# RESEARCH

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# Adoption of rimegepant in Denmark: a register-based study on uptake, prescribing patterns and initiator characteristics



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# Abstract

**Background** Rimegepant, an oral calcitonin gene-related peptide (CGRP) receptor antagonist, is the first drug within its class approved for both acute and preventive treatment of migraine. This study examines its uptake in Denmark.

**Methods** Using nationwide healthcare registry data, we analyze trends in rimegepant prescriptions from its introduction in October 2022 to December 2024. Parameters assessed include demographic and clinical characteristics of users, temporal trends in drug use, treatment adherence, and concomitant use of other migraine therapies.

**Results** By December 2024, over 140,000 defined daily doses (DDDs) of rimegepant had been dispensed in Denmark, primarily among females (88%), with a users' median age of 45 years. Most initiators had prior experience with triptans (79%) or NSAIDs (38%) for migraine treatment and 69% met criteria for medication overuse before initiation. Concomitant use of triptans (63%) and NSAIDs (17%) remained common, but a substantial decline in the overuse of acute headache medications was observed after rimegepant initiation. Early discontinuation was very common, with 45% of initiators filling only one prescription. Among the 55% who continued treatment, the most substantial drop occurred within the first 90 days, followed by a more gradual decrease over time.

**Conclusions** The study highlights the rapid uptake of rimegepant in Denmark, especially among middle-aged females with a history of triptan use and medication overuse. While rimegepant was associated with a reduction in acute medication overuse, early discontinuation rates suggest barriers to sustained use, potentially influenced by cost, efficacy, or patient preferences. There is a need for strategies to optimize long-term adherence and access to rimegepant in clinical practice.

Keywords CGRP, Drug utilization, Headache, Medication overuse headache, Pain, Treatment patterns

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# Background

Pharmacological treatments for migraine have evolved with the introduction of "gepants", small molecule antagonists of the calcitonin gene-related peptide (CGRP) receptor. Among these, rimegepant is the only gepant approved for both the acute treatment of migraine with and without aura, and prevention of episodic migraine in adults [1–4]. In the United States, rimegepant received approval for the acute treatment in February 2020 and its indication was expanded to include the prevention of migraine in June 2021 [5]. The European Union followed with its approval for both uses in April 2022 [6]. At the time of its introduction, other CGRP antagonists, specifically monoclonal antibodies (mAbs) targeting either the CGRP peptide or its receptor, were already available on the market [7]. Rimegepant is available as an orally disintegrating tablet that can be taken "as needed" for the acute treatment or every other day for prophylaxis. Due to its relatively high cost and modest efficacy [8], rimegepant is considered a third-line option for patients where standard treatments have inadequate efficacy or are contraindicated [9]. With this study, we aimed to describe the uptake of rimegepant in adults during the early phases after its launch in Denmark, including its impact on the use of other migraine therapies and its retention among early users. In addition, we present the characteristics of those initiating rimegepant for the acute treatment of migraine and those initiating it for the preventive treatment of migraine.

# Methods

We used nationwide data on filled prescriptions in Denmark to describe the use of rimegepant in adults with migraine from October 2022.

# Data sources

Data were obtained from three national registry sources. The National Prescription Registry has captured individual-level data on all prescription medications dispensed to Danish residents since 1995 [10]. This registry includes details such as drug name, dispensing date, tablet strength, and quantity dispensed. Dosage instruction was not consistently available, and drugs administered in hospitals were not available as individual-level data. Medications are classified using the Anatomical Therapeutic Chemical (ATC) system, developed by the World Health Organization, and dispensed quantities are recorded in terms of the number and strength of pharmaceutical units (e.g., tablet strengths) and DDDs for entire packages [11]. The indication for rimegepant, i.e., whether for acute or prophylactic use, was almost consistently recorded in the register (97% of users). The remaining indications were inferred from the pattern of dispensing [12]. Hospital diagnosis data was retrieved from the Danish National Patient Register, while data on birth dates, deaths, and immigration were obtained from the Danish Civil Registration System [13, 14]. These datasets were linked through a unique personal identification number (CPR number) assigned to all Danish residents since 1968. According to data privacy rules for the Danish National Patient Register, reporting of cell counts lower than five is not allowed.

