Budget impact of lasmiditan for the acute treatment of migraine in the United States

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What is already known about this subject

- In 2019 and 2020, the FDA approved 3 novel acute treatments for migraine—lasmiditan, rimegepant, and ubrogepant—for adults with migraine with and without aura.
- Unlike triptans, these treatments are not contraindicated in patients with cardiovascular conditions.
- These medications represent an increase in cost of treatment above that of generic oral triptans.

What this study adds

- This study performed a detailed analysis of potential budget impact of the novel acute treatments for migraine based on US prices and details of usage from the respective US labels.
- Costs in the broad population indicated in the US label were compared with a narrower population recommended in an American Headache Society consensus statement.
- The study also compares the budget implications of benefit designs requiring previous steps through 1 vs 2 oral triptans.

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J Manag Care Spec Pharm.
2021;27(12):1714-23

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ABSTRACT

BACKGROUND: Three novel acute treatments for migraine—lasmiditan, ubrogepant, and rimegepant—were approved by the FDA in 2019 and 2020 for adults with migraine with and without aura. American Headache Society guidance recommends that these novel acute treatments be considered for patients who are contraindicated to or fail to respond or tolerate oral triptans, the current standard of acute care.

OBJECTIVE: To estimate, from a US commercial plan perspective, the budget impact of adding lasmiditan as an option to a formulary that already includes ubrogepant and rimegepant.

METHODS: Epidemiologic data were drawn from US Census data, the American Migraine Prevalence and Preventive study, and the first wave of the OVERCOME US survey, a web-based survey that included 21,000 patients

with migraine. A model with a 3-year time horizon was built assuming that demand for the novel acute treatments would not vary based on whether lasmiditan is included in the formulary. The model examined a variety of populations, in particular beneficiaries with previous use of 1 or more oral triptans or contraindicated to triptans and beneficiaries with previous use of 2 or more oral triptans or contraindicated to triptans. Primary outcomes were the incremental differences in total cost and average cost per member per month (PMPM) between scenarios with and without lasmiditan. One-way sensitivity analyses with model parameters that were varied by plus or minus 15% were conducted to assess the effect of key parameters on the incremental total cost over 3 years.

RESULTS: The addition of lasmiditan to a formulary that already includes ubrogepant and rimegepant resulted in a total savings of \$927,657 (–1.5% compared with the scenario without lasmiditan) over a 3-year

time horizon in the population with previous history of using 1 or more oral triptans or contraindicated to a triptan. In the population with previous history of using 2 or more oral triptans or contraindicated, the addition of lasmiditan resulted in a total budget impact of –\$466,518 (–1.3%) over a 3-year time horizon. Most of the cost savings was attributable to reductions in drug acquisition cost. Savings in total costs resulted in average incremental cost per PMPM of –0.03 and –\$0.01, respectively.

CONCLUSIONS: The addition of lasmiditan to the formulary as a novel acute treatment option for migraine alongside ubrogepant and rimegepant resulted in lower budget impact on a 3-year time horizon from a US commercial payer's perspective. This result is important to US commercial payers as they seek to incorporate the emerging novel acute treatments for migraine into their benefit designs.

Migraine is a chronic neurologic disease typically characterized by moderate or severe throbbing headache pain; is often associated with photophobia and phonophobia, nausea, and/or vomiting; and can be exacerbated by physical activity.¹ Migraine may be preceded by aura, a preliminary symptom manifesting as visual, sensory, or other central nervous system symptoms that are then followed by primary migraine symptoms.¹ It is estimated that migraine affects 11.6% of the global population.² The prevalence of migraine is significantly higher in women than in men (13.8% vs 6.9%, respectively).² In the United States alone, migraine affects roughly 1 in 7 adults, 1 in 4 households, and more than 36 million individuals.^{1,3-6}

Migraine is associated with high levels of humanistic and economic burden in terms of reduced health-related quality of life and increased medical costs (direct and indirect).⁷ Annual direct health care expenditures associated with migraine in the United States are estimated at \$56.31 billion,⁸ and the annual indirect costs (ie, lost productivity, absenteeism, and short-term disability) can range widely from \$943 per person for episodic and \$3,300 for chronic migraine.^{9,10}

