Clinical Policy: Cenobamate (Xcopri)

Reference Number: CP.PMN.231
Effective Date: 03.01.20
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Cenobamate (Xcopri®) is a voltage-gated sodium channel inhibitor and a positive allosteric modulator of the γ-aminobutyric acid ($GABA_A$) ion channel.

FDA Approved Indication(s)

Xcopri is indicated for the treatment of partial-onset seizures in adult 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 Xcopri is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Partial-Onset Seizures (must meet all)**:**

1. Diagnosis of partial-onset seizures;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Failure of two preferred anticonvulsants indicated for partial seizures (*see Appendix B for examples*), unless clinically significant adverse effects are experienced or all are contraindicated;
5. Dose does not exceed 400 mg (2 tablets) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. 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: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; 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:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Partial-Onset Seizures (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Xcopri for a covered indication 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 400 mg (2 tablets) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. 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: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; 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: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

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

$GABA_A$: γ-aminobutyric acid-subtype A

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®, Equetro®, Tegretol®, Tegretol XR®)	Refer to prescribing information	Refer to prescribing information
felbamate (Felbatol®)		
gabapentin (Neurontin®)		
lamotrigine (Lamictal®, Lamictal CD®, Lamictal ODT®, Lamictal XR®)		
levetiracetam (Elepsia XR®, Keppra®, Keppra XR®, Roweepra®, Spritam®)		
oxcarbazepine (Oxtellar XR®, Trileptal®)		
phenobarbital (Luminal®)		
phenytoin (Dilantin®, Phenytek®)		
pregabalin (Lyrica®, Lyrica® CR)		
tiagabine (Gabitril®)		
topiramate (Qudexy XR®, Topamax®, Topamax Sprinkle®, Topiragen®, Trokendi XR®)		
valproic acid, divalproex sodium (Depakene®, Depakote Sprinkle®, Depakote ER®, Depakote®)		
zonisamide (Zonegran®)		

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):
  - Hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri
  - Familial short QT syndrome
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Partial-onset seizures	Dose titration: 12.5 mg PO QD for two weeks, then 25 mg PO QD for two weeks, then 50 mg PO QD for two weeks, then 100 mg PO QD for two weeks, then 150 mg PO QD for two weeks Maintenance dose: 200 mg PO QD	400 mg/day

Indication	Dosing Regimen	Maximum Dose
	If needed based on clinical response and tolerability, dose may be increased above 200 mg by increments of 50 mg PO QD every two weeks to 400 mg PO QD.	

VI. Product Availability

Tablets: 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, 200 mg

VII. References

1. Xcopri Prescribing Information. Paramus, NJ: SK Life Science, Inc.; April 2021. Available at: https://www.xcopri.com. Accessed November 19, 2021.
2. Krauss GL, Klein P, Brandt C, et al. Safety and efficacy of adjunctive cenobamate (YKP3089) in patients with uncontrolled focal seizures: a multicenter, double-blind, randomised, placebo-controlled, dose-response trial. *Lancet Neurology.* 2019; published online November 13, 2019; https://doi.org/10.1016/S1474-4422(19)30399-0.
3. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy. *Neurology.* 2018;91(2):74-81.
4. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs II: treatment-resistant epilepsy. *Neurology*. 2018;91(2):82-90.
5. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 19, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.07.20	02.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.22.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.19.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
Template changes applied to other diagnoses/indications.	10.06.22	

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.