# **Study population**

Rimegepant was introduced in Denmark in October 2022 (Vydura<sup> $\circ$ </sup> [oral]). We identified individuals aged  $\geq$  18 years who filled at least one prescription of rimegepant in the period.

1 October 2022 to 31 December 2024, regardless of whether they initiated rimegepant for acute treatment or preventive therapy.

#### Rimegepant

Rimegepant was identified and categorized according to the ATC index and drug utilization was expressed in DDDs, defined by the WHO as the assumed average maintenance dose per day for a drug used for its main indication in adults [11]. Drug use was defined as the filling of at least one prescription. One DDD corresponds to 37.5 mg of rimegepant [15]. DDD is a standardized measure that allows for international comparisons of drug utilization and does not necessarily reflect actual prescribed or reimbursed dosing patterns. New users were defined as individuals with a rimegepant prescription and no prior prescriptions since market approval.

# Statistical analysis

Data analysis was conducted using R software (version 4.3.3). Descriptive statistics were used to summarize patient characteristics, prescription patterns, and treatment persistence. Data were stratified based on age, sex, and indication for rimegepant use (acute vs. preventive) to explore variations in drug utilization. Normally distributed variables were compared by using the t-test, while non-normally distributed variables were analyzed using the Kruskal-Wallis rank sum test. All analyses were performed in accordance with Danish registry data regulations. The study was registered in the repository at the University of Southern Denmark (approval n. 11,570). As the study relied exclusively on registry data, it was exempt from ethics review board approval under Danish legislation.

## User characteristics

We characterized new users of rimegepant in Denmark according to: (1) sex and age at initiation (index date); (2) previous use of treatments for migraine within 1 year before index date; (3) fills of treatments for migraine

during 90 days before and after index date; and (4) the prescriber type of the first rimegepant prescription. Cardiovascular risk factors were assessed through the use of prescribed drugs, in addition to hospital diagnoses recorded in the Patient Registry, evaluated from the last year before the first individual prescription of rimegepant. We divided new users of rimegepant into those using it for acute treatment and those using it every other day for prophylaxis, by considering two factors: (1) indication code, (2) fill patterns. Fill patterns were constructed by assuming a daily intake of one DDD, while adding a 25% allowance to account for variability in use. If the duration of a prescription extended into the fill date of the subsequent prescription, both prescriptions were considered part of the same treatment episode. The number of dispensed prescriptions was analyzed to determine the indication: a single prescription was categorized as for an acute indication, while more than one prescription indicated preventive use.

#### Temporal trends

To describe changes in rimegepant use over time, we calculated the quarterly incidence rate, prevalence proportion, and quarterly quantity of rimegepant dispensed. Prevalence proportions were calculated as the number of individuals with a dispensation in the given quarter divided by the total adult population count on January 1st in the given year. Quarterly incidence rates were calculated by dividing the quarterly number of new users by the follow-up for the total adult population of Denmark each year. The total drug use was displayed as the cumulative number of dispensed DDDs each quarter. Incidence rate, prevalence proportion and total amount of DDDs were also stratified by age group (18–39, 40–64, and  $\geq$ 65 years), using census data for the group in question.

#### Treatment duration

To evaluate treatment duration, we used the 'proportion of patients covered' (PPC) method [16]. New rimegepant users were tracked starting from the date they filled their initial prescription. We first calculated the proportion of users who filled only one prescription, identifying them as early discontinuers. For the remaining users, we applied the PPC method starting from the date of their second prescription [16]. For each day during the observation period, we calculated the proportion of these continuing users who were alive, had not emigrated, and had an active rimegepant prescription. A person was classified as having an active prescription ("current user") based on a pre-set duration of 30 days per prescription. This approach allowed for the possibility that an individual might stop treatment temporarily but could later be reclassified as a "current user" if they filled a new prescription. This type of analysis is less sensitive than a conventional drug survival analysis to assumptions about the period of usage assigned to a single prescription [16]. Subgroup analyses of drug survival were performed by age and sex, and sensitivity analyses were conducted by assigning fixed prescription durations of 60 and 90 days.

