

Supplemental Material

Supplemental Table 1: CGRP inhibitor codes

Drug class	Drug	Earliest market date in US	NDC/HCPCS codes
Monoclonal antibody CGRP (mAb CGRP)	Erenumab	May 2018	NDC: 55513084001, 55513084100, 55513084101, 55513084301, 55513084201, 55513084300, 55513084002, 55513084102
	Galcanezumab	September 2018	NDC: 00002237727, 00002143601, 00002143627, 00002237711, 00002143611, 00002311501, 00002143661, 00002237701, 00002311509
	Fremanezumab	September 2018	NDC: 51759020411, 51759020222, 51759020410, 51759020211, 51759020210
	Eptinezumab	February 2020	NDC: 67386013051, 67386013091 HCPCS: C9063, J3032
Gepants (CGRP antagonist)	Atogepant	September 2021	NDC: 00074709530, 00074709430, 00074709604, 00074709404, 00074709630
	Rimegepant	May 2021	NDC: 72618300002, 72618300101, 72618300102

Abbreviations: CGRP = Calcitonin Gene-Related Peptide; NDC = National Drug Code; HCPCS = Prescription Claim of Administration Claim.

Supplemental Table 2: Other migraine-related medications

Treatment group	Pharmacological class	Generic names or NDC/HCPSC codes
Migraine-specific prophylactic medication		
	onabotulinumtoxinA	NDC: 54868412300; 00023114501; 00023114502; 00023392102; 00023392103; 00023391950; 00023923201 HCPSC: J0585
Non-specific migraine prophylactic medications		
	Antidepressants	Amitriptyline, nortriptyline, venlafaxine
	Antiepileptics	Gabapentin, topiramate, lamotrigine, divalproex sodium/sodium valproate
	Antihypertensives	Atenolol, metoprolol, nadolol, propranolol, timolol, candesartan, verapamil, flunarizine
Migraine-specific acute medications		
	Triptans	Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan (nasal spray, oral, subcutaneous) zolmitriptan (oral, nasal spray)
	Ergots	Dihydroergotamine, dihydroergotamine mesylate
	Gepants	Ubrogepant NDC: 00023649802, 00023650101, 00023650130, 00023649830, 00023650102, 00023649804, 00023649801, 00023650110, 00023649810, 00023649816, 00023650116 Zavegepant NDC: 00069350001, 00069350002
	Ditans	Lasmitidan NDC: 00002431208, 00002431261, 00002431262, 00002449108, 00002449161, 00002449162
Non-migraine-specific acute medications		
	Non-steroidal anti-inflammatory drugs (NSAIDs)	Diclofenac, ibuprofen, naproxen, ketorolac
	Opioids	Codeine, hydromorphone, morphine, oxycodone, tramadol, buprenorphine

Supplemental Table 3: Diseases, and their associated codes and weights included in the Charlson Comorbidity Index.

Disease ⁱ	ICD-10-CM codes	Weight
Myocardial infarction	I21, I22, I25.2	1
Congestive heart failure	I11.0, I13.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50, P29.0	1
Peripheral vascular disease	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.1, I79.8, K55.1, K55.8, K55.9, Z95.8, Z95.9	1
Cerebrovascular disease	G45, G46, I60, I61, I62, I63, I64, I65, I66, I67, I68, H34.0- H34.2	1
Dementia	F01, F02, F03, F04, F05, G30, F06.1, F06.8, G13.2, G13.8, G30, G31.0-G31.2, G91.4, R41.81, R54	1
Chronic pulmonary disease	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J68.4, J70.1, J70.3	1
Connective tissue disease	M05, M06, M31.5, M32, M33, M34, M35.1, M35.3, M36.0	1
Peptic ulcer disease	K25, K26, K27, K28	1
Mild liver disease	B18, K73, K74, K70.0, K70.1, K70.2, K70.3, K70.9, K71.7, K71.3, K71.4, K71.5, K76.0, K76.2, K76.3, K76.4, K76.8, K76.9, Z94.4	1
Moderate/severe liver disease	K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7, I85.0, I86.4	3
Diabetes (without complication)	E08-E11, E13 with E**.0x, E**.1x, E**.6x, E**.8x, E**.9x	1
Diabetes (with complication)	E08-E11, E13 with E**.2, E**.3, E**.4, E**.5	2
Hemiplegia and paraplegia	G81, G82, G04.1, G11.4, G80.0-G80.2, G83	2
Moderate or severe renal disease	N18.1-N18.6, N18.9, N19, N03, N05, I12.0, I12.9, I13.0, I13.2, I13.10, I13.11, N25, Z49, Z94.0, Z99.2	2
Cancer	C00-C29, C30-C34, C37-C41, C43, C45-C58, C60-C63, C76, C80.1, C81-C85, C88, C90-C99	2
Metastatic Carcinoma	C77-C79, C80.0, C80.2	6
HIV/AIDS	B20	6

