



# Migraine Characteristics, Comorbidities, Healthcare Resource Utilization, and Associated Costs of Early Users of Erenumab in the USA: A Retrospective Cohort Study Using Administrative Claims Data

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## ABSTRACT

**Introduction:** Erenumab is indicated for migraine preventive treatment in adults. The objective of this study was to provide descriptive information on real-world use of erenumab including patient profile and treatment patterns.

**Methods:** We completed a retrospective review of US data (through May 2019) from the IBM MarketScan® Early View Databases, identifying adult patients newly treated with erenumab with a migraine claim in the year prior to first erenumab claim (index) and at least 1 year of continuous pre-index medical and pharmacy insurance coverage, to assess pre- and post-erenumab migraine characteristics, comorbidities, healthcare resource utilization, and associated costs. All data were summarized using descriptive statistics.

**Results:** A total of 9753 patients met inclusion criteria. The average (SD) age was 46 (12) years,

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85% of patients were female, and 64% had at least one claim for chronic migraine; 70% of erenumab users had an initial dose of 70 mg; 77% of patients in the 6-month follow-up sample ( $n = 4437$ ) remained on their initial erenumab dose. Persistence at 6-month follow-up was 47.3% with a mean (95% CI) proportion of days covered of 0.68 (0.67, 0.68). In the post-erenumab period, claims for comorbidities of non-migraine headaches and anxiety were reduced and there was a shift to decreased use of acute and preventive medications. Reductions in overall use and associated cost of healthcare resources such as inpatient hospitalization and outpatient office visits were minimal, with slightly more pronounced reductions in the subgroup of patients that were persistent to erenumab.

**Conclusions:** We observed reductions in claims for important migraine characteristics, comorbidities, and a shift to decreased use of acute and preventive migraine medications—observations indicative of the real-world effectiveness of erenumab. Further examination is required as persistence to erenumab, which may be influenced by dose titration, appears to be an important factor in changes to healthcare resource utilization and costs.

**Keywords:** Cost; Erenumab; Healthcare resource utilization; Migraine; Persistence

## Key Summary Points

### Why carry out this study?

Erenumab-aooe was approved in the USA on 17 May 2018 for the preventive treatment of migraine in adults.

As a first-in-class option for migraine prevention, knowledge about the real-world experience of patients receiving erenumab is limited.

This study sought to examine the impact of erenumab treatment on migraine characteristics, comorbidities, healthcare resource utilization, and associated costs.

### What was learned from the study?

Reductions in claims for important migraine characteristics, comorbidities, and a shift to decreased use of acute and preventive migraine medications in the post-erenumab follow-up period are indicative of the real-world effectiveness of erenumab.

Persistence to erenumab is an important factor requiring further examination.

## INTRODUCTION

Migraine is a neurological disorder characterized by recurrent headache attacks of moderate to severe pain. It affects up to 18% of the female population and 6% of the male population. Reduced quality of life, functional impairment, reduced productivity, and high economic burden, are all associated with migraine, highlighting the need for effective therapeutic strategies [1–4]. The clinical management of migraine relies on the use of preventive medications to preempt migraine attacks and the use of acute medications to abort migraine attacks. Many of the available preventive medications, including tricyclic antidepressants, anticonvulsants, beta blockers, and calcium channel

blockers, were not developed specifically for migraine but have demonstrated efficacy in clinical trials [5, 6]. However, many patients have an inadequate response or do not continue treatment because of tolerability issues and thus fail to maintain control of their migraine [7, 8]. A recent retrospective analysis of claims for 8707 patients showed persistence of 25% after the first 6 months of treatment declining to 14% by 12 months, for the 14 most common medications used for migraine prevention [9]. These low rates of persistence may lead to increased burden of migraine as healthcare resource utilization has been shown to be greater among individuals who failed multiple migraine preventive therapies [10]. Importantly, there may also be substantial health risks when patients decide to alter their prescribed treatment plan without consulting their healthcare provider [11]. Thus, more effective and tolerable preventive treatments may promote wider use with the potential to reduce the burden of migraine to individuals and society.

Erenumab (erenumab-aooe in the USA) was approved in the USA by the Food and Drug Administration (FDA) on 17 May 2018 for the preventive treatment of migraine in adults. Information on the real-world experience of patients receiving erenumab is limited. We conducted a claims-based, retrospective observational study to examine the impact of erenumab treatment as a migraine preventive on migraine characteristics, comorbidities, healthcare resource utilization, and associated costs.