#### Overuse of acute headache medications

The presence of acute medication overuse was based on prescription fill patterns identifying  $\geq$  10 DDDs of ergotamines, triptans, opioids, or combination analgesics or  $\geq$  15 DDDs of acetaminophen or Non-steroidal antiinflammatory drugs (NSAIDs) in 3 or more consecutive months during the 6-month pre-index and post-index periods.

#### Results

The incidence rate and prevalence proportion of rimegepant use reached 0.85 per 10,000 person-years and 2.4 per 10,000 persons by December 2024 (Fig. 1A and B), mainly driven by individuals aged 40-64 years (Additional file 1). The total dispensed quantity of rimegepant in Denmark was 141,244 DDDs by the end of December 2024 filled by 2777 unique individuals (Fig. 1C). Rimegepant initiators were predominantly female (n = 2436, 88%), with a users' median age of 45 years (Table 1). The prevalence of cardiovascular comorbidities was low, with 9% (n = 241) having markers of cardiovascular disease, 5% (n = 130) having a hospital diagnosis for obesity, 2% (n = 60) having a history of stroke, and 1% (n = 20) a diagnosis of heart failure. Concomitant use of antihypertensive medications was common (n = 2450, 88%), whereas other concomitant therapies were less common, including antidiabetic medications (12%, n = 342), lipid lowering agents (14%, n = 402), and platelet inhibitors (15%, n = 422). The majority of rimegepant treatments were initiated by neurologists, who accounted for 2261 cases (81%), followed by general practitioners, responsible for 309 cases (11%). In the remaining 195 cases (7%), the prescriber was unknown (Fig. 2). At baseline, we identified a difference in the use of platelet inhibitors between acute and preventive users of rimegepant (16% vs. 7%, p = 0.01). Additionally, a higher proportion of patients in the acute group reported migraine with aura compared to the preventive group (20% vs. 13%, p = 0.04). Apart from these, no other significant differences were observed between the two groups (Table 1).

#### Previous use of migraine treatments

In the year preceding their first rimegepant prescription, the majority of rimegepant initiators had used triptans (79%, n = 2203) for migraine management (Table 2). NSAIDs (38%, n = 1064) and paracetamol (40%, n = 1109) were also commonly filled, albeit by a smaller proportion of patients. Use of opioids and combination analgesics



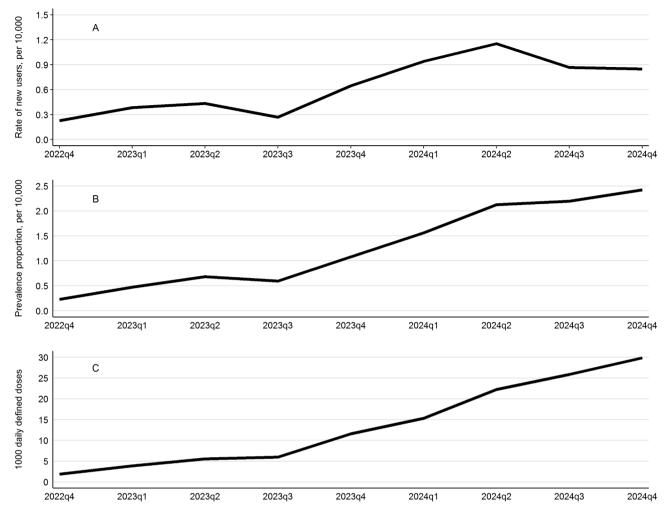


Fig. 1 (A) Quarterly incidence rate (per 10 000 person-years), (B) prevalence proportion (per 10 000 inhabitants) and (C) proportional distribution in total defined daily doses (DDDs; in thousands) of rimegepant for the period from 1 October 2022 to 30 September 2024 in Denmark

was relatively low (12%, n = 334), and no patients had use of ergot derivatives. For preventive treatments, candesartan was the most commonly prescribed (32%, n = 894), followed by beta-blockers such as metoprolol or propranolol (18%, n = 507) and topiramate (14%, n = 390). We identified a difference in the previous use of topiramate between acute and preventive users of rimegepant (14% vs. 21%, p = 0.02). Apart from this, no other significant differences were observed between the two groups (Table 2).

