# Clinical Policy: Galcanezumab-gnlm (Emgality)

Reference Number: HIM.PA.SP67
Effective Date: 10.01.20
Last Review Date: 08.25
Line of Business: HIM

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Galcanezumab-gnlm (Emgality®) is a calcitonin gene-related peptide (CGRP) receptor antagonist.

## FDA Approved Indication(s)

Emgality is indicated in adults for the:

- Preventive treatment of migraine
- Treatment of episodic cluster headache

## Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Emgality is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Migraine Prophylaxis** (must meet all)**:**

1. Diagnosis of episodic or chronic migraine;
2. Provider's attestation that member experiences ≥ 4 migraine days per month for at least 3 months;
3. Age ≥ 18 years;
4. Failure of at least 2 of the following oral migraine preventative therapies, each for 8 weeks and from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated: antiepileptic drugs (e.g., divalproex sodium, sodium valproate, topiramate), beta-blockers (e.g., metoprolol, propranolol, timolol), antidepressants (e.g., amitriptyline, venlafaxine);
5. If currently receiving treatment with Botox® for migraine prophylaxis and request is for concurrent use of Botox and Emgality (i.e., not switching from one agent to another), all of the following (a, b, and c):
   a. Sufficient evidence is provided from at least two high-quality*, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      **Case studies or chart reviews are not considered high-quality evidence*
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes such as a reduction in monthly migraine or headache days;

iv. Appropriate experimental design and method to address research questions (*see Appendix E for additional information*);

b. Member has experienced and maintained positive response to Botox monotherapy as evidenced by a ≥ 30% reduction in migraine days per month from baseline following at least 2 quarterly injection (6 months) of Botox monotherapy;

c. Despite Botox monotherapy, member continues to experience ≥ 4 migraine days per month and/or severe migraine headaches that result in disability and functional impairment;

6. Emgality is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig®, Ajovy®, Nurtec® ODT, Qulipta™, Ubrelvy™, Vyepti™, Zavzpret™);
7. Dose does not exceed:
   a. Loading dose: 240 mg (2 injections) once;
   b. Maintenance dose: 120 mg (1 injection) once monthly.

**Approval duration: 3 months**

**B. Episodic Cluster Headaches** (must meet all)**:**

1. Diagnosis of episodic cluster headaches;
2. Provider's attestation that member has a history of ≥ 2 cluster periods lasting from 7 days to 1 year each and separated by ≥ 3 months;
3. Age ≥ 18 years;
4. Failure of verapamil at a dose of 360 mg per day, unless contraindicated or clinically significant adverse effects are experienced;
5. Emgality is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig, Ajovy, Nurtec ODT, Qulipta, Ubrelvy, Vyepti, Zavzpret);
6. Dose does not exceed both of the following (a and b):
   a. 300 mg once monthly;
   b. 3 injections once monthly.

**Approval duration: 12 months**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

**II. Continued Therapy**

**A. Migraine Prophylaxis** (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member has experienced and maintained positive response to therapy as evidenced by provider's attestation of a reduction in migraine days per month from baseline;
3. Emgality is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig, Ajovy, Nurtec ODT, Qulipta, Ubrelvy, Vyepti, Zavzpret);
4. If request is for a dose increase, new dose does not exceed 120 mg (1 injection) once monthly.

**Approval duration: 6 months**

**B. Episodic Cluster Headaches** (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by provider's attestation of a reduction in cluster headache attack frequency;
3. Provider's attestation or pharmacy claims history to confirm that member meets one of the following (a or b):
   a. Member has not received more than 12 months of consecutive treatment;
   b. It has been at least 3 months since the member last received Emgality;
4. Emgality is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig, Ajovy, Nurtec ODT, Qulipta, Ubrelvy, Vyepti, Zavzpret);
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 300 mg once monthly;
   b. 3 injections once monthly.

**Approval duration: 12 months**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;

**B.** Chronic cluster headaches.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CGRP: calcitonin gene-related peptide
FDA: Food and Drug Administration
ICHD: International Classification of Headache Disorder

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Anticonvulsants such as: divalproex (Depakote®), topiramate (Topamax®), valproate sodium | **Migraine Prophylaxis** *Refer to prescribing information or Micromedex* | *Refer to prescribing information or Micromedex* |
| Beta-blockers such as: propranolol (Inderal®), metoprolol (Lopressor®)*, timolol, atenolol (Tenormin®)*, nadolol (Corgard®)* | **Migraine Prophylaxis** *Refer to prescribing information or Micromedex* | *Refer to prescribing information or Micromedex* |
| Antidepressants/tricyclic antidepressants* such as: amitriptyline (Elavil®), venlafaxine (Effexor®) | **Migraine Prophylaxis** *Refer to prescribing information or Micromedex* | *Refer to prescribing information or Micromedex* |
| verapamil* | **Episodic Cluster Headache** 120 mg PO TID | 360 mg/day |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*
**Off-label use*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