## METHODS

### Study Design

We used administrative claims data from the 2017–2019 IBM MarketScan® Early View Commercial Claims and Encounters (CCA) and Medicare Supplemental and Coordination of Benefits databases. The CCA database contains employer-sponsored private health insurance records encompassing employees, their spouses, and dependents. With the MarketScan® Early View Data Set, data are available within 45 days of the end of the service month. The Medicare

Supplemental and Coordination of Benefits database contains the data of retirees with employer-sponsored Medicare supplemental insurance. MarketScan® databases are in compliance with the Health Information Portability and Accountability Act of 1996 (HIPAA). Data from the MarketScan® database were used under a licensing agreement with IBM Watson Health. As this study did not involve the collection, use, or transmittal of individually identifiable data, it did not require institutional review board review or approval. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

### Patient Identification

Adult patients (at least 18 years of age) with at least one National Drug Code (NDC) claim for erenumab from May 2018 through May 2019 and a migraine diagnosis in the year prior to the first erenumab claim were identified. The date of the first claim of erenumab was set as the index date. Migraine diagnosis was based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes G43.xx and prescription claims using NDC or Healthcare Common Procedure Coding System (HCPCS) codes for acute migraine medications (e.g., triptans or ergotamines). Patients were required to have at least 1 year of continuous enrollment prior to the index date with both medical and pharmacy insurance coverage.

### Study Variables

Patient demographic characteristics assessed at the index date included age, sex, geographic region, and provider specialty. Provider specialties were identified on the basis of inpatient/outpatient migraine diagnosis (ICD-10-CM) and/or procedure (HCPCS) claims within 90 days prior and most proximal to or on the

erenumab index date. Patients may have had multiple provider specialties per claim.

Patient clinical characteristics for the full study population were characterized using ICD-10-CM codes for the 12-month pre-index period (baseline). Erenumab dispensing patterns included initial dose prescribed (70 mg vs 140 mg), switches in dose and time to switch (in days), and persistence. Persistence was evaluated using 30-day and 45-day allowable gaps in therapy as well as the proportion of days covered (PDC) method using stockpiling algorithm [12]. PDC was calculated as the ratio of number of days the patient was covered by erenumab in a period to the total number of days in the period. PDC was described at 3- and 6-months post-index.

In a sample of patients with 6-month follow-up data, pre- and post-erenumab migraine characteristics, comorbidities, treatment characteristics, healthcare resource utilization, and associated costs in US dollars (\$) were described 6 months pre- and post-index. Pre- and post-erenumab treatment characteristics were based on prescription claims using NDC or HCPCS codes. Acute treatments were identified as triptans, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, analgesics (non-NSAID, non-opioid analgesics), and ergotamines. Preventive treatments were identified as anticonvulsants, antidepressants, antihypertensives, botulinum toxins, and others. Analysis included measures of the number and type of acute and preventive treatments. Results include stratification by persistence and non-persistence to erenumab with persistence defined as having continuously filled erenumab prescriptions through day 180 of the follow-up period with a 30-day allowable gap between fills. Healthcare utilization was measured as prescription of medications used for the acute and preventive treatment of migraine, emergency room visits (service place code 23), outpatient care (service place code 22 [outpatient hospital] or 11 [office]), inpatient hospitalizations (service code 21) and inpatient length of hospital stay, brain imaging studies (Current Procedural Terminology [CPT] code or HCPCS code for an imaging procedure [e.g., CT Head 70,450–70,492, MRI Head 70,336, 76,390, 70,540–70,559] containing HCPCS modifier

code 26 to avoid double counting) and their associated costs for 6 months prior to and 6 months after the first claim of erenumab. For both commercial and Medicare patients in the study, healthcare costs were total reimbursed amount, including health plan payment and patients' out-of-pocket payment (copay, deductible, and coinsurance).

### Statistical Analysis

All data were summarized using descriptive statistics. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as mean/medians with corresponding standard deviations or standard errors. Subgroup analyses based on provider specialty were conducted for select baseline comorbidities and migraine characteristics. For these select subgroup analyses, patients were grouped on the basis of specialist visit during the pre-index baseline period as (1) patients who saw a neurologist and (2) patients who saw a family practice/internal medicine physician but no neurologist and no pain specialist/anesthesiologist.

## RESULTS

### Sample Size

After inclusion and exclusion criteria were met, 9753 patients with an erenumab claim comprised the full study population. Of these, 7280 patients had 3-month follow-up data and 4437 had 6-month follow-up data.

### Demographics and Baseline Characteristics

The average (SD) age at first erenumab claim for the full study population was 46.5 (12.1) years and 85.4% of users were women. Demographic characteristics for patients with 6-month follow-up data were similar to that of the full study population (Table 1). The 45–54 years age group made up the largest proportion of patients in the full study population (32.1%). Overall,

69.4% of patients had at least one comorbidity (Table 1). The most common comorbidities observed in the baseline period were other (non-migraine) headaches (29.0%), anxiety (21.8%), hypertension (18.4%), depression (16.5%), low back pain (15.5%), and osteoarthritis/spondylosis (14.5%).

Neurologists were the most common (47.3%) provider specialty seen by patients with migraine initiating erenumab, followed by other specialties including family practice (9.6%), nurse practitioner/physician's assistant (6.7%), and internal medicine (5.0%) (data not shown). As expected, additional analysis by provider type indicates that patients who saw a neurologist during the baseline period had a higher frequency of comorbidities in the year prior to erenumab use compared to patients who saw a family practice/internal medicine physician but no neurologist and no pain specialist/anesthesiologist during the 12-month baseline period (Supplemental Table 1).

