Azithromycin	189 (20%)	-
Influenza Virus Vaccine (Subvirion)	174 (18%)	-

Abbreviations: N = count of patients in specified category; n = subpopulation.

Nonmigraine medications identified during the baseline period among adult patients included ondansetron (41%), which was the most frequently encountered medication, followed by prednisone (36%). Additional medications include azithromycin (29%), promethazine hydrochloride (26%), cyclobenzaprine hydrochloride (25%), tizanidine hydrochloride (21%), and fluconazole (20%). During the follow up period, lower proportions of the population received prescriptions for medication overall. Some medications were identified both in the baseline and follow up period, these include ondansetron, prednisone, promethazine hydrochloride, cyclobenzaprine hydrochloride, and fluconazole.

10.4.2. Concomitant Migraine Medications

Table B005.10.9. Concomitant Migraine Medications among Lasmiditan Treated Patients Age <18 during the Period of 01 January 2020 through 31 June 2022

	Patients age <18 N=8	
Generic Drug Name	**Baseline n (%)**	**Follow up n (%)**
Acute Treatments		
Acetaminophen/Butalbital/Caffeine	2 (25%)	-
Acetaminophen/Hydrocodone Bitartrate	1 (13%)	1 (13%)
Acetaminophen/Hydrocodone Bitartrate	1 (13%)	-
Dihydroergotamine Mesylate	-	1 (13%)
Diclofenac Potassium	1 (13%)	
Meloxicam	2 (25%)	-
Naratriptan Hydrochloride	2 (25%)	-
Naratriptan Hydrochloride	2 (25%)	1 (13%)
Rizatriptan Benzoate	2 (25%)	-
Sumatriptan Succinate	2 (25%)	-
Preventive Treatments		
Candesartan Cilexetil	-	1 (13%)
Gabapentin	-	1 (13%)
Metoprolol Tartrate	-	1 (13%)
Pregabalin	-	1 (13%)
Topiramate	2(25%)	2(25%)

Abbreviations: N = count of patients in specified category; n = subpopulation.

Concomitant prescription migraine medication prescriptions among the adolescent population during the baseline period included acetaminophen/butalbital/caffeine, topiramate, sumatriptan, rizatriptan, naratriptan, and meloxicam among 25% (each) of the population. Other prescription migraine medications among the adolescent population that were prescribed less frequently (13% each) include diclofenac during the baseline period and gabapentin, metoprolol tartrate, and pregabalin during the follow-up period.

Concomitant acute migraine treatments among the adolescent population were limited. During the follow up period, 1 patient was identified as having a filled prescription for naratriptan hydrochloride, dihydroergotamine mesylate, and acetaminophen/hydrocodone bitartrate.

Table B005.10.10. Concomitant Migraine Medications among Lasmiditan Treated Adult Patients during the Period of 01 January 2020 through 31 June 2022

	Adult population N=941	
Generic Drug Name	**Baseline n (%)**	**Follow-up n (%)**
Acute Treatment		
Acetaminophen/Butalbital/Caffeine	206 (22%)	137 (15%)
Acetaminophen/Oxycodone Hydrochloride	145 (15%)	115 (12%)
Acetaminophen/Hydrocodone Bitartrate	220 (23%)	188 (20%)
Diclofenac Sodium	116 (12%)	100 (11%)
Ketorolac Tromethamine	182 (19%)	145 (15%)
Rizatriptan Benzoate	197 (21%)	95 (10%)
Sumatriptan Succinate	249 (26%)	122 (13%)
Ubrogepant	275 (29%)	228 (24%)
Preventive Medications		
Topiramate	295 (31%)	224 (24%)
Duloxetine Hydrochloride	-	137 (15%)
Erenumab-Aooe	229 (24%)	157 (17%)
Fremanezumab-Vfrm	-	151 (16%)
Galcanezumab-Gnlm	308 (33%)	274 (29%)
Gabapentin	229 (24%)	211 (22%)
Metoprolol Succinate	-	66 (7%)
Onabotulinum Toxin A	-	81 (9%)

	Adult population N=941	
Generic Drug Name	Baseline n (%)	Follow-up n (%)
Propranolol Hydrochloride	-	112 (12%)
Pregabalin	-	87 (9%)
Medications Used as Preventive or Acute		
Rimegepant	225 (24%)	224 (24%)

Abbreviations: N = count of patients in specified category; n = subpopulation .

