

Medical Policy



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Title: **CGRP (calcitonin gene-related peptide)**

➤ **Prime Therapeutics will review Prior Authorization requests**

Prior Authorization Form:

<https://www.bcbsks.com/CustomService/Forms/pdf/PriorAuth-6633KS-CGRP.pdf>

Link to Drug List (Formulary):

<https://www.bcbsks.com/drugs/>

Professional

Original Effective Date: May 22, 2018
Revision Date(s): May 22, 2018;
August 1, 2018; October 15, 2018;
October 22, 2018; October 29, 2018
Current Effective Date: October 29, 2018

Institutional

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Revision Date(s): May 22, 2018;
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October 22, 2018; October 29, 2018
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DESCRIPTION

The intent of the CGRP prior authorization with quantity limit is to encourage appropriate use according to clinical trial data.

FDA Labeled Indications¹⁻³

Agent	Indication	Dosage and Administration	Limitation of Use
Aimovig™ (erenumab) subcutaneous autoinjector, subcutaneous prefilled syringe	Preventive treatment of migraine in adults	Recommended dose is 70 mg once monthly Some patients may benefit from 140 mg once monthly	None
Ajovy™ (fremanezumab) subcutaneous prefilled syringe	Preventive treatment of migraine in adults	225 mg monthly, or 675 mg every 3 months (quarterly), which is administered as three consecutive subcutaneous injections of 225 mg each.	None
Emgality™ (galcanezumab) subcutaneous autoinjector, subcutaneous prefilled syringe	Preventive treatment of migraine in adults	240 mg loading dose (administered as two consecutive injections of 120 mg each), followed by monthly doses of 120 mg.	None

POLICY**Prior Authorization and Quantity Limit Criteria for Approval****Initial Approval**

Target Agents will be approved when ALL of the following are met:

1. ONE of the following:
 - a. The patient has a diagnosis of chronic migraine as defined by BOTH of the following:
 - i. ≥15 headache days per month of migraine-like or tension-like headache for a minimum of 3 months

AND

 - ii. ≥8 migraine headache days per month for a minimum of 3 months

OR

- b. BOTH of the following:
 - i. The patient has a diagnosis of episodic migraine AND ONE of the following:
 1. The patient has >4 migraine headaches per month

OR

2. The patient's migraine headaches last >12 hours
OR
3. The patient's migraine attacks cause significant disability or diminished quality of life despite appropriate acute treatment
OR
4. The patient has contraindications to acute therapies
OR
5. The patient has tried and received inadequate response to acute therapies
OR
6. The patient has serious side effects to acute therapies
OR
7. The patient is at risk of medication overuse headache without preventative therapy

AND

- ii. The request is for Aimovig (erenumab), Ajovy (fremanezumab), OR Emgality (galcaezumab)

AND

2. ONE of the following:
 - a. The patient has failed at least two migraine prophylaxis classes (anticonvulsants [divalproex, valproate, topiramate], beta blockers [atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [amitriptyline, venlafaxine]) after an adequate trial as defined by BOTH of the following:
 - i. The trial length was at least 6 weeks at generally accepted doses
AND
 - ii. The patient was $\geq 80\%$ adherent to the prophylaxis agent during the trial
 - b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to an anticonvulsant, a beta blocker, AND an antidepressant listed above

AND

3. The patient has not received botulinum toxin injection for headache prophylaxis in the past 4 months

AND

4. The patient will not be initiating botulinum toxin headache prophylaxis after starting the requested agent

AND

5. The patient has been evaluated for and does not have medication overuse headache

AND

6. ONE of the following:
 - a. The patient is not currently taking another CGRP agent
OR
 - b. The other CGRP agent will be discontinued prior to beginning therapy with the requested agent
AND
7. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist
AND
8. The patient does not have any FDA labeled contraindication(s) to the requested agent
AND
9. ONE of the following:
 - a. The requested quantity (dose) is NOT greater than the program quantity limit
OR
 - b. ALL of the following:
 - i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) is less than or equal to the maximum FDA labeled dose
AND
 - iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
 - c. ALL of the following:
 - i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) is greater than the maximum FDA labeled dose
AND
 - iii. The prescriber has submitted documentation in support of therapy with a higher dose for an accepted diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 3 months

For agents that require a loading dose for new starts, approve the loading dose noted with the quantity limits table above AND the maintenance dose for the remainder of 3 months.