#### Concomitant use of migraine treatments

In the 90 days surrounding rimegepant initiation, triptans were the most frequently filled medications for the acute treatment of migraine, with 63% (n = 1742) of rimegepant users filling them (Table 3). NSAIDs (17%, n = 485) and paracetamol (19%, n = 531) were less commonly filled, while opioids and combination analgesics were filled by a smaller subset (6%, n = 169). No patients filled ergot derivatives during this period. Regarding preventive

migraine treatments, candesartan was the most commonly prescribed (23%, n = 643), followed by beta-blockers such as metoprolol or propranolol (11%, n = 293) and topiramate (8%, n = 230). No significant differences were observed between acute and preventive users of rimegepant (Table 3).

#### **Treatment duration**

A substantial proportion of patients (45%) redeemed only one prescription, reflecting early discontinuation. Among those who filled a second prescription, retention rates declined over time, with the proportion of patients covered (PPC) showing a drop within the first 30 days and continuing to decrease at a slower pace thereafter (Fig. 3). The pattern observed within the first 30 days was consistent when analyzing retention over longer durations, including 60 and 90 days. Differences were not observed across age groups (Additional File 1). Female patients showed slightly higher retention rates with compared to male patients (Additional File 1). Patients using **Table 1** Characteristics of initiators of Rimegepant in Denmark for the acute and preventive treatment of migraine in the period from 1 October 2022 to 31 December 2024

	All	Acute	Preventive
	(n=2777)	( <i>n</i> =2642)	( <i>n</i> =135)
Age at initiation, years			
Median (IQR)	45.0	44.0	47.0
	(33.0–53.0)	(33.0–53.0)	(34.0–55.0)
Sex, n (%)			
Female	2436 (88%)	2314 (88%)	122 (90%)
Male	341 (12%)	328 (12%)	13 (10%)
Type of migraine, n (%)			
Migraine without aura	1190 (43%)	1131 (43%)	59 (44%)
Migraine with aura	548 (20%)	531 (20%)	17 (13%)
Other	611 (22%)	583 (22%)	28 (21%)
Cardiovascular risk factors <sup>a</sup> , n (%)			
Cardiovascular disease	241 (9%)	234 (9%)	7 (5%)
Heart failure	20 (1%)	19 (1%)	1 (0%)
History of stroke	60 (2%)	59 (2%)	1 (0%)
Chronic obstructive pulmonary disorder	17 (1%)	16 (1%)	1 (0%)
Obesity	130 (5%)	126 (5%)	4 (0%)
Concomitant medications <sup>a</sup> , n (%)			
Antihypertensives	2450 (88%)	2332 (88%)	118 (87%)
Antidiabetic medications	342 (12%)	322 (12%)	20 (15%)
Antilipemic agents	402 (14%)	383 (14%)	19 (14%)
Platelet inhibitors	422 (15%)	412 (16%)	10 (7%)
Prescriber responsible for initiating treatment, n	(%)		
General practitioner	309 (11%)	277 (10%)	32 (24%)
Neurologists	2261 (81%)	2164 (82%)	97 (72%)
Other specialty	12 (0%)	11 (0%)	1 (0%)
Unknown	195 (7%)	190 (7%)	5 (3%)

IQR, interquartile range; n, number of subjects; SD, standard deviation

<sup>b</sup> Based on all time available before index date unless otherwise specified

rimegepant for preventive indication had higher retention rates over time compared to those using it for acute indication (Additional File 1).