Concomitant medication use among patients treated with lasmiditan included galcanezumab (33%), topiramate (31%), and ubrogepant (30%) during the baseline period. Additional treatments identified ranging from 20% to 30% included acetaminophen/butalbital/caffeine (22%), sumatriptan (26%), erenumab (25%), gabapentin (25%), rimegapant (24%), acetaminophen/hydrocodone bitartrate (23%), and rizatriptan (21%).

Among the adult population, acetaminophen/hydrocodone bitartrate treatment was identified among 23% of adults during the baseline period and 20% of adults during the follow up period. Among 19% of adults during the baseline period and 15% of adults during the follow up period ketorolac tromethamine was identified. Triptan treatment was identified among 10% of patients.

10.4.3. Evaluation of Possible Misuse

Table B005.10.11. Application of Algorithm for Estimating Possible Misuse

Year	Misuse Estimation for Adult Population	(N=941)
2020	Possible Misuse	194
2020	Possible misuse with diagnosis of chronic migraine*	144
2021	Possible Misuse	226
2021	Possible misuse with diagnosis of chronic migraine	160
2022	Possible Misuse	47
2022	Possible misuse with diagnosis of chronic migraine	32

Abbreviation: N = count of patients in specified category.

* International Classification of Headache Disorders (ICHD)-3 definition for chronic migraine: Patients with chronic migraine have headache occurring on 15 or more days per month for more than 3 months, and the headaches have features of migraine on at least 8 days per month.

Misuse has been characterized using utilization-based misuse indicators that are commonly applied to opioids (Cochran 2017). The utilization-based misuse indicator was calculated by coding the number of prescribers, pharmacies used, and days supplied over 6-month periods (Parente et al. 2004). The total scores for 12-month periods were calculated and patients were

placed in the categories. The utilization-based misuse indicator was calculated for lasmiditan treated patients by coding number of prescribers (≤2 prescribers = 0, 3 to 4 prescribers = 1, ≥5 prescribers = 2), number of pharmacies used for medication filling (≤2 pharmacies = 0, 3 to 4 pharmacies = 1, ≥5 pharmacies = 2), days supplied (≤185 days = 0, 186 to 240 days = 1, >240 days = 2) over 6-month periods. Six-month periods were summated into 1-year periods. Total scores were divided into 3 categories: no misuse (0 to 1), possible misuse (2 to 4), and probable misuse (≥5). For the years 2020 and 2021, approximately 200 patients' treatment patterns could be categorized as possible misuse based on the applying the specified methodology. There were challenges with applying the algorithm to evaluate misuse in the population treated with lasmiditan. The algorithm required identification of prescribers of the medication of interest. Although this variable is available in the database, the values are sparsely populated. As a result, providers with visit codes within 3 days were used as an alternative to the prescriber variable, to assess the possibility of multiple providers. In addition, the code identifying unique pharmacies were sparsely populated, so assumptions were made to attempt to identify prescriptions filled at different pharmacies.

Table B005.10.12. Additional Assessment of Possible Misuse. Evaluation of Prescription Frequency for a 30-day Period