Renewal Approval

Target Agents will be approved when ALL of the following are met:

1. The patient has been approved for the requested agent previously through the Prime Therapeutics Prior Authorization process
AND
 2. The prescriber has submitted documentation indicating improvement in migraine prevention (e.g. reduced migraine headache days, reduced migraine frequency, reduced use of acute abortive migraine medication) with the requested agent
AND
 3. The patient has not received botulinum toxin injection for headache prophylaxis in the past 4 months
AND
 4. The patient will not be initiating botulinum toxin headache prophylaxis while using the requested agent
AND
 5. The patient has been evaluated for and does not have medication overuse headache
AND
 6. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist
AND
 7. The patient does not have any FDA labeled contraindication(s) to the requested agent
AND
 8. ONE of the following:
 - a. The requested quantity (dose) is NOT greater than the program quantity limit
OR
 - b. ALL of the following:
 - i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) is less than or equal to the maximum FDA labeled dose
AND
 - iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
- OR**

- c. ALL of the following:
- i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) is greater than the maximum FDA labeled dose
AND
 - iii. The prescriber has submitted documentation in support of therapy with a higher dose for an accepted diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

FDA Labeled Contraindications	
Agent	Contraindications
Aimovig (erenumab)	None
Ajovy (fremanezumab)	Patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients
Emgality (galcanezumab)	Patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients

Brand (generic)	Quantity Limit
Aimovig (erenumab)	
70 mg/mL autoinjector; 1 pack	1 autoinjector (1 mL) / 30 days ^a
70 mg/mL autoinjector; 2 pack	2 autoinjectors (2 mL) / 30 days ^a
70 mg/mL prefilled syringe	2 prefilled syringes (2 mL) / 30 days ^a
Ajovy (fremanezumab)	
225 mg/1.5 mL prefilled syringe	3 prefilled syringes (4.5 mL) / 90 days
Emgality (galcanezumab)	
120 mg/mL autoinjector	1 autoinjector (1 mL) / 30 days ^b

a – quantity limit is cumulative to 2 x 70 mg injections per month between dosage forms

b – Loading dose is 2 autoinjectors (2 mL) / 30 days

RATIONALE

The calcitonin gene-related peptide (CGRP) is a therapeutic target in migraine because of its hypothesized role in mediating trigeminovascular pain transmission and the vasodilatory component of neurogenic inflammation.⁴

The diagnostic criteria for chronic migraine requires the inclusion of all of the following:¹⁰

- A. Headache (migraine-like or tension-like) on ≥ 15 days per month for >3 months and fulfilling criteria B and C
- B. Occurring in a patient who has had at least five attacks fulfilling of migraine without aura and/or migraine with aura

- C. On ≥ 8 days per month for >3 months, fulfilling any of the following:
 1. Migraine without aura
 2. Migraine with aura
 3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative
- D. Not better accounted for by another ICHD-3 diagnosis.

Migraine prevention may be of benefit in those with the following:^{4,9,13}

- Frequent or long lasting migraine headaches (>4 headaches/month or headaches lasting >12 hours)
- Migraine attacks that cause significant disability or diminished quality of life despite appropriate acute treatment
- Contraindication to acute therapies
- Failure of acute therapies
- Serious adverse effects of acute therapies
- Risk of medication overuse headache
- Menstrual migraine (when acute abortive therapies are incomplete or unsatisfactory)¹²

Preventative pharmacotherapy for chronic migraine is less well studied than for episodic migraine. However, use of recommended episodic prevention agents is also recommended in chronic migraine. Clinical trials suggest efficacy is often first noted at four weeks and can continue to increase for three months.⁴

The American Headache Society and the American Academy of Neurology suggest the following agents for the prevention of migraine:⁹

- Established as effective
 - Antiepileptic drugs (AEDs)
 - Divalproex
 - Valproate
 - Topiramate
 - Beta blockers
 - Metoprolol
 - Propranolol
 - Timolol
 - Triptans
 - Frovatriptan for short term menstrually associated migraines (MAMs) prevention
- Probably effective
 - Antidepressants
 - Amitriptyline
 - Venlafaxine
 - Beta blockers
 - Atenolol
 - Nadolol
 - Triptans
 - Naratriptan, zolmitriptan for short term MAMs prevention