A goal of acute treatment of migraine is to alleviate attacks rapidly and consistently without recurrence and to minimize the use of rescue medications.¹¹ Current pharmacotherapies recommended by the American Academy of Neurology and the American Headache Society (AHS) include analgesics, ergots, nonsteroidal anti-inflammatory drugs, opioids (butorphanol nasal spray 1 mg), and triptans.¹² The American Migraine Prevalence and Prevention (AMPP) study found that 41% of patients treated for episodic migraine had at least 1 unmet treatment need from among treatment dissatisfaction, moderate or severe migraine-related disability, excessive use of opioids or barbiturates, recurrent use of emergency department, or a history of cardiovascular events indicating a possible contradiction to triptan use.¹³ While triptans are efficacious for the acute treatment of migraine, up to 40% of attacks (and 30% of patients) fail to respond to a particular triptan.^{14,15} Triptans are also associated with peripheral vasoconstriction due to effects mediated by activation of (5HT) 1B receptors and are, therefore, contraindicated in people with cardiovascular risks.

Three novel compounds have been approved by the US Food and Drug Administration in the past year for the acute treatment of migraine with and without aura in adults. The AHS position statement recommends consideration of these emerging novel acute treatments for patients who have contraindications to the use of triptans or failed to respond to or tolerate oral triptans, as determined

by either a validated patient-reported outcome questionnaire (such as the Migraine Treatment Optimization Questionnaire [mTOQ] or other instrument) or health care provider attestation.¹⁶ Lasmiditan, the first oral selective serotonin (5HT) 1F receptor agonist, was approved in October 2019.¹⁷ Ubrogapant and rimegepant, both oral calcitonin gene-related peptide (CGRP) receptor antagonists, received approval in December 2019 and February 2020, respectively.^{18,19} The near simultaneous approval of these medications complicates budget impact modeling, since in practice, plans may consider a variety of subsets of the 3 medications for their formularies.

For simplicity, we compared scenarios that partitioned based on the 2 mechanistic classes of drugs: selective serotonin (5HT) 1F receptor agonist and oral CGRP receptor agonists. We did not distinguish uptake or usage between the 2 oral CGRP receptor agonists other than with respect to potential second doses, which are excluded from the US label for rimegepant but permitted for ubrogapant.

This study aimed to estimate the budget impact of adopting lasmiditan alongside the other novel acute treatments ubrogapant and rimegepant from a third-party commercial payer perspective in the United States.

Methods

MODEL OVERVIEW

A decision-analytic economic model was developed to evaluate the costs of including lasmiditan as an acute treatment option for adults with migraine in the United States. For convenience in adapting results to various actual plan sizes, the displayed model calculated the number of patients who are eligible to receive novel acute treatments within a hypothetical plan with 1 million members. Patients were allocated to different treatment options each year based on the estimated market share data. Market share for other treatment options decreased with a corresponding uptake in market share of novel acute treatments. The overall cost of the market mix was calculated based on the drug unit costs and administration costs (when applicable) for each treatment, as well as the treatment's dosing regimen and annual frequency of use.

A scenario that reflected current and new treatments in the market without lasmiditan was compared with one that included lasmiditan. Growth in total market share for the novel acute treatments was assumed to remain the same in both scenarios whether or not lasmiditan was included on formulary. The budget impact to a payer was the difference in projected expenditures between the 2 scenarios.

FIGURE 1 Size of Eligible Target Population

^a“Low mTOQ score” refers to a score of less than 6.
mTOQ=Migraine Treatment Optimization Questionnaire.

The model framework was developed from the perspective of a third-party commercial payer in the United States over a time horizon of 3 years. Primary outcomes were average cost per member per month (PMPM), total cumulative 3-year cost, cost per treated member per month, and the

incremental difference between those outcomes in the scenario with and without lasmiditan.