Abbreviations: HIV/AIDS = Human immunodeficiency virus / acquired immunodeficiency syndrome; ICD-10-CM = International classification of diseases, tenth revision, Clinical Modification.

Supplemental Table 4: Case definitions using administrative data to identify comorbid conditions

Comorbidity	Algorithm	ICD-10-CM codes	Other codes
Anxiety ¹	1 hospitalization or 2 claims OR 1 claim and 2 prescription dispensations in ≤2 years	F40, F41	Generic name: Lorazepam, alprazolam (oral, EV, IM, if applicable)
Asthma ²	1 hospitalization or 3 ambulatory care visits in ≤2 years	J45	
Cardiovascular disease (any of the below) ^{3 4 5}			
			ICD-9-PCS : 0066, 3601, 3602, 3603, 3605, 3606, 3607, 3609, 361, 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619, 362, 0210
Atrial fibrillation	1 hospitalization or 2 claims in ≤2 years	I48.0	ICD-10-PCS: 0270346, 027034Z, 0270356, 027035Z, 0270366, 027036Z, 0270376, 027037Z, 02703D6, 02703DZ, 02703ZZ, 0270046, 0271346, 027134Z, 0271356, 027135Z, 0271366, 027136Z, 0271376, 027137Z, 02713D6, 02713DZ, 02714E6, 02713EZ, 02714EZ, 02723FZ, 02733GZ, 02713E6, 02723F6, 02733G6, 0272366, 0273376, 027236Z, 027337Z, 02C03ZZ, 02C13ZZ, 02C23ZZ, 02C33ZZ, 02C03Z6, 02C13Z6, 02C23Z6, 02C33Z6, 021009W, 02100A3, 02100A8, 02100A9, 02100AC, 02100AF, 02100AW CPT: 33510 – 33514, 33516 – 33519, 33520 – 33523, 33530, 33533 – 33536, 33572, 33545, 37184, 37185, 37186, 37187, 37188, 92920 – 92921, 92924 – 92925, 92928 – 92929, 92933 – 92934, 92937 – 92938, 92941, 92943-92944, 92973, 92980 – 92982, 92984, 92995 – 92996
Chronic heart failure	1 hospitalization or 2 claims in ≤2 years	I09.9, I25.5, I42.0, I42.5–I42.9, I43, I50	
Coronary artery disease	1 hospitalization or 1 ambulatory care visit or 1 procedure or 2 claims in ≤2 years	I20–I25	
Peripheral artery disease	1 hospitalization or 1 ambulatory care visit or 1 claim in any years	I70.2	
Stroke	1 most responsible stroke hospitalization or emergency department OR 1 other diagnosis stroke and 1 most responsible z-code hospitalization or ambulatory care* in any years	G45 (excluding subcode G45.4), H34.0, H34.1, I60, I61, I62.9, I63, I64, I67.6; Z50 (excluding subcodes Z50.2, Z50.3, Z50.4), Z54.8, Z54.9, *only Z51.5 applies to ambulatory care	

¹Marrie RA, Fisk JD, Yu BN, et al (2013) Mental comorbidity and multiple sclerosis: validating administrative data to support population-based surveillance. BMC Neurol 13:16.

² Tonelli M, Wiebe N, Fortin M, et al (2015) Methods for identifying 30 chronic conditions: application to administrative data. BMC Med Inform Decis Mak 15:31.