### Erenumab Dispensing Patterns and Persistence

A majority (70.2%) of erenumab users were administered an initial dose of 70 mg; 76.9% of patients in the 6-month follow-up sample remained on their initial erenumab dose; 833 patients (26.6%) starting on 70 mg switched to 140 mg and 194 patients (14.9%) starting on 140 mg switched to 70 mg (Table 2). Persistence at 3-month follow-up was 67.1% using a 30-day gap and 72.6% using a 45-day gap; persistence at 6-month follow-up was 41.8% and 47.3%, respectively. Mean (95% CI) PDC for the 3-month follow-up after erenumab initiation was 0.80 (0.79, 0.80) and for the 6-month follow-up was 0.68 (0.67, 0.68) (Table 2). There was no difference in persistence based on erenumab dose or provider specialty (data not shown). There were, however, notable differences in erenumab dose switching for persistent and non-persistent patients. Thirty two percent of persistent patients, versus 17% of non-persistent patients, switched from their initial dose. Seventy five percent of persistent patients and 67% of non-persistent patients started at 70 mg;

**Table 1** Patient demographics and baseline clinical characteristics in the full study population and 6-month follow-up sample

	<b>All patients N = 9753</b>	<b>6-month follow-up patients* N = 4437</b>
Age, mean (SD)	46.5 (12.1)	46.7 (11.8)
Age category, <i>n</i> (%)		
18–34	1550 (15.9)	655 (14.8)
35–44	2458 (25.2)	1104 (24.9)
45–54	3134 (32.1)	1497 (33.7)
55–64	2180 (22.4)	1000 (22.5)
65–74	353 (3.6)	148 (3.3)
75+	78 (0.8)	33 (0.7)
Sex (female), <i>n</i> (%)	8329 (85.4)	3808 (85.8)
Geographic region, <i>n</i> (%)		
Northeast	1047 (10.7)	507 (11.4)
Midwest	2134 (21.9)	934 (21.1)
South	2998 (30.7)	1287 (29.0)
West	1373 (14.1)	633 (14.3)
Unknown	2201 (22.6)	1076 (24.3)
Year of index date		
2018	6185 (63.4)	4437 (100.0)
2019	3568 (36.6)	0 (0.0)
Comorbidities		
Asthma	727 (7.5)	174 (3.9)
Hypertension	1790 (18.4)	457 (10.3)
Acute myocardial infarction	37 (0.4)	8 (0.2)
Ischemic stroke	77 (0.8)	23 (0.5)
Constipation	306 (3.1)	76 (1.7)
Irritable bowel syndrome	232 (2.4)	48 (1.1)
Complications of constipation	187 (1.9)	44 (1.0)
Anxiety	2125 (21.8)	646 (14.6)
Depression	1606 (16.5)	500 (11.3)
Other (non-migraine) headaches	2829 (29.0)	810 (18.3)
Low back pain	1511 (15.5)	463 (10.4)
Osteoarthritis/spondylosis	1411 (14.5)	393 (8.9)

**Table 1** continued

	All patients N = 9753	6-month follow-up patients* N = 4437
Fibromyalgia	549 (5.6)	171 (3.9)
No comorbidities	2981 (30.6)	2056 (46.3)
Migraine characteristics		
Migraine with aura, including persistent aura	2611 (26.8)	915 (20.6)
Migraine with aura, excluding persistent aura	2530 (25.9)	890 (20.1)
Chronic migraine	6274 (64.3)	2904 (65.4)
Menstrual migraine	259 (2.7)	103 (2.3)
Status migrainosus	2607 (26.7)	1103 (24.9)

*SD* standard deviation

\*Comorbidities and migraine characteristics for the 6-month follow-up period were based on a 6-month baseline period whereas the same elements for all patients were based on a 12-month baseline period

36% of the persistent patients starting at 70 mg switched to 140 mg at a mean of 135 days and 19% of non-persistent starting at 70 mg switched to 140 mg at a mean of 126 days. Of the 25% of persistent patients starting at 140 mg, 21% switched to 70 mg at a mean of 130 days. Of the 33% of non-persistent patients starting at 140 mg, 12% switched to 70 mg at a mean of 121 days.

### Pre- and Post-erenumab Comorbidities and Migraine Characteristics

In the sample of patients with 6-month follow-up data, claims submitted for migraine with aura including and excluding persistent aura, chronic migraine, menstrual migraine, and status migrainosus were reduced in the 6-month post-index period as compared with the 6-month pre-index period with reductions in claims for chronic migraine and status migrainosus being slightly more pronounced for persistent patients (Table 3). Medical claims for comorbidities submitted during the 6-month pre-index period and the 6-month post-index period remained relatively consistent except for non-migraine headaches (18.3% vs 13.2%) and anxiety (14.6% vs 13.6%), which decreased in the 6-month post-compared with

the 6-month pre-index period; these decreases were consistent for persistent and non-persistent patients (Table 3).