The model was developed in accordance with guidelines and recommendations from the Academy of Managed Care Pharmacy and the International Society for

Pharmacoeconomics and Outcomes Research.^{20,21}

DATA INPUTS

Population. Published epidemiological data were used to estimate the number of adults with migraine in the United States,²²⁻²⁴ accounting for annual population growth over 3 years. The size of the target population was obtained by estimating the percentage of adults with migraine who were eligible for the emerging novel acute treatments using the first cohort of OVERCOME US, a recent web-based survey.²⁵ Baseline data for the initial OVERCOME US cross-sectional survey were collected from September to November 2018 using a phased approach. First, a representative sample of respondents of the US population was sought using 5 commercial consumer panels. Inclusion criteria were (1) aged 18 years or older, (2) US resident, (3) online survey panel member, (4) internet access, (5) ability to read and write English, and (6) ability to provide electronic informed consent. Sample performance was monitored daily vs quota targets.

The sample of respondents (N=97,478) reflected the US marginal distribution of geography (Northeast, Midwest, South, and West); age (18-34, 35-44, 45-54, 55-64, and 65+ years); and race (American Indian/Alaska native, Asian/Asian American/Native Hawaiian/Asian or Pacific Islander, Black/African American, White/Caucasian, and other), each nested in sex. OVERCOME US included 21,000 patients that met the criteria for migraine based on a validated American Migraine Study/AMPP migraine diagnostic screener or a self-report of migraine diagnosis by a health care professional.

The study considered 4 alternative criteria for the target populations for treatment (Figure 1). These criteria

TABLE 1 Market Share Inputs as a Percentage of Target Population Over 3 Years and Non-Novel Acute Treatment at Baseline

	Population 1 Previous history of 1 or more oral triptan or contraindicated to triptans	Population 2 Previous history of 2 or more oral triptans or contraindicated to triptans
Novel treatments market uptake^a		
Year 1	2.6%	1.9%
Year 2	4.7%	3.5%
Year 3	8.0%	5.9%
Percentage of patients on non-novel treatment at baseline^b		
Oral triptans	40.8%	37.3%
Non-oral triptans	29.4%	25.7%
Ergots	7.6%	9.2%
Prescription NSAIDs	25.8%	27.3%
Opioids	31.7%	33.5%
Barbiturates	15.3%	16.8%
Antiemetics	3.8%	4.7%
Antihistamines	5.2%	5.5%

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probed eligibility requirements derived from the AHS position statement regarding use of the novel acute treatments comparing 1 vs 2 steps through oral triptans, as well as a comparison with a narrower subset of patients who are currently on an oral triptan but doing “poor” or “very poorly” on their current acute treatment (mTOQ score <6).

- Benefit-eligible populations
 - Population 1: previous history of using 1 or more oral triptan or contraindicated to triptans.
 - Population 2: previous history of using 2 or more oral triptans or contraindicated to triptans.
- “Most likely to use” populations
 - Population 3: currently on oral triptan but with mTOQ <6.
 - Population 4: currently on second or later oral triptan but with mTOQ <6.

The mTOQ-6 is a validated patient-reported questionnaire that focuses on how often over the past 3 months patients achieved treatment success in various domains: return to normal function, 2-hour pain freedom, sustained 24-pain relief, tolerability, comfort in being able to make plans, and perceived control. Since it was not anticipated that plans would have access to data such as mTOQ-6, this

questionnaire was relevant to establishing the size of the population that fails to tolerate or receive adequate efficacy from current treatment. As such, the patients identified by using mTOQ-6 give insight on the size of the population that may be prescribed and submit claims for the novel acute treatments.²⁶ Contraindications to oral triptans were based on medical history reported in OVERCOME US.²⁵

Treatment Options. The market size of novel acute treatments for population 1 (previous history of using 1 or more oral triptans or contraindicated to triptans) was drawn from a hypothetical forecast scenario, whereas for population 2 (previous history of using 2 or more oral triptans or contraindicated to triptans), market size was estimated to be approximately 50% of that for population 1. For the narrower populations (but thought to be the most likely to use), the market size for population 3 was assumed to be about 90% of that for population 1, and for population 4, about 90% of that for population 2. The adoption of the novel agents within the plan was assumed to be independent of the number and mix of novel agents (lasmiditan, rimegepant, and ubrogepant) included in the formulary. Baseline market shares of the non-novel treatments were informed by the OVERCOME US survey (Table 1).