Erenumab

Erenumab was studied in chronic migraine in a randomized, double-blind, placebo-controlled, phase 2 study. 656 men and women aged 18-65 years with a history of chronic migraine (with or without aura) were enrolled. In each of the 3 months before screening, patients had to have had 15 or more headache days per month, of which 8 or more of those days were migraine days. Patients were also required to be 80% compliant with their headache logs. Patients were excluded if they were older than 50 years at migraine onset and if they had a history of cluster headache or hemiplegic migraine, or chronic migraine with continuous pain. Patients were also excluded from the study if they had no therapeutic response (reduction in frequency, duration, or severity of headache) with prophylaxis of more than three treatment categories after an adequate trial (at least 6 weeks of treatment at generally accepted doses). Migraine preventive drugs were prohibited during the study and 2 months before the start of the baseline phase. Botulinum toxin injections in the head or neck region were prohibited during the study and for at least 4 months before the start of the baseline phase. At baseline, the monthly migraine days was 18.2 (SD 4.7) for the placebo group, 17.9 (SD 4.4) for the erenumab 70 mg group, and 17.8 (SD 4.7) for the 140 mg erenumab group. Monthly headache days was 21.1 (SD 3.9) for placebo, 20.5 (SD 3.8) for 70 mg erenumab group, and 20.7 (SD 3.8) mg for 140 erenumab group. Monthly acute migraine-specific drug use days was 9.6 (SD 7.6) for placebo, 8.8 (SD 7.2 for erenumab 70 mg, and 9.7 (SD 7.0) for erenumab 140 mg. Study outcomes were assessed after 12 weeks:⁵

- Monthly migraine days reduction was -4.2 (SE 0.4) days for placebo, 6.6 (SE 0.4) days for erenumab 70 mg and 140 mg.
- Both doses of erenumab showed a statistically significant difference in reduction of -2.5 (CI -3.5 to -1.4) days in monthly migraine days vs. placebo.
- Erenumab also exhibited statistically significant higher number of patients who were 50% responders (decrease of at least 50% migraine days vs. baseline) vs placebo. However, the percentage of 50% responders in both dosage strengths was in the minority (40% for 70 mg, 41% for 140 mg, 23% for placebo).
- There was a statistically significant difference in reduction of monthly acute migraine-specific drug treatment days for erenumab vs. placebo (-1.9 days vs placebo for 70 mg, -2.6 days vs placebo for 140 mg).
- There was not a statistically significant difference in cumulative monthly headache hours vs. placebo.

Erenumab's efficacy in episodic migraines was examined in two studies. Study 1 included 955 patients with episodic migraines. Patients were randomly assigned to either placebo, 70 mg of erenumab, or 140 mg erenumab. Patients had to have at least 4 and fewer than 15 migraine days per month and fewer than 15 headache days per month on average during the 3 month screening period. Exclusion criteria included having received botulinum toxin within 4 months before or during the baseline phase, used devices or procedures for migraine prevention within 2 months before the baseline phase, or had had no therapeutic response to more than two migraine-preventive treatment categories. The study allowed enrollment of patients with concomitant use of 1 migraine preventative medication at a stable dose. Study outcomes were assessed after 24 weeks. Baseline and outcomes results are presented in Table 1 below.⁶

Table 1.

	Placebo	Erenumab 70 mg	Erenumab 140 mg
Baseline migraine days per month	8.2 (SD 2.5)	8.3 (SD 2.5)	8.3 mg (SD 2.5)
Baseline days of acute migraine-specific medication per month	3.4 (SD 3.4)	3.2 (SD 3.4)	3.4 (SD 3.5)
Monthly MPFID score	13.7 (SD 9.1)	14.0 (SD 8.9)	13.1 (SD 8.3)
Monthly MPFID physical-impairment score	12.2 (SD 9.4)	12.6 (SD 9.6)	12.0 (SD 9.0)
Primary endpoint - reduction from baseline in migraine days per month	-1.8 (SE 0.2)	-3.2 (SE 0.2)	-3.7 (SE 0.2)
Difference in reduction from baseline in migraine days per month vs. placebo	NA	-1.4 (95% CI -1.9 to -0.9)	-1.9 (95% CI -2.3 to -1.4)
Change from baseline in days of use of acute migraine-specific medication per month	-0.2 (SE 0.1)	-1.1 (SE 0.1)	-1.6 (SE 0.1)
Difference in reduction from baseline in days of use of acute migraine-specific medication vs. placebo	NA	-0.9 (95% CI -1.2 to -0.6)	-1.4 (95% CI -1.7 to -1.1)
Change in monthly MPFID everyday-activities score	-3.3 (SE 0.4)	-5.5 (SE 0.4)	-5.9 (SE 0.4)
Difference in reduction in monthly MPFID everyday-activities score vs. placebo	NA	-2.2 (95% CI -3.3 to -1.2)	-2.6 (95% CI -3.6 to -1.5)
Change in monthly MPFID physical-impairment score	-2.4 (SE 0.4)	-4.2 (SE 0.4)	-4.8 (SE 0.4)
Difference in reduction in monthly MPFID physical-impairment score vs. placebo	NA	-1.9 (95% CI -3.0 to -0.8)	-2.4 (95% CI -3.5 to -1.4)