	Age: 18+					
	Total Population			Chronic Migraine Population		
30-day Prescription Frequency	N=941 n (%)	Mean Dose Mean (Std dev)	n (%) (>800 mg)	N=618 n (%)	Mean Dose Mean (Std dev)	n (%) (>800 mg)
All patients with 2 or more filled prescriptions in a 30-day period						
Total sample	189 (20%)	687.8 (169.1)	150 (16%)	147 (24%)	583.3 (166.7)	118 (19%)
2 filled prescriptions	189 (20%)	685.4 (170.1)	149 (16%)	147 (24%)	600.0 (200.0)	118 (19%)
3-4 filled prescriptions	8 (0.85%)	705.9 (162.6)	8 (0.85%)	6 (0.97%)	666.7 (188.6)	6 (0.97%)
5 filled prescriptions	1 (0.11%)	800.0 (0.00)	1 (0.11%)	1 (0.16%)	800.0 (0.00)	1 (0.16%)
Annual evaluations						
Year 2020: All patients with 2 or more filled prescriptions in a 30-day period						
Total sample	88(100%)	684.4 (167.6)	65 (74%)	72 (100%)	600.0 (200.0)	55 (76%)
2 filled prescriptions	88 (100%)	667.4 (173.1)	65 (74%)	72 (100%)	600.0 (200.0)	55 (76%)
3-4 filled prescriptions	4 (4.5%)	800.0 (0.00)	4 (4.5%)	4 (5.6%)	800.0 (0.00)	4 (5.6%)
5+ filled prescriptions	1 (1.1%)	800.0 (0.00)	1 (1.1%)	1 (1.4%)	800.0 (0.00)	1 (1.4%)
Year 2021: All patients with 2 or more filled prescriptions in a 30-day period						
Total sample	89 (100%)	691.0 (168.7)	74 (83%)	71 (100%)	583.3 (166.7)	59 (83%)
2 filled prescriptions	89 (100%)	699.5 (164.7)	73 (82%)	71 (100%)	600.0 (200.0)	59 (83%)
3-4 filled prescriptions	4 (4.5%)	533.3 (170.6)	4 (4.5%)	2 (2.8%)	666.7 (188.6)	2 (2.8%)

	Age: 18+					
	Total Population			Chronic Migraine Population		
30-day Prescription Frequency	N=941 n (%)	Mean Dose Mean (Std dev)	n (%) (>800 mg)	N=618 n (%)	Mean Dose Mean (Std dev)	n (%) (>800 mg)
5+ filled prescriptions	0	0	0	0	0	0
Year 2022: All patients with 2 or more filled prescriptions in a 30-day period						
Total sample	36	687.7 (176.3)	27 (75%)	24 (100%)	600.0 (200.0)	19 (79%)
2 filled prescriptions	36 (100%)	687.7 (176.3)	27 (75%)	24 (100%)	600.0 (200.0)	19 (79%)
3-4 filled prescriptions	0	0	0	0	0	0
5+ filled prescriptions	0	0	0	0	0	0

Abbreviations: N = count of patients in specified category; n = subpopulation; Std dev = standard deviation.

Additional analyses were conducted to better understand treatment patterns among the lasmiditan-treated cohort. Table B005.10.12 summarizes the proportion of patients with 2 or more prescriptions filled in a 30-day period. No adolescent patients with 2 or more prescriptions in a 30-day period were identified. Among adults (total N=941), 189 patients had 2 or more prescriptions filled within a 30-day period during the observation window. For patients with 2 or more prescriptions filled within a 30-day period during the observation window, 150 patients had total doses exceeded 800 mg within a 30-day period. For all patients with 2 or more prescriptions filled, all had an instance of 2 filled prescriptions filled within a 30-day period, 8 had an instance of 3 to 4 filled prescriptions filled within a 30-day period, and 1 had an instance of 5 filled prescriptions within a 30-day period. Among patients with 2 or more prescriptions filled in a 30-day period (n=189), the majority (approximately 68%) had a diagnosis code for chronic migraine (n=147) during the study period. ICHD-3 definition for chronic migraine: Patients with chronic migraine have headache occurring on 15 or more days per month for more than 3 months, and the headaches have features of migraine on at least 8 days per month.

When evaluating each year separately, the total sample for year 2020 included 88 patients with 2 or more filled prescriptions and approximately 82% (n=72) of these patients also had a diagnosis code for chronic migraine during the study period. For the total sample (n=88), all patients had an instance of 2 filled prescriptions during the observation window, 4 had an instance of 3 to 4 filled prescriptions, and 1 included an instance with 5 or more filled prescriptions. In year 2021, the trends were similar, where a total sample of 89 patients had an instance of 2 prescription fills, 4 had an instance of 3 to 4 prescription fills, and none had an instance of 5 or more prescription fills. In year 2022, a total of 36 patients had an instance of 2 filled prescriptions in a 30-day period, and no patients had an instance of 3 or more prescription fills. Among the cohort of patients with a diagnosis code of chronic migraine, 72, 71, and 24 patients had 2 or more filled prescriptions in a 30-day period during years 2020, 2021, and 2022 respectively. The count of patients with 3 or more filled prescriptions was 4, 2, and 0 for years 2020, 2021, and 2022 respectively.