The distribution of market share among the 3 novel acute treatments was hypothetical based on preapproval market research estimates. In the scenario without lasmiditan, it was assumed that 50% were treated with ubrogepant and 50% were treated with rimegepant. When lasmiditan was included, the distribution was assumed to be 40%, 30%, and 30% for lasmiditan, ubrogepant, and rimegepant, respectively. Lasmiditan and ubrogepant are approved for use at more than 1 dose. The distribution over the 3 doses of lasmiditan was assumed to be 20%, 60%, and 20% for the 50 mg, 100 mg, and 200 mg doses, respectively. The distributions were assumed to remain constant over the 3-year time horizon.

Costs. The model was built from a US commercial payer perspective and considered only drug acquisition and administration costs. Indirect costs were not considered. Drug acquisition costs were based on wholesale acquisition costs obtained from Micromedex RED BOOK Online (October 2019 for non-novel treatments and March 2020 for novel treatments).²⁷ Drug dosing and frequency were obtained from the prescribing information for each product, while the annual dosing frequency measured by the number of single-treatment doses per patient per year was informed by the MarketScan Commercial Claims and Encounters database, based on historical triptan data.²⁸

TABLE 1 Market Share Inputs as a Percentage of Target Population Over 3 Years and Non-Novel Acute Treatment at Baseline (continued)

	Population 3 Currently on oral triptan but with low mTOQ score	Population 4 Currently on second or later oral triptan but with low mTOQ score
Novel treatments market uptake^a		
Year 1	7.1%	8.2%
Year 2	13.1%	15.2%
Year 3	22.1%	25.7%
Percentage of patients on non-novel treatment at baseline^b		
Oral triptans	107.1%	107.2%
Non-oral triptans	69.4%	63.4%
Ergots	11.3%	19.5%
Prescription NSAIDs	49.9%	57.2%
Opioids	56.8%	61.3%
Barbiturates	29.6%	39.3%
Antiemetics	8.2%	12.1%
Antihistamines	10.1%	11.4%

^aThese percentages for market uptake should yield numbers of patients taking novel therapies that follow these rationales: (1) number of beneficiaries using novel acute treatments among those with previous history of using 1 or more oral triptan or contraindicated is drawn from a market forecast scenario; (2) number of beneficiaries using novel acute treatments among those with previous history of using 2 or more oral triptans or contraindicated is approximately 50% of scenario 1; (3) number of beneficiaries using novel acute treatments among those currently on oral triptan but with low mTOQ represents about 90% of scenario 1; and (4) number of beneficiaries using novel acute treatments among those currently on second or later oral triptan but with low mTOQ represents about 90% of scenario 2.

^bGiven that a single patient can receive multiple treatments over the course of a year, the total patient treatment share in the model exceeds 100%.

mTOQ=Migraine Treatment Optimization Questionnaire; NSAID=nonsteroidal anti-inflammatory drug.

Based on analysis of insurance claims data for triptans, the annual number of treated migraine episodes was estimated to be 27. The annual dosing frequency of novel acute treatments to treat the 27 episodes varied depending on the assumed use of rescue dosing. Almost 40% of ubrogepant patients in the phase 3 clinical studies used a rescue dose,^{29,30} and 45%–48% used a rescue dose in the longer-term open label follow-up study.³¹ The model reflected this in the annual dosing frequency of ubrogepant. Conversely, labeled usage of lasmiditan and rimegepant precluded use of a second dose,^{17,19} and their annual dosing frequency equaled 27 (Table 2). The 200 mg dose of lasmiditan is

available only as two 100 mg pills.¹⁷ The cost per episode for lasmiditan 200 mg was, therefore, taken as 2 times the cost per episode of 100 mg of lasmiditan. The 50 mg and 100 mg doses of lasmiditan were priced the same on a per pill basis, as were the 50 mg and 100 mg doses of ubrogepant.²⁷