MPFID - Migraine Physical Function

Study 2 was a randomized, multi-center, 3-month, placebo-controlled, double-blind study evaluating erenumab for the preventive treatment of episodic migraine. A total of 577 patients with a history of episodic migraine were randomized to receive either erenumab 70 mg (N = 286) or placebo (N = 291) by subcutaneous injection once monthly for 3 months. Exclusion criteria included use of botulinum toxin, patients with no response to >2 prophylactic treatments for migraine, and patients with medication overuse headache. Patients were allowed use of only 1 prophylactic medication during the study if the dosing for the prophylactic medication was stable within 2 months prior to the start of therapy. Results of the study are summarized in table 2 below:¹¹

Table 2.

	Aimovig 70 mg once monthly	Placebo
Monthly Migraine Days (MMD)		
Change from baseline	-2.9	-1.8
Difference from placebo	-1.0	
p-value	<0.001	
≥50% MMD responders		
% Responders	39.7%	29.5%
Difference from placebo	10.2%	
Odds ratio relative to placebo	1.6	
p-value	0.01	

	Aimovig 70 mg once monthly	Placebo
Monthly acute migraine-specific medication days		
Change from baseline	-1.2	-0.6
Difference from placebo	-0.6	
p-value	0.002	

In the episodic studies, 10-20% of patients on erenumab either did not see a reduction or saw an increase in migraine days per month vs. 25-30% for placebo.^{6,11}

Fremanezumab

Fremanezumab was studied in a double-blind, randomized, placebo-controlled, phase 3 trial with 1130 patients. Individuals were randomized to receive placebo, fremanezumab quarterly, or fremanezumab monthly. Inclusion criteria included an age of 18-70 years, a history of migraine for at least 12 months, history of chronic migraine (headache of any duration or severity on ≥ 15 days and migraine headache on ≥ 8 days) during the 28 days prior to intervention. Up to 30% of patients using a stable dose of one migraine-preventive medication for at least 2 months were allowed to continue these medications. Key exclusion criteria were the use of onabotulinum toxin A during the 4 months before screening, the use of interventions or devices for migraine such as nerve blocks and transcranial magnetic stimulation during the 2 months before screening, the use of opioids or barbiturates on more than 4 days prior to intervention, and lack of efficacy of at least two or four clusters of preventative medications after an adequate therapeutic trial. Study outcomes were assessed after 12 weeks:⁷

- The primary endpoint of least squares mean change from baseline of average number of headache days per month was -4.3 (SE 0.3) for fremanezumab administered quarterly, -4.6 (SE 0.3) for fremanezumab administered monthly, and -2.5 (SE 0.3) for placebo. The difference between placebo and the two fremanezumab arms were statistically significant.
- The least squares mean change from baseline in average number of migraine headache days per month was -4.9 (SE 0.4) for fremanezumab administered quarterly, -5.0 (SE 0.4) for fremanezumab administered monthly, and -3.2 (SE 0.4) for placebo. The difference between placebo and the two fremanezumab arms were statistically significant.
- The percentage of patients with $\geq 50\%$ reduction in average number of headache days per month was 38% for fremanezumab administered quarterly, 41% for fremanezumab administered monthly, and 18% for placebo.
- The least squares mean change from baseline in average number of days of use of any acute headache medication per month was -3.7 (SE 0.3) for fremanezumab administered quarterly, -4.2 (SE 0.3) for fremanezumab administered monthly, and -1.9 (SE 0.3) for placebo. The difference between placebo and the two fremanezumab arms were statistically significant.
- 79% of the fremanezumab administered quarterly, 77% of the fremanezumab administered monthly, and 79% of placebo arms were not receiving concomitant preventative medications. The least squares mean change from baseline in average number of headache days per month for these patients was -4.6 (SE 0.3) for fremanezumab administered quarterly, -4.8 (SE 0.3) for fremanezumab administered monthly, and 2.6 (SE 0.3) for placebo. The difference between placebo and the two fremanezumab arms were statistically significant.
- The average number of headache days per month showed statistically significant differences between the two fremanezumab arms and placebo during the 4 weeks period after the first dose.