#### Overuse of acute headache medications

In the periods leading up to the index date, the proportions of patients meeting overuse criteria for acute headache medications was relatively stable (Table 4). Overall, 69% (n = 1929) of patients met at least one overuse criterion. The use of  $\geq 10$  DDD of triptans varied between 54% and 57%, while the use of  $\geq$  15 DDD of NSAIDs was steady at 14–15%. Similarly,  $\geq$  15 DDD of paracetamol showed little variation, maintaining values between 18% and 19%, and the use of  $\geq$  10 DDD of opioids was consistent between 3% and 4%. After initiation of rimegepant, there was a decline in the proportions of patients overusing acute headache medications. After the index date, the proportion of patients meeting at least one overuse criterion decreased up to 51% (n = 1425). After the index date, triptan overuse was observed in 38-47% of patients, while the overuse of opioids was stable around 2-4%. Overuse of NSAIDs dropped to 11-14%, and paracetamol overuse was around 16–19%. No significant differences were observed between acute and preventive users of rimegepant (Additional File 1).

# Discussion

This nationwide register-based study provides comprehensive insights into the uptake and utilization patterns of rimegepant in Denmark from October 2022 to December 2024. The findings reflect several aspects of real-world use, including user demographics, concomitant therapies, and adherence trends. Current guidelines recommend the use of rimegepant as a third-line option for the acute treatment of migraine, reserved for patients who have insufficient response to or contraindications for triptans [17]. In Denmark, reimbursement for rimegepant is granted for up to 8 tablets per month for the acute treatment of migraine, whereas there is no reimbursement for its preventive use. Rimegepant users were predominantly middle-aged women, and most of them used the drug for the acute treatment of migraine. We identified only a small proportion of patients (5%) using rimegepant for prevention, suggesting that few patients

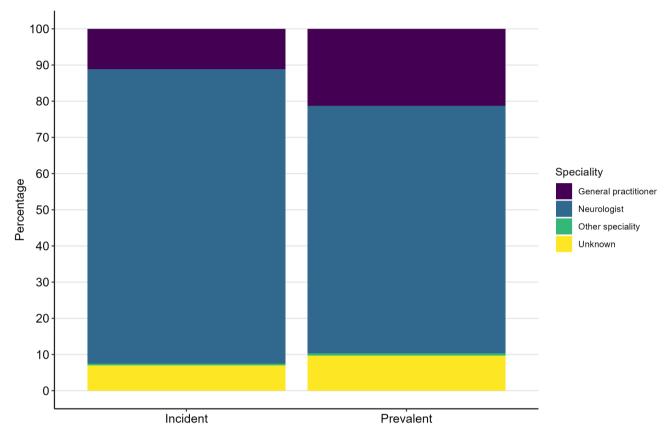


Fig. 2 Proportion of all rimegepant prescriptions initiated and maintained by different prescribers

<b>Table 2</b> Migraine treatments used in the year preceding the first Rimegepant i	treatments used in	n the vear i	precedina	the first	Rimedepant prescription
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	All	Acute	Preventive	<i>p</i> -value
	(n=2777)	(n=2642)	( <i>n</i> = 135)	
Paracetamol	1109 (40%)	1057 (40%)	52 (39%)	0.80
NSAIDs	1064 (38%)	1004 (38%)	60 (44%)	0.16
Triptans	2203 (79%)	2092 (79%)	111 (82%)	0.46
Ergots	0 (0%)	0 (0%)	0 (0%)	Not performed
Opioids and combinations	334 (12%)	318 (12%)	16 (12%)	1.00
Candesartan	894 (32%)	849 (32%)	45 (33%)	0.84
Metoprolol/propranolol	507 (18%)	482 (18%)	25 (19%)	1.00
Topiramate	390 (14%)	361 (14%)	29 (21%)	0.02