ANALYSIS

We used the presented input values to calculate the annual and 3-year total costs for the 4 target populations, as well as the PMPM cost for the markets with and without lasmiditan. One-way sensitivity analyses were conducted to assess the effect of key parameters on the total cost impact in 3 years. Model parameters varied by plus or minus 15% to assess uncertainty in model parameters and key model drivers. While plus or minus 15% may not precisely cover the plausible range of each parameter, the variation does provide directional and approximate estimates of relative magnitude of impact.

Results

BASE-CASE ANALYSES

The addition of lasmiditan to a formulary alongside the other 2 novel acute agents ubrogepant and rimegepant resulted in a total savings over a 3-year time horizon of −\$927,657 (−1.5%) in Population 1 (previous history of using 1 or more oral triptan or contraindicated to a triptan) and −\$830,796 (−1.8%) in population 3 (currently on an oral triptan but with a mTOQ<6). In population 2 (previous history of using 2 or more oral triptans or contraindicated), the addition of lasmiditan resulted in a total budget impact of −\$466,518 (−1.3%); whereas in population 4 (currently using a second or later oral triptan but with mTOQ<6), the savings were −\$415,601 (−2.0%) over a 3-year time horizon (Table 3). Most of the cost savings was attributable to reductions in drug acquisition cost. Savings in total costs resulted in average incremental cost PMPM of −\$0.01 to −0.03 in the 4 target population groups. Detailed results may be found in [Supplementary Table 1](#) (available in online article).

SENSITIVITY ANALYSES

Sensitivity analyses of the 4 target population groups were consistent (Figure 2). They suggested that drug acquisition costs of novel acute treatments, annual treated migraine episodes, and the uptake of novel treatments are key cost drivers. In addition, none of the tornado diagram bars crossed the line to positive incremental costs triggered by the introduction of lasmiditan to the formulary.

TABLE 2 Drug Acquisition and Administration Costs and Dosing Frequency

Treatments	Dosing	Acquisition cost per unit ^a	Annual dosing frequency	Annual cost, \$
Novel treatments				
Lasmiditan	20% on 50 mg 60% on 100 mg 20% on 200 mg	\$80 per pill (50 or 100 mg, 200 mg dose = 2 × 100 mg pills)	32.4 (= 27 × 20% + 27 × 60% + 54 × 20%)	2,592
Ubrogepant	25% on 50 mg 75% on 100 mg	\$85 per pill (50 or 100 mg)	38 (= 27 × 1.4) Assume 40% of patients using second dose as a rescue medication ^b	3,230
Rimegepant	100% on 75 mg ODT	\$106.25 per pill	27	2,869
Non-novel treatment class				
Oral triptans	Single-agent oral triptans	\$3.72	26	96.79
	Sumatriptan/naproxen	\$26.96	36	970.63
Non-oral triptans	Zolmitriptan (nasal)	\$80.94	18	1,456.92
	Sumatriptan (nasal)	\$49.96	16	799.29
	Sumatriptan (SC)	\$57.22	6	343.35
Ergots	Dihydroergotamine (nasal)	\$210.46	8	1,683.71
	Other ergotamine	\$12.45	36	448.09
Prescription NSAIDs	Diclofenac and others	\$0.80	57	45.74
Opioids	Butorphanol (nasal)	\$7.25	21	152.18
	Other opioids and combinations	\$1.21	37	44.68
Barbiturates	Butalbital and combinations	\$2.60	60	155.92
Antiemetics	Metoclopramide	\$0.35	30	10.40
	Prochlorperazine	\$0.70	30	21.09
Antihistamines	Promethazine	\$0.47	30	14.12
SC administration cost^c				
SC injection for sumatriptan		\$29.67	6	178.02

^aWholesale acquisition cost considering 98% generic use if available; accessed October 2019 for non-novels and February 2020 for novels.²⁷

^bA second dose of ubrogepant 50 mg and 100 mg was taken by 39.48% (184/466) and 40.82% (198/485) of patients, respectively, in the ubrogepant group from the ACHIEVE trial (ie, an average of 40% of all patients). This is reflected as an increase in the annual dosing frequency.³⁰

^cFrom InHealth Professional Services.³⁸

NSAID = nonsteroidal anti-inflammatory drug; ODT = orally disintegrating tablet; SC = subcutaneous.