### Pre- and Post-erenumab Medications, Healthcare Resource Utilization, and Costs

In the follow-up sample at baseline, almost all patients were using at least one acute and one preventive migraine medication prior to the erenumab index date with most patients using two or more (Table 4). The majority of patients were using triptans and a substantial proportion were using NSAID, opioids, or other analgesics, with few using ergotamines. During baseline, the most commonly used preventive migraine medications were anticonvulsants and antidepressants, followed by antihypertensives and botulinum toxin. Use of acute and preventive medications in the baseline period was similar for persistent and non-persistent patients with the exception of triptans where 72.4% of persistent patients were using triptans in the pre-index period versus 65.6% of non-persistent patients.

The use of these acute medications declined from pre-index to post-index period (Table 4). There was a greater percentage of patients using zero or one acute medication in the post-index

**Table 2** Erenumab dispensing patterns and persistence in the full study population and 6-month follow-up sample stratified by persistence

	All patients ( <i>N</i> = 9753)	6-month follow-up patients		
		All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non-persistent ( <i>N</i> = 2584)
Remained on initial dose, <i>n</i> (%)	8236 (84.4)	3410 (76.9)	1261 (68.1)	2149 (83.2)
Switched from initial dose, <i>n</i> (%)	1517 (15.6)	1027 (23.1)	592 (31.9)	435 (16.8)
70 mg initial dose	<i>n</i> = 6845 (70.2)	<i>n</i> = 3136 (70.7)	<i>n</i> = 1394 (75.2)	<i>n</i> = 1742 (67.4)
Switched to 140 mg, <i>n</i> (%)	1202 (17.6)	833 (26.6)	497 (35.7)	336 (19.3)
Time to switch (days)				
Mean (SD)	114.2 (65.0)	131.3 (67.8)	135.0 (64.9)	125.8 (71.6)
95% CI	(110.5, 117.9)	(126.7, 135.9)	(129.3, 140.7)	(118.2, 133.5)
140 mg initial dose	<i>n</i> = 2908 (29.8)	<i>n</i> = 1301 (29.3)	<i>n</i> = 459 (24.8)	<i>n</i> = 842 (32.6)
Switched to 70 mg, <i>n</i> (%)	315 (10.8)	194 (14.9)	95 (20.7)	99 (11.8)
Time to switch (days)				
Mean (SD)	104.3 (71.2)	125.6 (78.3)	130.1 (79.7)	121.3 (77.7)
95% CI	(96.5, 112.2)	(114.5, 136.7)	(114.0, 146.2)	(105.8, 136.8)
Erenumab proportion of days covered	3-month follow-up			
<i>n</i>	7280	4437	1853	2584
Mean (SD)	0.80 (0.24)	0.68 (0.28)	0.94 (0.07)	0.48 (0.21)
95% CI	(0.79, 0.80)	(0.67, 0.68)	(0.94, 0.95)	(0.47, 0.49)

*CI* confidence interval, *SD* standard deviation

period compared to the pre-index period (44.6% vs 38.3%) with an accompanying reduction in the percentage of patients using each class of medication except for opioids which increased slightly from 37.9% pre-index to 38.3% post-index. Closer inspection of these results using subgroup analyses for patients who were persistent and non-persistent at 6 months revealed a small difference in the post-index proportion of patients on zero or one acute medication, increasing by 7.3% (from 37.8% to 45.1%) for persistent patients and 5.9% (from 38.5% to 44.4%) for non-persistent patients. Similar small differences were observed between persistent and non-persistent patients and the use of triptans, decreasing by 7.9% (from 72.4% to

64.5%) for persistent patients and 6.9% (from 65.6% to 58.7%) for non-persistence patients. The slight increase in opioid use was consistent for persistent, increasing by 0.4% (from 36.7% to 37.1%), and non-persistent patients, increasing by 0.3% (from 38.8% to 39.1%). For preventive medications, the proportion of patients using anticonvulsants in the post-erenumab period decreased by 9.3% (from 49.0% to 39.7%) for persistent patients and 8.2% (from 51.9% to 43.7%) for non-persistent patients.

Differences in the costs associated with acute medications aligned with the overall reduction in use between pre- and post-erenumab index periods. Overall, a minor reduction in costs was observed from an average of \$1206 in the

**Table 3** Patient migraine characteristics and comorbidities in the 6 months pre- and post-erenumab stratified by persistence