Table 3	Migraine treatments	used 90 days before and	l after Rimegepant initiation
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	All	Acute	Preventive	<i>p</i> -value
	(n=2777)	(n=2642)	( <i>n</i> = 135)	
Paracetamol	531 (19%)	507 (19%)	24 (18%)	0.77
NSAIDs	485 (17%)	466 (18%)	19 (14%)	0.34
Triptans	1742 (63%)	1647 (62%)	95 (70%)	0.07
Ergots	0 (0%)	0 (0%)	0 (0%)	Not performed
Opioids and combinations	169 (6%)	157 (6%)	12 (9%)	0.23
Candesartan	643 (23%)	615 (23%)	28 (21%)	0.56
Metoprolol/propranolol	293 (11%)	283 (11%)	10 (7%)	0.28
Topiramate	230 (8%)	218 (8%)	12 (9%)	0.92

NSAID: nonsteroidal anti-inflammatory drug

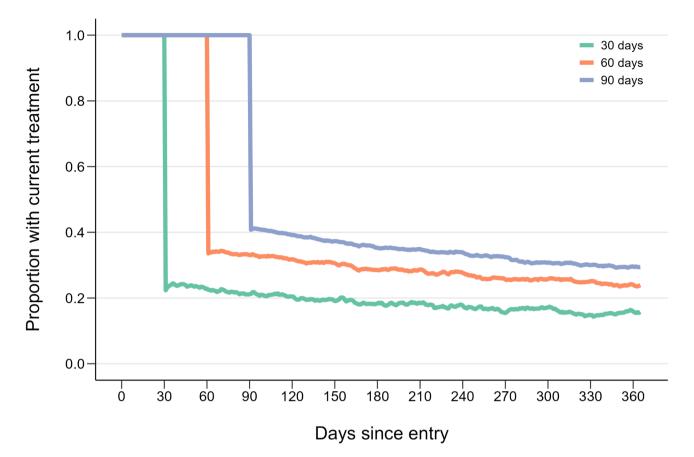


Fig. 3 Retention of rimegepant among early initiators (2022–2023) over a 360-day period, under the assumption of a 30-day, 60-day, and 90-day duration of prescription. Data were analyzed using the proportion of patients covered technique

<b>Table 4</b> Overall prevalence of acute medication overuse among Rimegepant users in Denmark in the period from 1 October 20	)22 to
30 September 2024	

	One or the other criteria	Use of ≥ 10 DDDs of triptans	Use of ≥ 10 DDDs of opioids	Use of ≥ 15 DDDs of NSAIDs	Use of ≥ 15 DDDs of
					paracetamol
Days relative to index date: -180 to -90	1841 (66%)	1500 (54%)	107 (3.9%)	382 (14%)	511 (18%)
Days relative to index date: -150 to -60	1820 (66%)	1482 (53%)	107 (3.9%)	395 (14%)	516 (19%)
Days relative to index date: -120 to -30	1834 (66%)	1504 (54%)	96 (3.5%)	379 (14%)	526 (19%)
Days relative to index date: -90 to 0	1929 (69%)	1582 (57%)	101 (3.6%)	414 (15%)	526 (19%)
Days relative to index date: -60 to 30	1827 (66%)	1482 (53%)	105 (3.8%)	374 (13%)	492 (18%)
Days relative to index date: -30 to 60	1759 (63%)	1398 (50%)	108 (3.9%)	386 (14%)	486 (18%)
Days relative to index date: 0 to 90	1699 (61%)	1299 (47%)	106 (3.8%)	388 (14%)	521 (19%)
Days relative to index date: 30 to 120	1571 (57%)	1197 (43%)	88 (3.2%)	328 (12%)	481 (17%)
Days relative to index date: 60 to 150	1517 (55%)	1144 (41%)	87 (3.1%)	318 (11%)	455 (16%)
Days relative to index date: 90 to 180	1425 (51%)	1064 (38%)	78 (2.8%)	304 (11%)	439 (16%)