10.5. Other Analyses

Not applicable

10.6. Adverse Events/Adverse Reactions

Not applicable

11. Discussion

11.1. Key Results

This study describes patient characteristics of patients treated with lasmiditan from 01 January 2020 through 30 June 2022. The study cohort included 941 adults and 8 patients younger than 18 years old had a filled prescription for lasmiditan. For adolescent patients, the age range was from 15 to 17 years, and adult ages ranged from 18 through 81 years. The majority of adults treated (54%) were age 30 to 49 and were female (88%). Among the adolescent population treated with lasmiditan, the mean count of prescriptions filled was 1.25 while among the adult population, the mean count of filled prescriptions was 3.36. Among the adult population, the count of prescriptions filled during the study period ranged from 1 to 32.

In the US, the pack size for filled prescriptions can be 8×100-mg tablets or 8×50-mg tablets. A single prescription can deliver a maximum of 800 mg (8×100-mg tablets). If a person with frequent headaches primarily uses lasmiditan to treat attacks, then 4 to 8 attacks can be managed with 1 prescription depending on the dose used/headache attack. If 4 attacks in 1 month are treated, then a refill will be required in 1 to 2 months, depending on the dose used. The maximum count of prescriptions filled among adults during the study period was 32, and the corresponding maximum length of therapy was 1041 days, which translates to 2.85 years. This would indicate approximately 1 prescription fill each month. The majority of the adolescent patients (75%) and adults (49%) treated with lasmiditan had a diagnosis code for migraine. Patients treated with lasmiditan were also diagnosed with chronic migraine, 4(50%) of adolescent patients, and 66% of adults. The most common baseline condition diagnosed among the adolescent population was anxiety disorder. Among adults, the most common conditions were cervicalgia (40%) and anxiety disorder (37%).

The concomitant medication use among the adolescent population included antibiotic and antiviral medications while among the adult population, the treatments observed in the baseline and follow up period treat symptoms that could be associated with migraine or chronic migraine. The range of patients with prescriptions for concomitant migraine medications ranged from 13% to 25% among the adolescent population and from 21 to 33% during the baseline period for adults. The most frequently prescribed among adults was galcanezumab (33%) followed by topiramate (31%). Among the adolescent population, several drugs were prescribed concomitantly during the baseline period with equal frequency.

The evaluation of misuse was adapted from an opioid based algorithm for identifying nonmedical use of lasmiditan by applying a utilization-based misuse measure. This approach evaluated prescription fill behaviours using 6-month treatment intervals. The initial assumption made during the development of this study was that patients treated with lasmiditan would not likely include patients treated for multiple migraine headaches per month or those patients with chronic migraine (who, by ICHD-3 definition, have headache occurring on 15 or more days per month for more than 3 months), and as a result, the initially presumed frequency of prescriptions would be on average 2 per year. Using this approach, an annual evaluation identified 194, 226, and 47 patients in the years 2020, 2021, and 2022 respectively that were categorized as possible

misuse. Of these patients, the majority also had a diagnosis of chronic migraine. In the year 2020, 69% of 195 patients in the possible misuse category, in 2021, 59% of 229 patients in the possible misuse category, and in 2022, and 57% of 48 patients in the possible misuse category had a chronic migraine diagnosis during the study period. Additional analyses were conducted to further evaluate the performance of the algorithm used to identify misuse/abuse. What was observed is that the majority patients treated with lasmiditan have a diagnosis of chronic migraine and that patients are treated in a more routine fashion with monthly refills. The algorithm highlighted more frequent use of lasmiditan, mainly by patients with chronic migraine, rather than misuse. The additional analysis has identified 1 person with a diagnosis of chronic migraine that has an instance of 5 or more prescription fills in a 30-day period.