DISCUSSION

The potential budget impact of the novel acute treatments has been explored by the Institute for Clinical and Economic Review (ICER).^{32,33} The target cohort used was similar to the cohorts examined here: patients for whom triptans had not been effective, were not tolerated, or were contraindicated. The ICER analysis was conducted at a US national level with results expressed as the proportion of patients that could be treated given an assumed total annual national expenditure of \$819 million and various costs per quality-adjusted

life-year derived from ICER's cost-effectiveness modeling. The estimated proportions that could be treated without exceeding the budget threshold were 12%, 16%, and 16%, respectively, for lasmiditan, ubrogepant, and rimegepant.

At the time of the ICER analysis, the wholesale acquisition cost (WAC) for rimegepant was unknown and assumed to be the same as that for ubrogepant. Our model used the actual launch WAC for rimegepant (\$106.25) per pill rather than that of ubrogepant (\$85 per pill). The ICER analysis pooled the various doses of lasmiditan and ubrogepant,

TABLE 3 Results Comparing Scenarios With and Without Lasmiditan Over 3 Years

Target population	Scenario without lasmiditan		Scenario with lasmiditan		Incremental results		
	Total cost, \$	PMPM, \$	Total cost, \$	PMPM, \$	Incremental total costs, \$	Incremental PMPM, \$	% change
Previous history of using 1 or more oral triptans or contraindicated to triptans	60,306,449	1.65	59,378,793	1.63	−927,657	−0.03	−1.5
Previous history of using 2 or more oral triptans or contraindicated to triptans	37,126,026	1.01	36,659,509	1.00	−466,518	−0.01	−1.3
Currently on oral triptan but with low mTOQ score	46,004,093	1.26	45,173,296	1.24	−830,796	−0.02	−1.8
Currently on second or later oral triptan but with low mTOQ score	21,172,170	0.58	20,756,569	0.57	−415,601	−0.01	−2.0

mTOQ=Migraine Treatment Optimization Questionnaire; PMPM=per member per month.

and as discussed further in this section, did not distinguish between the differences in label-approved usage for a second dose within a single episode of migraine.

Our model concluded that the introduction of lasmiditan alongside oral CGRP receptor antagonists as an option for the treatment of migraine with and without aura in adults resulted in a decrease in a US commercial payer's budget over a 3-year time horizon. The acquisition cost per pill difference is smaller between lasmiditan and ubrogepant (\$80 vs \$85), but this may not reflect the full drug cost/migraine attack, since a second dose of ubrogepant may be administered if needed. Approximately 40% of ubrogepant patients in the phase 3 clinical studies used a rescue dose. On the other hand, two 100 mg pills of lasmiditan are required to achieve the 200 mg dose. It is not yet known what proportion of patients will opt to use the 200 mg dose of lasmiditan at the higher cost per episode.

US commercial plans may implement a variety of designs regarding use of the novel acute treatments. The AHS guidance suggests a step through 2 or more oral triptans if not contraindicated; however, plans may choose to give access after only 1 step to avoid their beneficiaries delaying trial of a treatment with a different mechanism of action. Switching from one triptan to another is not associated with significant improvements in headache-related disability compared with consistent treatment.³⁴ Furthermore, inadequate acute treatment efficacy was associated with an increased risk of new-onset chronic migraine over the course of 1 year.³⁵

In addition to benefit eligible populations, the model explored 2 smaller populations of patients thought to be more likely to receive therapy. These populations were based on patients currently receiving an oral triptan but reporting a low mTOQ (<6) score, indicating that they

were not adequately treated. While considerably smaller in terms of the number of beneficiaries, these populations were thought to have a high likelihood of receiving the novel acute treatments and in the end account for approximately 90% of the total market of the larger benefit eligible populations. Future analyses of claims data will be needed to assess the number and characteristics of beneficiaries who actually initiate the novel acute treatments.