Galcanezumab

Galcanezumab was studied in a phase 2b trial in patients with episodic migraine. 936 patients were randomized to 1 of 5 treatment groups (2:1:1:1:1 ratio) to receive either placebo or 1 galcanezumab dose level (5, 50, 120, or 300mg), respectively. The study was separated into 4 study periods (SP). SP 1 (4-45 days) was for screening and washout. SP 2 (28-38 days) was the prospective baseline period for evaluating the frequency of migraine headache days (MHDs). SP 3 (3 months) was the double-blinded treatment period. And SP 4 (3 months) was the post-treatment period. Galcanezumab or placebo was administered by subcutaneous (SC) injection once monthly during office visits. Patients were required to track daily headache information starting in SP2. During the study, acute migraine treatments were allowed as needed (opioids or barbiturates were not permitted). Concomitant medications allowed included acetaminophen, nonsteroidal anti-inflammatory drugs, aspirin, triptans, corticosteroids (periodic topical or inhaled but not oral or injected), and ergotamines and their derivatives. Preventive treatments were permitted only during SP 4 at the discretion of the investigator. Patients were men and women 18 to 65 years of age with a history of migraine, with or without aura, for at least 1 year prior to enrollment. For inclusion, patients had to experience a frequency of 4 to 14 MHDs and at least 2 migraine attacks in a 28-day period during SP 2. Migraine onset must have occurred prior to age 50 years. Use of botulinum toxin A and B administered in the head or neck area must have been discontinued at least 4 months prior to SP 2. Patients were excluded from study participation for any of the following reasons: currently enrolled in or discontinued within the last 30 days from a clinical trial using any investigational drug or device; any current or previous exposure to a CGRP or nerve growth factor antibody; history of hemiplegic, ophthalmoplegic, or basilar-type migraine; history or presence of other medical illness indicating a medical problem that would preclude study participation; failure to respond to more than 2 effective migraine preventive treatments; evidence of significant active psychiatric disease; and pregnancy or lactation. Patients should have completed at least 80% of daily headache log entries during SP 2. The mean (SD) MHDs per month at baseline was 6.6 (2.7) and 6.7 (2.6) for placebo and galcanezumab respectively. The mean (SD) migraine attacks per month was 4.7 (1.5) and 4.7 (1.6) for placebo and galcanezumab respectively. The primary objective was to assess whether at least 1 dose of galcanezumab was superior to placebo in the prevention of migraine. The posterior probability of greater improvement in MHDs with galcanezumab, 120 mg (99.6%; -4.8 MHDs, 90% BCI, -5.4 to -4.2 MHDs) compared with placebo (-3.7 MHDs, 90% BCI, -4.1 to -3.2 MHDs) was greater than the specified threshold (95%) for the mean change from baseline in the number of MHDs at month 3. Least square (LS) mean change from baseline for secondary outcomes was statistically significantly different between galcanezumab, 120mg, and placebo at month 3 except for headache days: migraine plus probable MHDs (-5.9; 95% CI, -6.7 to -5.1; P < .001) vs placebo (-4.0; 95% CI, -4.6 to -3.4), probable MHD (-0.9; 95% CI, -1.3 to -0.6; P = .049) vs placebo (-0.5; 95% CI, -0.8 to -0.3), migraine attacks (-3.5; 95% CI, -3.9 to -3.0; P = .003) vs placebo (-2.7; 95% CI, -3.0 to -2.3), 50% response rate (47/62 [75.8%]; P = .03) vs placebo (78/126 [61.9%], and 100% response rate (22/62 [35.5%]; P = 0.04) vs. placebo (29/126 [23.0%]).⁸