11.2. Limitations

Secondary use of data studies is subject to potential limitations, as claims data are collected administratively for billing purpose and are subject to inaccuracies. It is uncertain how many patients with migraine use lasmiditan, as it is a new medication for migraine. The IBM MarketScan contains commercially insured patients, as well as patients treated using Medicare and Medicaid, thus there are limits to the generalizability of study findings to the population without third party payer coverage. Insofar as their patterns of care, and that disease incidence and prevalence may differ from that seen in our study population, results from this study may not hold true in this group. ICD-10-CM code algorithm sensitivity and specificity for the identification of comorbidities and concomitant medications can lead to misclassification (Chandler et al. 2021). Data on migraine frequency are not available; therefore, it is difficult to determine treatment frequency for lasmiditan. Also, given that lasmiditan is used as needed, the study assumed that a 30-day supply was used within 120 days.

Another very important limitation to this project is related to the estimation of misuse among patients treated with lasmiditan. The algorithm applying a misuse indicator required coding the number of prescribers and number of pharmacies filling the prescriptions. The database MarketScan includes variables for identifying prescribers along with pharmacies, by unique ID. While conducting the analysis, it was discovered that the IDs were sparsely populated for both providers and prescribers. As a result, providers with visit codes within 3 days were used as an alternative to the prescriber variable, to assess the possibility of multiple providers. In addition, the code identifying unique pharmacies were sparsely populated so assumptions were made to attempt to identify prescriptions filled at different pharmacies. To identify pharmacies, the date with the pharmacy indicator on the prescription fill date was used. These modifications result in a less precise estimation of misuse given it was not possible to identify utilization of different providers to obtain lasmiditan treatment. The results of this analysis identified approximately 200 patients as possible misuse using the original framework with less precise measures applies.

During the planning phase for this study, it was assumed that patients treated with lasmiditan would include patients who would infrequently use lasmiditan to treat migraine headaches. The algorithm chosen to evaluate misuse was applied based on an assumption that patients would only fill 2 to 3 prescriptions on an annual basis. This assumption, not reflective of what was observed, limited the utility of the misuse algorithm as real-world use of lasmiditan includes

patients with frequent migraine and patients that require monthly refills to manage their migraine. The misuse algorithm selected was not appropriate for estimating misuse among this study population. The study assumed intermittent use whereas this real-world data shows frequent refills. In addition, over 60% of patients had a diagnosis of chronic migraine, which indicates a need to manage more frequent migraines.

11.3. Interpretation

The findings from this utilization study provide a summary of use patterns among adults and adolescent patients treated with lasmiditan. Assessment of characteristics at baseline and during the follow up period provide a better understanding of patients treated with lasmiditan in the real world. From the period January 2020 through December 2022, the Marketscan database identified 941 adults and 8 adolescent patients treated with lasmiditan. The adolescent population treated included adolescents aged 15 through 17 years, and among adults, the mean age was approximately 44 years. Overall, the number of patients treated with lasmiditan in the US is low, and within this MarketScan database, the count was 949 patients. Evaluation of the misuse algorithm applied shows that the selected algorithm was not appropriate for estimating misuse among patients treated with lasmiditan. These data do not suggest misuse among patients treated with lasmiditan but instead treatment patterns that differ the expectation that patients would use lasmiditan infrequently. Patients with monthly filled prescriptions also show routine visits with healthcare professionals. In addition, the majority of patients with 2 or more prescriptions filled in a 30-day period have a diagnosis of chronic migraine, which may require the frequent use of an acute treatment such as lasmiditan to treat migraine headaches.

11.4. Generalisability

This real-world study included an evaluation of patients with filled prescriptions for lasmiditan. The study period included data from January 2020 through December 2022. The large administrative claims database, MarketScan database, and coverage of the US population allow for generalisable findings characterizing the US population that are covered by third party payers. There are limitations however if applying study findings to the population without third party payer coverage.

12. Other Information

Not applicable.

13. Conclusions

This study summarizes data available on the real-world use of lasmiditan for the acute treatment of migraine. This claims-based, retrospective, observational study assessed real-world utilization patterns for patients treated with lasmiditan, including identification of potential patterns of lasmiditan misuse or abuse. The results describe utilization patterns in the US for patients treated with lasmiditan in routine clinical practice using IBM MarketScan commercial administrative claims data. The results show that utilization of lasmiditan to treat patients with migraine is low (N=941 adults, N=8 adolescents). Among children, the age range for lasmiditan treated patients was 15 to 17 years and adults were treated from age 18 through 81 years. Treatment patterns by gender were as anticipated where the majority (>85%) were female gender. An unexpected finding was that approximately 66% patients treated with lasmiditan had a diagnosis of chronic migraine during the study period.