The univariate sensitivity analyses suggested that drug acquisition costs of novel acute treatments, annual treated migraine episodes, and the uptake of novel treatments were the most influential parameters on results. The addition of lasmiditan maintained cost savings even if the costs of the novel acute medications were decreased by 15%.

This study drew heavily on US real-world data. The size of the eligible population and market shares of current treatments were based on data from the OVERCOME US study, whereas the dosing frequencies were based on information from the MarketScan claims database.

LIMITATIONS

As with all economic analyses, several limitations should be noted. First, the generalizability of all insurance plans will depend on how well data sources and assumptions represent the plan members' patterns of migraine management and associated medical costs. As noted, use of data from a representative US patient survey was likely a plus for this analysis.

Second, the model was developed for cost comparison only and did not consider product safety, efficacy, or outcomes. As such, uptake of novel therapies by eligible patients was not adjusted for any potential differences between the agents on these attributes. The label for lasmiditan includes these warnings: Patients are advised not

FIGURE 2 One-Way Sensitivity Analysis: Impact of Changes of Input Parameters ($\pm 15\%$) on the Change in Total Cost in 3 Years (Target Population: Patients With Previous History of 1 or More Oral Triptans)

to drive or operate machinery until at least 8 hours after taking each dose of lasmiditan. Patients may not be able to assess their own driving competence and the degree of impairment. Lasmiditan may cause central nervous system (CNS) depression and should be used with caution if used in combination with alcohol or other CNS depressants. Reactions consistent with serotonin syndrome were reported in patients treated with lasmiditan, and patients should discontinue lasmiditan if symptoms of serotonin syndrome occur. Detoxification may be necessary in case of medication overuse headaches.

The label for rimegepant warns that if a serious hypersensitivity reaction occurs, patients are to discontinue rimegepant and initiate appropriate therapy. Severe hypersensitivity reactions have included dyspnea and rash and can occur days after administration.

In GLADIATOR,^{36,37} the long-term open-label extension study of lasmiditan, more patients discontinued because of adverse events than in ubrogepant and rimegepant long-term extension studies. The most common adverse event leading to discontinuation with lasmiditan was dizziness. Discontinuation because of dizziness was dose dependent

and more likely to occur after the first or second treated attack than after subsequent attacks, suggesting the possibility that the impact may be mitigated in clinical practice by dose adjustment, which was not permitted in the trial.

Third, the model did not include the costs related to health care resource utilization (HCRU). The phase 3 registration studies for the 3 drugs were based on single episodes of care and did not include longer-term evaluations of resource utilization. We chose not to speculate on HCRU until more definitive data were available. We also did not consider patient cost sharing (ie, copayment or coinsurance); pharmaceutical incentives (ie, rebates); or dispensing fees, since this would introduce complexity related to shifts between medical and pharmacy benefits due to changes in care locations and routes of administration and would in the end have minimal effect on the analysis.

Finally, these analyses assumed the distribution for the 3 doses of lasmiditan (20% on 50 mg, 60% on 100 mg, and 20% on 200 mg) and of the proportion of patients on ubrogepant taking a second dose (40% based on a phase 3 clinical trial). Budget impact results may change if these proportions differ from real-world practice.

Conclusions

The addition of lasmiditan to the formulary as a novel acute treatment option for migraine alongside ubrogepant and rimegepant resulted in lower budget impact from a US commercial payer perspective.

DISCLOSURES

This work was funded by Eli Lilly and Company. Milev and Sun are employed by Evidera, which received funding from Eli Lilly and Company for work on this project. Pohl, Mason, Njuguna, and Loo are employees and stockholders of Eli Lilly and Company.

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