³ Boklage SH, Malangone-Monaco E, Lopez-Gonzalez L, et al (2018) Statin Utilization Patterns and Outcomes for Patients with Acute Coronary Syndrome During and Following Inpatient Admissions. Cardiovasc Drugs Ther 32:273-280

⁴ Kumar A, Lutsey PL, St Peter WL, et al (2023) Prescription patterns of P2Y12 inhibitors following revascularization in the United States: 2013-2018. Clin Transl Sci 16:1886-1897.

⁵ Hwang YJ, Chang HY, Metkus T, et al (2024) Risk of Major Bleeding Associated with Concomitant Direct-Acting Oral Anticoagulant and Clopidogrel Use: A Retrospective Cohort Study. Drug Saf 47:251-260.

			HCPCS: C9600 - C9606, G0290 - G0291
Depression ⁶	1 hospitalization or 2 claims in ≤2 years	F32-F33, F34.1	
Epilepsy ⁷	1 hospitalization or 2 claims in ≤2 years	G40, G41	
Hypertension ²	1 hospitalization or 2 claims in ≤2 years	I10–I13, I15	
Obstructive sleep apnea ⁸	1 hospitalization or 2 claims in ≤2 years	G47.3	

⁶ Doktorchik C, Patten S, Eastwood C, et al (2019) Validation of a case definition for depression in administrative data against primary chart data as a reference standard. BMC Psychiatry 19:9.

⁷ Reid AY, St Germaine-Smith C, Liu M, et al (2012) Development and validation of a case definition for epilepsy for use with administrative health data. Epilepsy Res 102:173-179.

⁸ Laratta CR, Tsai WH, Wick J, et al (2017) Validity of administrative data for identification of obstructive sleep apnea. J Sleep Res 26:132-138.

Supplemental Table 5: Definition of medical healthcare encounters

Healthcare encounter type	Definition
Migraine-related hospitalization	Hospitalization records where the main diagnosis ⁹ indicates G43
Migraine-related emergency department (ED) visit ¹⁰	Include both inpatient and outpatient ED visits where any of the four diagnosis fields indicate G43 and the last two digits of the service sub-category code (SVCSCAT variable) are 20 (e.g., code 12220, which indicates a Facility Outpatient Emergency Room).
Migraine-related ambulatory care visits ¹⁰	Include all records classified as ED visits (see above), as well as both inpatient and outpatient records where any of the four diagnosis fields indicate G43 and the place of service (variable STDPLAC) is 22 (Outpatient Hospital).
Migraine-related outpatient physician visits ¹⁰	Include outpatients encounters where any of the four diagnosis fields indicate G43 and the variable STDPLAC is 11 (Office) or 22 (Outpatient Hospital) and the SVCSCAT variable is a physician visit/procedure (indicated by any of the following codes): 21115, 21124, 21125, 21199, 21215, 21224, 21225, 21299

⁹ In MarketScan, the main hospital diagnosis is represented by the principal diagnosis, which typically reflects the primary reason for admission and is usually the discharge diagnosis.

¹⁰ Multiple visits occurring on the same date were combined into a single occurrence

Supplemental Table 6: Demographic and baseline clinical characteristics of Calcitonin Gene-Related Peptide (CGRP) inhibitors users, MarketScan, US, 2018 – 2022

Characteristics ¹¹	CGRP inhibitor users N = 55,212
Demographic	
Age (years)	
Mean (SD)	43.9 (11.8)
Median (Q1-Q3)	45 (36-52)
Age (years): n (%)	
18-44	27,064 (49.0)
45-64	27,242 (49.3)
65+	906 (1.6)
Female sex: n (%)	47,412 (85.9)
Urban residence location: n (%)	48,096 (87.1)
Comorbidities	
Charlson comorbidity index	
Mean (SD)	0.6 (1.3)
Median; (Min, Max)	0 (0-1)
Category, n (%)	
0: no comorbid condition	38,469 (69.7)
1-2: mild comorbidity	12,079 (21.9)
≥3: moderate/severe comorbidity	4664 (8.5)
Comorbid condition¹², n (%)	

¹¹ Characteristics of CGRP inhibitor users were assessed within one year prior to the first dispensation date of a CGRP inhibitor.