An algorithm for identifying opioid misuse was adapted to assess misuse among patients treated with lasmiditan. The algorithm required identification of prescribers of the medication of interest. Although this variable is available in the database, the values are sparsely populated. As a result, providers with visit codes within 3 days were used as an alternative to the prescriber variable, to assess the possibility of multiple providers. In addition, the code identifying unique pharmacies were sparsely populated so assumptions were made to attempt to identify prescriptions filled at different pharmacies.

Additional analyses were conducted to understand treatment patterns among the lasmiditan treated cohort by identifying the frequency of lasmiditan prescription fills in a 30-day period. This additional analysis shows that approximately 20% of adult patients filled 2 or more prescriptions in a 30-day period and the majority (129 out of 189) of these patients have a diagnosis of chronic migraine during the study period. Chronic migraine patients experience 15 or more days within a 30-day period and, therefore, a lasmiditan prescription that contains 8 tablets may not be sufficient to meet the patients' migraine management requirements. The findings from the misuse calculation highlight utilization patterns that differ from what was anticipated during study planning. The original expectation was that lasmiditan would be used infrequently to treat migraine and, consequently, the treated population would only require a small number of prescriptions annually. What was identified, however, is that the lasmiditan-treated population includes a high proportion of patients diagnosed with chronic migraine (66%), which require frequent treatment to address their migraine management needs. These data do not suggest misuse among patients treated with lasmiditan, but instead treatment patterns that differ from the expectation that patients would use lasmiditan infrequently.

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Annex 1. List of Standalone Documents

Not applicable.

Annex 2. Additional Information

Demographic Characteristics Stratified by Calendar Year

Variable	Categories	Age: 0-17 2020 (N=5)	Age: 0-17 2021 (N=3)	Age: 18+ 2020 (N=421)	Age: 18+ 2021 (N=386)	Age: 18+ 2022 (N=134)
Age at index	Mean (Std dev)	16.2 (0.84)	16.67 (0.58)	44.04 (11.36)	44.4 (11.79)	44.38 (12.05)
	Median [25%,75%]	16 [16,17]	17 [16,17]	44 [36,53]	45 [37,53]	45.5 [37,53]
	Min-Max	15-17	16-17	18-75	18-81	18-79
Age categories	n(%)					
	0-17 years	5 (100%)	3 (100%)			
	1829 years			46 (10.93%)	43 (11.14%)	17 (12.69%)
	30–49 years			232 (55.11%)	206 (53.37%)	66 (49.25%)
	50+ years			143 (33.97%)	137 (35.49%)	51 (38.06%)
Geographic region	n(%)					
	Northeast	1 (20%)		38 (9.03%)	35 (9.07%)	17 (12.69%)
	South	2 (40%)	2 (66.67%)	142 (33.73%)	148 (38.34%)	66 (49.25%)
	West	1 (20%)	1 (33.33%)	45 (10.69%)	56 (14.51%)	21 (15.67%)
	Unknown	1 (20%)		97 (23.04%)	60 (15.54%)	
	North Central			99 (23.52%)	87 (22.54%)	30 (22.39%)
Gender	n(%)					
	Male	1 (20%)		48 (11.4%)	49 (12.69%)	13 (9.7%)
	Female	4 (80%)	3 (100%)	373 (88.6%)	337 (87.31%)	121 (90.3%)
# Prescriptions filled	Mean (Std dev)	1.2 (0.45)	1.33 (0.58)	4.12 (5.08)	3.14 (3.07)	1.6 (0.88)
	Median [25%,75%]	1 [1,1]	1 [1,2]	2 [1,5]	2 [1,4]	1 [1,2]
	Min-Max	1-2	1-2	1-32	1-17	1-5
Total dosage	Mean (Std dev)	720 (521.5)	933.33 (611.0)	2823.75 (3688)	2195.85 (2222)	1098.51 (659.3)
	Median [25%,75%]	400 [400,800]	800 [400,1600]	1200 [800,3200]	800 [800,3200]	800 [800,1600]
	Min-Max	400-1600	400-1600	400-25,600	400-11,200	400-3600
# of tablets (at index)	Mean (Std dev)	8 (0.00)	8 (0.00)	8 (0.00)	8 (0.00)	8 (0.00)
	Median [25%,75%]	8 [8,8]	8 [8,8]	8 [8,8]	8 [8,8]	8 [8,8]
	Min-Max	8-8	8-8	8-8	8-8	8-8
Dosage frequency – 50 mg (at index)	n(%)	3 (60%)	1 (33.33%)	163 (38.72%)	113 (29.27%)	41 (30.6%)
Dosage frequency – 100 mg (at index)	n(%)	2 (40%)	2 (66.67%)	258 (61.28%)	273 (70.73%)	93 (69.4%)
Dosage frequency – 50 mg	n(%)	3 (60%)	1 (33.33%)	168 (39.9%)	114 (29.53%)	41 (30.6%)