	Pre-erenumab			Post-erenumab		
	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)
Comorbidities						
Asthma	174 (3.9)	68 (3.7)	106 (4.1)	176 (4.0)	63 (3.4)	113 (4.4)
Hypertension	457 (10.3)	186 (10.0)	271 (10.5)	425 (9.6)	168 (9.1)	257 (9.9)
Acute myocardial infarction	8 (0.2)	1 (0.1)	7 (0.3)	9 (0.2)	3 (0.2)	6 (0.2)
Ischemic stroke	23 (0.5)	7 (0.4)	16 (0.6)	20 (0.5)	8 (0.4)	12 (0.5)
Constipation	76 (1.7)	28 (1.5)	48 (1.9)	85 (1.9)	29 (1.6)	56 (2.2)
Irritable bowel syndrome	48 (1.1)	20 (1.1)	28 (1.1)	52 (1.2)	26 (1.4)	26 (1.0)
Complications of constipation	44 (1.0)	18 (1.0)	26 (1.0)	52 (1.2)	19 (1.0)	33 (1.3)
Anxiety	646 (14.6)	238 (12.8)	408 (15.8)	604 (13.6)	224 (12.1)	380 (14.7)
Depression	500 (11.3)	192 (10.4)	308 (11.9)	477 (10.8)	173 (9.3)	304 (11.8)
Other (non- migraine) headaches	810 (18.3)	299 (16.1)	511 (19.8)	584 (13.2)	201 (10.8)	383 (14.8)
Low back pain	463 (10.4)	192 (10.4)	271 (10.5)	440 (9.9)	158 (8.5)	282 (10.9)
Osteoarthritis/ spondylosis	393 (8.9)	168 (9.1)	225 (8.7)	431 (9.7)	166 (9.0)	265 (10.3)
Fibromyalgia	171 (3.9)	62 (3.3)	109 (4.2)	146 (3.3)	53 (2.9)	93 (3.6)
No comorbidities	2056 (46.3)	893 (48.2)	1163 (45.0)	2207 (49.7)	972 (52.5)	1235 (47.8)
Migraine characteristics, <i>n</i> (%)						
Migraine with aura, including persistent aura	915 (20.6)	372 (20.1)	543 (21.0)	700 (15.8)	287 (15.5)	413 (16.0)
Migraine with aura, excluding persistent aura	890 (20.1)	364 (19.6)	526 (20.4)	682 (15.4)	280 (15.1)	402 (15.6)
Chronic migraine	2904 (65.4)	1216 (65.6)	1688 (65.3)	2531 (57.0)	1041 (56.2)	1490 (57.7)
Menstrual migraine	103 (2.3)	37 (2.0)	66 (2.6)	77 (1.7)	33 (1.8)	44 (1.7)
Status migrainosus	1103 (24.9)	442 (23.9)	661 (25.6)	806 (18.2)	296 (16.0)	510 (19.7)



**Table 4** Patient use of acute and preventive migraine treatment in the 6 months pre- and post-erenumab stratified by persistence

	Pre-erenumab			Post-erenumab		
	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)
Number of acute medications used, <i>n</i> (%)						
0	402 (9.1)	146 (7.9)	256 (9.9)	610 (13.7)	242 (13.1)	368 (14.2)
1	1294 (29.2)	554 (29.9)	740 (28.6)	1373 (30.9)	593 (32.0)	780 (30.2)
2	114 (25.8)	488 (26.3)	656 (25.4)	1077 (24.3)	446 (24.1)	631 (24.4)
3	777 (17.5)	332 (17.9)	445 (17.2)	674 (15.2)	284 (15.3)	390 (15.1)
4	404 (9.1)	153 (8.3)	251 (9.7)	355 (8.0)	162 (8.7)	193 (7.5)
5+	416 (9.4)	180 (9.7)	236 (9.1)	348 (7.8)	126 (6.8)	222 (8.6)
Type of acute medication used, <i>n</i> (%)						
Triptans	3037 (68.4)	1342 (72.4)	1695 (65.6)	2712 (61.1)	1196 (64.5)	1516 (58.7)
Ergotamines	214 (4.8)	90 (4.9)	124 (4.8)	168 (3.8)	65 (3.5)	103 (4.0)
NSAIDs	1646 (37.1)	685 (37.0)	961 (37.2)	1517 (34.2)	627 (33.8)	890 (34.4)
Opioids	1682 (37.9)	680 (36.7)	1002 (38.8)	1699 (38.3)	688 (37.1)	1011 (39.1)
2+ opioid claims	1150 (25.9)	457 (24.7)	693 (26.8)	1125 (25.4)	456 (24.6)	669 (25.9)
Analgesics <sup>a</sup>	825 (18.6)	329 (17.8)	496 (19.2)	741 (16.7)	280 (15.1)	461 (17.8)
Number of preventive medications used, <i>n</i> (%)						
0	564 (12.7)	235 (12.7)	329 (12.7)	878 (19.8)	402 (21.7)	476 (18.4)
1	1131 (25.5)	515 (27.8)	616 (23.8)	1235 (27.8)	528 (28.5)	707 (27.4)
2	1195 (26.9)	491 (26.5)	704 (27.2)	1110 (25.0)	461 (24.9)	649 (25.1)
3	804 (18.1)	312 (16.8)	492 (19.0)	673 (15.2)	260 (14.0)	413 (16.0)
4	451 (10.2)	186 (10.0)	265 (10.3)	334 (7.5)	138 (7.4)	196 (7.6)
5+	292 (6.6)	114 (6.2)	178 (6.9)	207 (4.7)	64 (3.5)	143 (5.5)
Type of preventive medication used, <i>n</i> (%)						
Anticonvulsant	2249 (50.7)	908 (49.0)	1341 (51.9)	1863 (42.0)	735 (39.7)	1128 (43.7)
Antidepressant	2206 (49.7)	879 (47.4)	1327 (51.4)	2001 (45.1)	779 (42.0)	1222 (47.3)
Antihypertensive	1540 (34.7)	642 (34.6)	898 (34.8)	1335 (30.1)	542 (29.2)	793 (30.7)
Botulinum toxin	1302 (29.3)	575 (31.0)	727 (28.1)	1048 (23.6)	452 (24.4)	596 (23.1)
Anti-CGRP (excluding erenumab)	0 (0.0)	0 (0)	0 (0)	552 (12.4)	43 (2.3)	509 (19.7)
Other <sup>b</sup>	744 (16.8)	277 (14.9)	467 (18.1)	690 (15.6)	249 (13.4)	441 (17.1)