¹² To be considered as having one of the listed diseases, a subject must have ≥1 hospitalization (associated ICD-10-CM code listed in any diagnostic field) or ≥2 physician claims (associated ICD-10-CM codes listed in any diagnostic field) of the corresponding ICD within ≤1-years

Cardiovascular disease	2,324 (4.2)
Depression	13,527 (24.5)
Anxiety	16,833 (30.5)
Asthma	5,556 (10.1)
Epilepsy	1,542 (2.8)
Hypertension	13,112 (23.8)
Obstructive sleep apnea	6,320 (11.5)

CGRP = Calcitonin Gene-Related Peptide; SD = Standard Deviation; Q1-Q3 = First and Third quartiles

Supplemental Table 7: Treatment pattern (one-year follow-up) according to initial Calcitonin Gene-Related Peptide (CGRP) inhibitors, MarketScan, US, 2018 – 2022.

N=	Initial CGRP					
	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant ¹³
	29,582	24,532	12,257	167	124	6,596
Switching to a subsequent CGRP inhibitor, n (%)						
Overall	3,709 (12.5)	1,875 (7.6)	1,184 (9.7)	16 (9.6)	12 (9.7)	741 (11.2)
Erenumab	-	707 (37.7)	378 (31.9)	1 (6.3)	1 (8.3)	165 (22.3)
Galcanezumab	1,916 (51.7)	-	498 (42.1)	2 (12.5)	1 (8.3)	266 (35.9)
Fremanezumab	1,191 (32.1)	514 (27.4)	-	1 (6.3)	1 (8.3)	187 (25.2)
Eptinezumab	22 (0.6)	35 (1.9)	18 (1.5)	-	2 (16.7)	14 (1.9)
Atogepant	42 (1.1)	48 (2.6)	36 (3.0)	1 (6.3)	-	109 (14.7)
Rimegepant ¹³	538 (14.5)	571 (30.5)	254 (21.5)	11 (68.8)	7 (58.3)	-
Switching to onabotulinumtoxinA injection, n (%)	3,163 (10.7)	2,226 (9.1)	1,229 (10.0)	26 (15.6)	15 (12.1)	824 (12.5)
Switching to non-migraine specific prophylaxis, n (%)	8,861 (30.0)	8,029 (32.7)	3,580 (29.2)	46 (27.5)	28 (22.6)	1,737 (26.3)
Concomitant treatment with onabotulinumtoxinA injection, n (%)	1,668 (5.6)	998 (4.1)	654 (5.3)	26 (15.6)	5 (4.0)	390 (5.9)
Concomitant treatment with non-specific migraine prophylaxis, n (%)	4,130 (14.0)	3,461 (14.1)	1,872 (15.3)	30 (18.0)	14 (11.3)	562 (8.5)
Treatment break, n (%)	462 (1.6)	344 (1.4)	194 (1.6)	3 (1.8)	1 (0.81)	297 (4.5)
Discontinuation, n (%)	3,419 (11.6)	3,297 (13.4)	1,653 (13.5)	13 (7.8)	32 (25.8)	1,452 (22.0)

CGRP = Calcitonin Gene-Related Peptide

¹³Individuals on rimegepant were included as of May 27, 2021 onwards and only for dispenses with 30 or more days' supply

Supplemental Table 8: Longitudinal treatment patterns of Calcitonin Gene-Related Peptide (CGRP) inhibitor users, MarketScan, US, 2018 – 2022

	Time from CGRP inhibitor initiation (in days)		Probability of event (%)	
	Mean (SE)	Median	At 1 year (95% CI)	At 2-year (95% CI)
First switch from an initial to a subsequent CGRP inhibitor	1,269 (1.8)	NE	11.3 (11.1-11.5)	16.8 (16.6-17.1)
First switch from a CGRP inhibitor to onabotulinumtoxinA injection	1,319.3 (1.7)	NE	11.9 (11.7-12.1)	13.4 (13.2-13.6)
First treatment break	1,415.1 (1.0)	NE	2.4 (2.3-2.5)	4.8 (4.6-5.0)
Discontinuation	1,177.3 (2.6)	1,575 (1553-1591)	15.7 (15.4-15.9)	29.3 (29.0-29.7)

CGRP = Calcitonin Gene-Related Peptide; NE: Not Estimated; SE = Standard Error; CI = Confidence Interval