Safety

Erenumab has no FDA labeled contraindications or black box warnings.¹

Contraindications to fremanezumab include:²

- patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients

Fremanezumab has no black box warnings.²

Contraindications to galcanezumab include:³

- patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients

Galcanezumab has no black box warnings.³

REVISIONS	
05-22-2018	Policy published 05-23-2018. Policy retro-effective to 05-22-2018.
	Policy added to the bcbsks.com web site.
08-01-2018	<p>In Policy section:</p> <p><u>Initial Approval</u></p> <ul style="list-style-type: none"> ▪ Removed "The patient is within the age range as recommended by the FDA label" ▪ In Item 1 added "b. BOTH of the following: <ol style="list-style-type: none"> i. The patient has a diagnosis of episodic migraine AND ONE of the following: <ol style="list-style-type: none"> 1. The patient has >4 migraine headaches per month OR 2. The patient's migraine headaches last >12 hours OR 3. The patient's migraine attacks cause significant disability or diminished quality of life despite appropriate acute treatment OR 4. The patient has contraindications to acute therapies OR 5. The patient has tried and received inadequate response to acute therapies OR 6. The patient has serious side effects to acute therapies OR 7. The patient is at risk of medication overuse headache without preventative therapy ii. The request is for Aimovig (erenumab)" <p><u>Initial and Renewal Approval</u></p> <ul style="list-style-type: none"> ▪ In Item 9 b ii and 8 b ii added "maximum" to read "The requested quantity (dose) is less than or equal to the maximum FDA labeled dose" ▪ In Item 9 c ii and 8 c ii added "maximum" to read "The requested quantity (dose) is greater than the maximum FDA labeled dose" ▪ In Item 9 c iii and 8 c iii removed "the intended" and added "an accepted" to read "The prescriber has submitted documentation in support of therapy with a higher dose for an accepted diagnosis..." ▪ Quantity Limit chart updated <p>Rationale section updated</p> <p>References updated</p>
10-15-2018	<p>Policy Published November 7, 2018. Policy retro-effective to October 15, 2018.</p> <p>Description section updated to add Ajovy as a target agent.</p> <p>In Policy section:</p> <ul style="list-style-type: none"> ▪ In Item 1 b ii added "OR Ajovy (fremanezumab)" to read "The request is for Aimovig (erenumab) OR Ajovy (fremanezumab)" ▪ Updated FDA Labeled Contraindications and Quantity Limits charts to add Ajovy <p>Rationale section updated</p> <p>References updated</p>
10-22-2018	<p>Policy Published November 7, 2018. Policy retro-effective to October 22, 2018.</p> <p>In Policy section:</p> <ul style="list-style-type: none"> ▪ In Initial Approval Item 7 and Renewal Approval Item 6 added "pain management specialist; or specialist with" to read "The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist"

REVISIONS	
10-29-2018	Policy Published November 7, 2018. Policy retro-effective to October 29, 2018.
	Description section updated to add Emgality as a target agent.
	In Policy section: <ul style="list-style-type: none"> ▪ In Item 1 b ii added "OR Emgality (galcaezumab)" to read "The request is for Aimovig (erenumab), OR Ajovy (fremanezumab), OR Emgality (galcaezumab)" ▪ In Length of Approval added "For agents that require a loading dose for new starts, approve the loading dose noted with the quantity limits table above AND the maintenance dose for the remainder of 3 months." ▪ Updated FDA Labeled Contraindications and Quantity Limits charts to add Emgality
	Rationale section updated
	References updated

REFERENCES

1. Aimovig prescribing information. Amgen, Inc. May 2018.
2. Ajovy prescribing information. TEVA Pharmaceuticals. July 2018.
3. Emgality prescribing information. Eli Lilly. September 2018.
4. Preventative treatment of migraine in adults. UptoDate. Current through 12/2017. Last updated 12/2017
5. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomized, double-blind placebo-controlled phase 2 trial. *Lancet Neurology*. 2017; 16: 425–34.
6. Goadsby PJ, Reuter U, Hallström Y, et al. A controlled trial of erenumab for episodic migraine. *The New England Journal of Medicine*. 2017; 377: 2123-32.
7. Pending launch of drug - Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the preventive treatment of chronic migraine. *The New England Journal of Medicine*. 2017; 377: 2113-22.
8. Pending launch of drug - Skljarevski V, Oakes TM, Zhang Q, et al. Effect of different doses of galcanezumab vs placebo for episodic migraine prevention - a randomized clinical trial. *JAMA Neurology*. Published online December 18, 2017.
9. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78(17):1337.
10. ICHD-3 Classification. International Headache Society. 2018. Accessed 2/12/2018
11. Dodick DW, Ashina M, Brandes JL, et al. ARISE: A Phase 3 randomized trial of erenumab for episodic migraine. *Cephalalgia*. 2018;38(6).
12. Estrogen-associated migraine. UptoDate. Current through 5/2018. Last updated 5/2017.
13. Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. September 26, 2000; 55 (6)