*Appendix D: General Information*

- In clinical trials, a migraine day was defined as any calendar day in which the patient reported either a headache that lasted at least 2 consecutive hours and met International Classification of Headache Disorder (ICHD)-3 diagnostic criteria for migraine (with or without aura) or probable migraine (subtype in which only 1 migraine criterion is absent), or a day when a headache of any duration was treated with migraine-specific medications (triptans or ergots).
- Although Emgality given as either 120 mg SC once monthly or 240 mg SC once monthly showed a statistically significant decrease in migraine days per month compared to placebo as the primary outcome in the EVOLVE-1, EVOLVE-2, and REGAIN pivotal trials, there was no clinically significant difference between the two dosing regimens, and thus no significant additional benefit conferred from using a higher dose of Emgality. This is consistent with the FDA-approved maintenance dose of 120 mg SC once monthly.
- According to the ICHD-3 diagnostic criteria for cluster headaches, episodic cluster headaches occur in periods lasting from seven days to one year and are separated by periods of remissions that are at least 3 months. Chronic cluster headaches (affecting 10-15% of patients), on the other hand, occur for longer than a year without remission or with a remission that lasts less than 3 months. Of note, Emgality has only demonstrated efficacy in episodic cluster headaches. It failed to meet its primary endpoint in its chronic cluster headache phase 3 trial.

*Appendix E: Appropriate Experimental Design Methods*

- Randomized, prospective controlled trials are generally considered the gold standard; however:
  - In some clinical studies, it may be unnecessary or not feasible to use randomization, double-blind trials, placebos, or crossover.
  - Non-randomized prospective clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- Case reports and chart reviews are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Migraine prophylaxis | Loading dose: 240 mg SC once<br>Maintenance dose: 120 mg SC once monthly | 120 mg/month |
| Episodic cluster headaches | 300 mg (administered as three consecutive injections of 100 mg each) SC at the onset of the cluster period, and then monthly until the end of the cluster period | 300 mg/month |

## VI. Product Availability

- Single-dose prefilled pen: 120 mg/mL
- Single-dose prefilled syringe: 100 mg/mL, 120 mg/mL

## VII. References

1. Emgality Prescribing Information. Indianapolis, IN: Eli Lilly and Company; May 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761063s006lbl.pdf. Accessed July 15,2024.
2. Silberstein SD, Holland S, Freitag F, et al. American Academy of Neurology: Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Neurology 2012; 78: 1337-45.
3. Stauffer VL, Dodick DW, Zhang Q, et al. Evaluation of galcanezumab for the prevention of episodic migraine: the EVOLVE-1 randomized clinical trial. JAMA Neurol. 2018; 75(9):1080-1088.
4. Skljarevski V, Matharu M, Millen BA, et al. Efficacy and safety of galcanezumab for the prevention of episodic migraine: results of the EVOLVE-2 phase 3 randomized controlled clinical trial. Cephalalgia. 2018; 38(8):1442-1454.
5. Detke H, Wang S, Skljarevski V, et al A phase 3, randomized, double-blind, placebo-controlled study of LY2951742 in patients with chronic migraine – the REGAIN study. Poster session presented at: International Headache Congress; Sept 7-10, 2017; Vancouver, Canada.
6. Headache Classification Committee of the International Headache Society. The International classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013; 33(9): 629-808.
7. Francis BJ, Becker WJ, and Pringsheim TM. Acute and preventative pharmacologic treatment of cluster headache. Neurology. 2010; 75: 463-473.
8. Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, and Schwedt TJ. Treatment of cluster headache: The American Headache Society evidence-based guidelines. Headache. 2016; 56: 1093-1106.
9. Digre KB. The American Headache Society Position Statement on integrating new migraine treatments into clinical practice. Headache 2019; 59: 1-18.
10. Charles AC, Digre KB, Goadsby PJ, et al. The American Headache Society: Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache. 2024; 64: 333–341.

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J3590 | Unclassified biologics |
| C9399 | Unclassified drugs or biologicals |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added coding implications; references reviewed and updated. | 11.18.20 | 02.21 |
| Revised requirement on concurrent use with other CGRP inhibitors to include oral products with Nurtec and Ubrelvy listed as additional examples. | 06.28.21 | |
| 1Q 2022 annual review: no significant changes; references reviewed and updated. | 09.14.21 | 02.22 |
| Clarified the following "…not prescribed concurrently with Botox or other injectable **or** oral CGRP inhibitors." | 05.31.22 | |
| 4Q 2022 annual review: Added criteria for concurrent use with Botox requiring supportive evidence from published studies or clinical practice guidelines, positive response with Botox monotherapy, and continued migraine burden; references reviewed and updated; template changes applied to other diagnoses/indications. Template changes applied to other diagnoses/indications and continued therapy section. | 07.19.22 | 11.22 |
| 4Q 2023 annual review: no significant changes; references reviewed and updated. | 07.12.23 | 11.23 |
| 4Q 2024 annual review: added Zavzpret to list of CGRP inhibitors that should not be prescribed concurrently with Emgality, removed references to "injectable or oral CGRP" as Zavzpret is a nasal product; references reviewed and updated. | 07.15.24 | 11.24 |
| Per June SDC: for episodic cluster headaches, changed approval duration from 3 months to 12 months for initial approval criteria and continued therapy, removed the following verbiage from continued therapy approval duration: "up to a total of 12 months per cluster period". | 06.10.25 | 08.25 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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