Variable	Categories	Age: 0-17 2020 (N=5)	Age: 0-17 2021 (N=3)	Age: 18+ 2020 (N=421)	Age: 18+ 2021 (N=386)	Age: 18+ 2022 (N=134)
Dosage frequency – 100 mg	n(%)	2 (40%)	2 (66.67%)	300 (71.26%)	291 (75.39%)	95 (70.9%)
Length of therapy (in days)	Mean (Std dev)	202.4 (50.09)	192.33 (21.36)	325.43 (203.0)	281.99 (131.3)	205.41 (36.13)
	Median [25%,75%]	180 [180,180]	180 [180,217]	220 [180,402]	216.5 [180,361]	180 [180,226]
	Min-Max	180-292	180-217	180-1041	180-715	180-325
# of treatment episodes	Mean (Std dev)	1 (0.00)	1 (0.00)	1 (0.00)	1 (0.00)	1 (0.00)
	Median [25%,75%]	1 [1,1]	1 [1,1]	1 [1,1]	1 [1,1]	1 [1,1]
	Min-Max	1-1	1-1	1-1	1-1	1-1
# of treatment episodes (age: 0-17)	Mean (Std dev)	1 (0.00)	1 (0.00)			
	Median [25%,75%]	1 [1,1]	1 [1,1]			
	Min-Max	1-1	1-1			
Average days between prescriptions filled	Mean (Std dev)	31.93 (71.41)	43.67 (75.63)	37.61 (47.77)	32.34 (40.11)	18.72 (27.06)
	Median [25%,75%]	0 [0,0]	0 [0,131]	29.4 [0,54.93]	27.3 [0,48.83]	0 [0,35]
	Min-Max	0-159.67	0-131	0-311	0-209	0-145
Chronic use (>2 Prescriptions filled)	n(%)	0 (0.00%)	0 (0.00%)	160 (38%)	136 (35.23%)	18 (13.43%)
	Mean (Std dev)	1.2 (0.45)	1.33 (0.58)	2.61 (2.05)	2.45 (1.86)	1.6 (0.88)
	Median [25%,75%]	1 [1,1]	1 [1,2]	2 [1,4]	2 [1,3]	1 [1,2]
	Min-Max	1-2	1-2	1-13	1-10	1-5
Length of therapy >365 days	n(%)	0 (0.00%)	0 (0.00%)	122 (28.98%)	93 (24.09%)	0 (0.00%)
# of treatment episodes (age: 18-29)	Mean (Std dev)			1 (0.00)	1 (0.00)	1 (0.00)
	Median [25%,75%]			1 [1,1]	1 [1,1]	1 [1,1]
	Min-Max			1-1	1-1	1-1
# of treatment episodes (age: 30-49)	Mean (Std dev)			1 (0.00)	1 (0.00)	1 (0.00)
	Median [25%,75%]			1 [1,1]	1 [1,1]	1 [1,1]
	Min-Max			1-1	1-1	1-1
# of treatment episodes (age: 50+)	Mean (Std dev)			1 (0.00)	1 (0.00)	1 (0.00)
	Median [25%,75%]			1 [1,1]	1 [1,1]	1 [1,1]
	Min-Max			1-1	1-1	1-1

Abbreviations: Max = maximum; Min = minimum; N = count of patients in specified category; n = subpopulation; Std dev = standard deviation.