Clinical Policy: Carbamazepine ER (Equetro)

Reference Number: CP.PMN.137
Effective Date: 03.13.18
Last Review Date: 05.19
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Carbamazepine extended-release (Equetro®) is an antiepileptic drug and mood stabilizer.

FDA Approved Indication(s)

Equetro is indicated for the treatment of:

- Acute manic or mixed episodes associated with bipolar I disorder
- Pain associated with trigeminal neuralgia
- Partial seizures with complex symptomatology (e.g., psychomotor, temporal lobe), generalized tonic-clonic seizures (grand mal), and mixed seizure patterns, which include the seizure types listed here or other partial or generalized seizures.

Limitation(s) of use: Equetro is not indicated for the treatment of absence seizures (petit mal).Carbamazepine has been associated with increased frequency of generalized convulsions in these patients.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

A. Bipolar Disorder, Trigeminal Neuralgia, or Epilepsy (must meet all)**:**

1. One of the following diagnoses (a, b, or c):
   a. Bipolar disorder;
   b. Trigeminal neuralgia;
   c. Epilepsy (partial seizures, generalized tonic-clonic seizures [grand mal], or mixed types)
2. If diagnosis is bipolar disorder or trigeminal neuralgia, age ≥ 18 years;
3. Member has experienced clinically significant adverse effects to immediate-release carbamazepine or has contraindication(s) to its excipients;
4. Member has experienced clinically significant adverse effects to extended-release carbamazepine (e.g., Tegretol® XL) or has contraindication(s) to its excipients;
5. Dose does not exceed:
   a. Bipolar disorder, epilepsy: 1600 mg/day;
   b. Trigeminal neuralgia: 1200 mg/day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Bipolar Disorder, Trigeminal Neuralgia, or Epilepsy (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. Documentation supports that member is currently receiving Equetro for bipolar disorder or epilepsy and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed:
   a. Bipolar disorder, epilepsy: 1600 mg/day;
   b. Trigeminal neuralgia: 1200 mg/day.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Absence seizures (petit mal).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

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
carbamazepine (Carbatrol, Epitol®, Tegretol®, Tegretol-XR)	**Adults: Bipolar Disorder** • Immediate-release products: Initially, 200 mg PO twice daily. Usual daily dose range is 600 to 1600 mg/day in divided doses. **Adults: Trigeminal neuralgia** • Carbatrol extended-release capsule: Initial: 200 mg PO once on day 1; may increase by 200 mg/day given every 12 hours as needed for efficacy and tolerability (range, 200 to 1200 mg/day; most patients, 400 to 800 mg/day) to max 1200 mg/day • Immediate-release, chewable, or extended-release tablet: Initial: 100 mg PO twice daily on day 1; may increase by 100 mg every 12 hours as needed for pain control (range, 200 to 1200 mg/day; most patients, 400 to 800 mg/day) to max 1200 mg/day • Suspension: Initial: 50 mg orally 4 times daily on day 1; may increase by 200 mg/day (50 mg 4 times daily) as needed for pain control (range, 200 to 1200 mg/day; most patients, 400 to 800 mg/day) to max 1200 mg/day. **Adults: Epilepsy, partial, generalized, and mixed types** • Carbatrol extended-release capsule: Initial: 200 mg PO twice daily for the first week; may increase by adding up to 200 mg/day in 2 divided doses at weekly intervals to the minimum effective level (usually 800 to 1200 mg/day); generally, do not exceed 1200 mg/day and rarely, up to 1600 mg/day may be given • Extended-release tablet: Initial: 200 mg PO twice daily for the first week; may increase by adding up to 200 mg/day in 2 divided doses at weekly intervals to the minimum effective level (usually 800 to 1200 mg/day); generally, do not exceed 1200 mg/day and rarely, up to 1600 mg/day may be given	*Oral formulations:* 1200 mg/day for trigeminal neuralgia. In rare instances, 1600 mg/day for epilepsy or bipolar disorder

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Immediate-release or chewable tablet: Initial: 200 mg PO twice daily for the first week; may increase by adding up to 200 mg/day in 3 or 4 divided doses at weekly intervals to the minimum effective level (usually 800 to 1200 mg/day); generally, do not exceed 1200 mg/day, and rarely, up to 1600 mg/day may be given • Suspension: Initial, 100 mg PO 4 times daily for the first week; may increase by adding up to 200 mg/day in 3 or 4 divided doses at weekly intervals to the minimum effective level (usually 800 to 1200 mg/day); generally, do not exceed 1200 mg/day, and rarely, up to 1600 mg/day may be given	

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.

Appendix C: Contraindications/Boxed warnings

- Contraindication(s): history of bone marrow depression, concomitant use or use within 14 days of an MAOI, concomitant use of non-nucleoside reverse transcriptase inhibitors that are substrates for CYP3A4, hypersensitivity to carbamazepine or other tricyclic compounds
- Boxed warning(s): serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), have been reported, especially in patients with the inherited allelic variant HLA-B*1502 who are almost exclusively of Asian ancestry. Avoid use of carbamazepine in patients testing positive for the allele unless the benefit clearly outweighs the risk. Discontinue if you suspect that the patient has a serious dermatologic reaction. Aplastic anemia and agranulocytosis have also been reported. Obtain a pretreatment complete blood count (CBC) and periodically monitor CBC. Consider discontinuing carbamazepine if significant bone marrow depression develops.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Acute manic or mixed episodes associated with bipolar I disorder	200 mg PO twice daily; the dose may be increased by 200 mg per day to achieve optimal clinical response. Doses higher than 1600 mg per day have not been studied in mania associated with bipolar disorder.	1600 mg/day

Indication	Dosing Regimen	Maximum Dose
Trigeminal neuralgia	Initial: On the first day, start with one 200 mg capsule PO once daily. This dose may be increased by up to 200 mg/day using increments of 100 mg every 12 hours only as needed to reach an effective and tolerated dose. Do not exceed a total daily dose of 1200 mg. Maintenance: Control of pain can be maintained in most patients with 400 mg to 800 mg daily. However, some patients may be maintained on as little as 200 mg daily, while others may require as much as 1200 mg daily.	1200 mg/day
Epilepsy	Adults and children over 12 years of age: The recommended initial dose is 200 mg PO twice daily. Increase in weekly increments of 200 mg a day, administered as an equally divided, twice daily dose, until an optimal response is obtained. Dosage generally should not exceed 500 mg twice daily in children 12 to 15 years old; 600 mg twice daily in children 15 to 18 years old; and 800 mg twice daily in adults. Children under 12 years of age: Ordinarily, optimal clinical response is achieved at daily doses below 35 mg/kg	1600 mg/day

VI. Product Availability

Extended-release capsules: 100 mg, 200 mg, and 300 mg

VII. References

1. Equetro Prescribing Information. Parsippany, NJ: Validus Pharmaceuticals LLC; October 2016. Available at: http://equetro.com/full-prescribing-information/. Accessed February 12, 2019.
2. American Psychiatric Association Practice Guideline for the Treatment of Patients with Bipolar Disorder: Second Edition (2010). Available at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf. Accessed online March 5, 2018.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.

4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 12, 2019

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.13.18	05.18
2Q 2019 annual review: no significant changes; added contraindications and boxed warning for SJS/TEN in HLA-B*1502; removed HIM LOB; Commercial: added LOB; references reviewed and updated.	02.12.19	05.19

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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