DDD: Defined daily dose; NSAID: nonsteroidal anti-inflammatory drug

are willing to pay out of pocket, as the monthly cost for preventive use is approximately  $\notin$ 400. Among all users, the proportion of adults with migraine who had previously used triptans was not as high as expected (79%), potentially reflecting suboptimal triptan utilization before transitioning to newer therapies. This may also indicate the presence of patients with contraindications to triptans who require alternative treatment options. Concomitant use of triptans and NSAIDs remained common during the early stages of rimegepant therapy, while the reduction in acute headache medications after rimegepant initiation suggests its efficacy in addressing acute migraine episodes. Previous studies in the United States have similarly reported that long-term rimegepant use reduced the need for adjunctive treatments [18, 19]. The decline in the prevalence of acute medication overuse observed after rimegepant initiation supports its potential role in mitigating medication overuse headache, a common complication of migraine. Previous preclinical studies suggested that rimegepant is not associated with medication overuse headache and may offer a safer alternative for patients with complex headache profiles [20]. The rapid decline in rimegepant adherence within the first 30 days of initiation, followed by continued attrition over time, is noteworthy. Similar patterns are observed across various preventive migraine treatments, often attributed to factors such as side effects, costs, and lack of efficacy [21]. Reimbursement policies may have played a role in shaping prescriber behavior and patient access. Further research should focus on patient-reported outcomes, including quality of life and functional impairment, to better understand the broader impact of rimegepant. Economic evaluations comparing rimegepant with other preventive therapies could also inform reimbursement decisions.

#### **Study limitations**

This study has limitations. First, our analysis was based on nationwide healthcare registry data, which primarily capture prescription records from filled prescriptions and community pharmacies. Certain migraine treatments, including anti-CGRP mAbs and onabotulinumtoxin A, are administered in hospital settings and recorded in hospital-based registries rather than prescription databases. Since we did not have access to hospital records, we could not accurately assess the use of these treatments. Future evaluations should focus on potential interactions between these therapies and rimegepant, as well as the feasibility of combination therapy in real-world clinical practice. Second, we lack detailed clinical data on the reasons for treatment discontinuation. The absence of these factors limits our ability to determine whether discontinuation was driven by inadequate efficacy, side effects, cost-related barriers, or other patient-specific considerations. Additionally, the lack of reimbursement for preventive treatment may have influenced treatment initiation and continuation patterns. Since only patients who could afford out-of-pocket costs had access to rimegepant for migraine prophylaxis, our findings on adherence and utilization may not be generalizable to settings where reimbursement policies differ.

#### Conclusion

This register-based study provides insights into the realworld utilization of rimegepant in Denmark, revealing significant uptake among middle-aged female patients with prior exposure to triptans, as expected. Despite its promising role in migraine management, declining adherence rates highlight the need for strategies to optimize long-term use. The potential of rimegepant

#### **Supplementary Information**

The online version contains supplementary material available at https://doi.or g/10.1186/s10194-025-02028-w.

Supplementary Material 1

#### Acknowledgements

None.

#### Author contributions

L.P., J.H., and A.P. conceived the study. M.T.E. performed the statistical analysis. T.P.D. provided inputs during the initial stages of the study and later contributed to the writing of the manuscript. All authors contributed to the writing of the manuscript and provided critical revisions. All authors read and approved the final manuscript.

#### Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

#### Data availability

Data are provided within the manuscript and supplementary information files.

#### Declarations

#### **Competing interests**

L.P. was formerly employed by Lundbeck. T.P.D. has received personal fees from Teva that are unrelated to this manuscript. J.H. and A.P. reports participation in research projects funded by Alcon, Almirall, Astellas, Astra-Zeneca, Boehringer-Ingelheim, Novo Nordisk, Servier, Pfizer and LEO Pharma (all regulatormandated Phase IV studies), and an unrestricted research grant from Novo Nordisk, all with funds paid to the institution where they were employed (no personal fees) and with no relation to the work reported in this paper. M.T.E. reports no conflict of interests.

#### Received: 27 February 2025 / Accepted: 7 April 2025 Published online: 18 April 2025

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