**Table 4** continued

	Pre-erenumab			Post-erenumab		
	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)
Associated costs, mean (SD)						
Acute migraine treatment costs	\$1206 (\$8164)	\$1463 (\$12,298)	\$1021 (\$2437)	\$1054 (\$7214)	\$1245 (\$10,845)	\$916 (\$2235)
Preventive migraine treatment costs (excluding anti-CGRPs)	\$1321 (\$2028)	\$1346 (\$2034)	\$1303 (\$2024)	\$1124 (\$1959)	\$1120 (\$1908)	\$1127 (\$1995)
Total acute and preventive migraine treatment costs (excluding anti-CGRPs)	\$2526 (\$8453)	\$2809 (\$12,470)	\$2324 (\$3334)	\$2178 (\$7540)	\$2365 (\$11,028)	\$2043 (\$3225)
Anti-CGRP costs (excluding erenumab)	\$0 (\$0)	\$0 (\$0)	\$0 (\$0)	\$171 (\$6)	\$24 (\$2)	\$276 (\$7)

<sup>a</sup> Non-NSAID/non-opioid analgesics

<sup>b</sup> Other agents prescribed for migraine prevention such as memantine, milnaciprin, etc.

6-month period pre-index versus \$1054 in the 6-month post-erenumab period. Again, closer inspection of cost results by persistent and non-persistent patients identified important differences. Reflective of higher use of triptans in the pre-index period, costs for acute medications in the pre-index period were \$1463 for persistent patients and \$1021 for non-persistent patients. In the post-index period, reductions in costs were slightly higher for persistent patients (– \$218, \$1245 post versus \$1463 pre) than non-persistent patients (– \$105, \$916 post versus \$1021 pre).

As was observed for acute medications, a similar picture of overall reduction from pre- to post-erenumab periods was seen with the preventive medications used prior to erenumab (Table 4). There was a greater percentage of patients using zero or one preventive medication in the post-index period (47.6% post versus 38.2% pre) with an accompanying reduction in the percentage of patients using each class of medication. These reductions were slightly higher for persistent versus non-persistent patients.

With these changes, the average costs for preventive medication decreased slightly between pre- and post-erenumab periods with slightly higher reductions for persistent than non-persistent patients; – \$226 (\$1120 post versus \$1346 pre) for persistent patients and – \$176 (\$1127 post versus \$1303 pre) for non-persistent patients. Importantly, we noted some concomitant use of non-erenumab CGRP pathway antagonists in the persistent group (*n* = 43 or 2.3%), but also switching to a non-erenumab CGRP pathway antagonist in non-persistent patients (*n* = 509 or 19.7%). We completed a sensitivity analysis excluding patients prescribed non-erenumab CGRP pathway antagonists from the analysis and noted similar patterns of change as the primary analysis for both acute and preventive medications. As expected, removing a larger number of non-erenumab CGRP pathway antagonists from the non-persistent subgroup resulted in a reduction in associated costs for preventive medications in the subgroup (data not shown).

Aligned to overall reductions in the use of acute and preventive medications in the pre-

index period, total costs for acute and preventive medications were reduced with slightly higher reductions in costs for persistent (– \$444, \$2365 post versus \$2809 pre) versus non-persistent (– \$281, \$2043 post versus \$2324 pre) patients.

The use of inpatient, ER, and imaging resource was low in the 6-month baseline period, for example 0.1 hospitalizations and 0.5 ER visits on average (Table 5). The most used resource was outpatient office visits, with a mean 8.5 visits in the 6-month pre-erenumab period. Associated costs ranged from a mean (SD) of \$170 (\$606) for imaging to \$1680 (\$9995) for inpatient hospital admissions contributing to a total cost of \$3651 (\$11,736) across non-medication healthcare resources.

For the overall population, only minor differences in the use and associated costs for non-medication healthcare resources were observed in the 6 months post-erenumab compared to the 6 months pre-erenumab (Table 5). Closer inspection of differences in the use and associated costs for these resources pre-index by persistent and non-persistent patients revealed a slightly longer mean length of stay during inpatient hospitalizations and higher use of outpatient visits for non-persistent versus persistent patients: 5.6 days versus 4.6 days and 8.7 visits versus 8.2 visits, respectively. Aligned to this, the associated pre-index costs for these services were higher in non-persistent versus persistent patients. Post-index reductions in the use of resources were slightly more pronounced for persistent patients with the exception of brain imaging studies which were almost identical for persistent and non-persistent patients. For costs estimates, a notable finding was the substantial uncertainty (large standard deviation relative to the mean) in post-index inpatient hospitalization cost estimates for non-persistent patients, suggesting that a few outlier patients with higher costs likely contributed to higher mean post-index costs. Acknowledging this, and that the uncertainty in cost estimates overall was substantial, there remained a pattern of greater reductions in costs for persistent patients compared to non-persistent patients. This contributed to an overall reduction in total costs of – 23% for persistent patients (\$3334

pre-index to \$2564 post-index) and a slight increase in total costs of 3.0% for non-persistent patients (\$3879 pre-index to \$3980 post-index) with the caveat that this increase will be influenced by the skewed cost estimate for inpatient hospitalization. Of note, this pattern was still observed in our non-erenumab CGRP pathway antagonist censored sensitivity analysis (data not shown).

## DISCUSSION

We completed a retrospective, claims-based analysis designed to understand the real-world impact of erenumab as a migraine preventive including changes in migraine characteristics, comorbidities, healthcare resource utilization, and associated costs. In the overall population of patients, the average age of the predominantly female population was 46 years. Comorbid non-migraine headaches, hypertension, anxiety, and depression were common. Almost two-thirds of patients had chronic migraine. Demographic and migraine characteristics were similar in the 6-month follow-up sample where we observed reductions in claims for migraine with aura, chronic migraine, menstrual migraine, and status migrainosus. Similarly claims for comorbidities of hypertension, anxiety, depression, and non-migraine headaches were reduced in the post-erenumab period. There was a shift to decreased use of acute and preventive medications. Reductions in the overall use and associated cost of healthcare resources such as inpatient hospitalization and outpatient office visits were minimal. Reductions that were observed in the 6-month follow-up period were generally more pronounced for the subgroup of patients that were persistent to erenumab. A notable exception was observed in the use of opioids which increased slightly overall but consistently for persistent and non-persistent patients. We also note some potentially important differences in erenumab prescribing patterns between persistent and non-persistent patients that suggest dose titration may have a role to play in persistence.

The main strengths of our study include the relatively large sample size of patients initiating

**Table 5** Patient use of healthcare utilization and associated costs in the 6 months pre- and post-erenumab stratified by persistence

	Pre-erenumab			Post-erenumab		
	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)	All ( <i>N</i> = 4437)	Erenumab persistent ( <i>N</i> = 1853)	Erenumab non- persistent ( <i>N</i> = 2584)
Inpatient hospitalizations						
Mean (SD)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.0 (0.2)	0.1 (0.3)
95% CI	(0.1, 0.1)	(0.0, 0.1)	(0.1, 0.1)	(0.0, 0.1)	(0.0, 0.1)	(0.1, 0.1)
Length of stay, days						
Mean (SD)	5.2 (3.9)	4.6 (2.5)	5.6 (4.5)	5.2 (4.3)	4.4 (3.2)	5.5 (4.7)
95% CI	(4.7, 5.7)	(4.0, 5.1)	(4.9, 6.3)	(4.6, 5.8)	(3.7, 5.2)	(4.7, 6.3)
Mean (SD) costs	\$1680 (\$9995)	\$1403 (\$8316)	\$1879 (\$11,040)	\$1696 (\$19,939)	\$957 (\$6515)	\$2227 (\$25,527)
ER visits						
Mean (SD)	0.5 (2.2)	0.5 (2.9)	0.4 (1.4)	0.4 (1.4)	0.4 (1.4)	0.4 (1.4)
95% CI	(0.4, 0.5)	(0.4, 0.6)	(0.4, 0.5)	(0.3, 0.4)	(0.3, 0.4)	(0.4, 0.5)
Mean (SD) costs	\$657 (\$3581)	\$636 (\$4227)	\$673 (\$3035)	\$533 (\$2401)	\$500 (\$2738)	\$557 (\$2127)
Outpatient office visits						
Mean (SD)	8.5 (7.9)	8.2 (7.5)	8.7 (8.2)	8.0 (7.8)	7.7 (7.2)	8.3 (8.2)
95% CI	(8.2, 8.7)	(7.9, 8.5)	(8.4, 9)	(7.8, 8.2)	(7.3, 8.0)	(8.0, 8.6)
Mean (SD) costs	\$1143 (\$1951)	\$1128 (\$2381)	\$1154 (\$1572)	\$1049 (\$1473)	\$1024 (\$1676)	\$1067 (\$1308)
Brain imaging <sup>a</sup> studies						
Mean (SD)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)
95% CI	(0.2, 0.2)	(0.1, 0.2)	(0.2, 0.2)	(0.1, 0.1)	(0.1, 0.1)	(0.1, 0.2)
Mean (SD) costs	\$170 (\$606)	\$166 (\$643)	\$173 (\$577)	\$110 (\$503)	\$84 (\$459)	\$129 (\$531)
Total associated costs <sup>b</sup> mean (SD)	\$3651 (\$11,736)	\$3334 (\$10,921)	\$3879 (\$12,285)	\$3389 (\$20,457)	\$2564 (\$7786)	\$3980 (\$25,969)

<sup>a</sup> (CT + MRI + Nuclear Med + Angiography)<sup>b</sup> Total associated costs include inpatient, ER, office visits, and brain imaging studies

preventive treatment for migraine with erenumab, the comprehensive capture of healthcare resource utilization in the MarketScan database, and the pre–post design. There are also inherent weaknesses with claims-based analyses. Use of ICD-10-CM codes and NDC/HCPCS codes to identify comorbid conditions and concomitant medications, respectively, may misclassify comorbid conditions because of sensitivity and specificity of ICD-10-CM code algorithms. Although we can assess use of prescription medications, we cannot assess use of over-the-counter prescription medications used for migraine treatments including non-prescription NSAIDs and other supplements. No data on migraine frequency or severity were available nor were reasons for non-persistence. Our results also represent patients predominantly younger than 65 years of age with commercial health insurance. Results may not be representative of the full US population. A high level of variability was observed in all cost estimates, limiting comparisons between time periods and subgroups.

Our results are generally consistent with other early real-world use reports. As expected, our erenumab patient profile was almost identical to that observed in a preliminary analysis of 1181 patient also based on MarketScan® Early View data [13] and similar to the profile observed in early analysis of other databases [14, 15]. A preliminary review of changes in acute migraine-specific medications pre- and post-erenumab initiation using pharmacy data also observed reductions in acute medication use post-erenumab [16]. Using a combined electronic health record and claims database, Tepper and colleagues [17] observed significant reductions in migraine-specific acute medication use and healthcare resource utilization. Reporting interim results from a retrospective chart-review study with select US headache centers and focusing on clinical versus medication use outcomes, Faust and colleagues [18] observed reductions in the mean number of migraine/headache days per month and the average duration of migraine/headache attacks, but also noted the continued use of a polypharmacy approach to management in their chronic migraine population. Similarly,

on the basis of data from headache centers in Italy, Ornello and colleagues [19] observed reductions in monthly migraine days, median monthly days of analgesic use, and median monthly days of triptan use.

We note that 6-month persistence was less than 50%. Although this is higher than claims-based analysis for classes of non-migraine specific medications traditionally used for migraine prevention (around 34% at 6 months for beta-blockers, tricyclic antidepressants, and topiramate with a 90-day gap to define persistence) [20], it is still lower than ideal; however, the context of our analysis is important. The time frame for our analysis covers a period of initial approval and use of a totally new class of medications and the associated evolution of understanding of this new class and the place of the class in migraine prevention. Although there was an overall reduction in the use of acute medications, preventive medications, and healthcare resource utilization for migraine in the 6-month post-erenumab period, it is important to consider the differences observed between persistent and non-persistent patients. For acute medications, the higher use of more expensive triptans in the post-erenumab period by erenumab-persistent patients was aligned with a small increase in associated costs. At the same time, increased use of less expensive opioids in non-persistent patients was aligned with a decrease in costs. As has been shown in more recent research, patients using opioids have greater overall healthcare costs compared to patients not using opioids—up to double for patients using the highest doses of opioids [21]. Thus, the trade-off between increased use of a more expensive migraine-specific acute medication and the reduced use of a less expensive but more costly overall non-migraine-specific and addictive pain medication may be more than justified.

### Limitations

This was a study of medical claims from US-centric databases. The findings from this study are specific to the US healthcare system and may not be generalizable to other countries.

Claims data lack information on frequency or severity of migraine attacks and do not distinguish among migraine subtypes. Although there is a specific ICD-10-CM code for chronic migraine (G43.7), there is no similar code for episodic migraine. This limits the ability to stratify patients by migraine category, thus potential imbalances in healthcare resource utilization between patients with varying degrees of migraine severity may make the estimates calculated less precise. However, focusing the analysis on all migraine patients is consistent with previous studies and the US prescribing information for erenumab. Additional research with adjudicated claims, longer follow-up time, and larger sample size will likely support a better characterization of the potential economic benefits of erenumab.

## CONCLUSION

In this claims-based, retrospective observational study we observed reductions in claims for important migraine characteristics, comorbidities, and a shift to decreased use of acute and preventive migraine medications in the post-erenumab follow-up period—observations indicative of the real-world effectiveness of erenumab. Further examination is required as persistence to erenumab, which may be influenced by dose change, appears to be an important factor in changes to healthcare resource utilization and costs.

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**Data Availability.** In alignment with the IBM Watson Health licensing agreement, the dataset generated and analyzed during the current study is not publicly available.

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