Clinical Policy Title:	cenobamate
Policy Number:	RxA.631
Drug(s) Applied:	Xcopri®
Original Policy Date:	05/21/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Xcopri® is indicated for the treatment of partial-onset seizures in adult patients. The precise mechanism of cenobamate (Xcopri®) is unknown. It has been demonstrated to inhibit voltage-gated sodium channels, reducing repetitive neuronal firing. It also acts as a positive allosteric modulator of $GABA_A$ ion channels.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
cenobamate (Xcopri®)	Focal (partial) onset seizures	Slowly titrated up over time - • Weeks 1 + 2: 12.5 mg once daily; • Weeks 3 + 4: 25 mg once daily; • Weeks 5 + 6: 50 mg once daily; • Weeks 7 + 8: 100 mg once daily; • Weeks 9 + 10: 150 mg once daily; • Week 11 + so on: 200 mg once daily	May increase by increments of 50 mg Q2 weeks. Max dose: 400 mg once daily In mild or moderate hepatic impairment, the maximum recommended dosage is 200 mg once daily.

Dosage Forms

- Tablet: 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Partial-onset seizures (must meet all)**:**

1. Diagnosis of partial onset seizures with baseline seizure frequency;
2. Age ≥ 18 years;
3. Prescribed by a neurologist or in consultation with a neurologist;
4. Documentation supports that the member does not have Familial Short QT syndrome;

5. Documented trial of at least 2 other antiepileptic drugs titrated to an appropriate maintenance dose or documented failure of at least two other antiepileptic drugs due to intolerable adverse effects;
6. Does not exceed maximum recommended 400 mg/day dosing.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Partial-onset seizures (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member has experienced and maintained positive response to therapy as evidenced by a reduction in partial onset seizure frequency;
3. If request is for a dose increase, new dose does not exceed maximum recommended 400 mg/day dosing.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
$GABA_A$: γ-aminobutyric acid-subtype A

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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 (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®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
valproic acid, divalproex sodium (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):
  - Familial Short QT syndrome;
  - Hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri®.

- Boxed Warning(s):
  - None.

APPENDIX D: General Information

- Although the product labeling for Xcopri® is broad (indicated for treatment in adults with partial-onset seizures), the drug was studied in patients who had refractory seizures to between 1 and 3 antiepileptic therapies (80% on at least 2 concomitant antiepileptic drugs).
- The 2018 Joint American Academy of Neurology/American Epilepsy Society guideline update in 2018 provide specific recommendations regarding antiepileptics that can be considered for treatment-resistant adult focal epilepsy (TRAFE). Below table is adapted from the guideline update:

Level of Recommendation	Antiepileptic Drug	Recommendation for TRAFE
A	Pregabalin (immediate release) Fycompa (perampanel)	Established as effective to reduce seizure frequency
A	Vigabatrin Banzel (rufinamide)	Should be considered as effective for decreasing seizure frequency but are not first-line agents (retinopathy risk with vigabatrin and modest benefit with rufinamide)
B	Aptiom (eslicarbazepine) Topiramate extended-release Vimpat (lacosamide)	Should also be considered to decrease seizure frequency
C	Clobazam Oxtellar XR (oxcarbazepine extended release)	May be considered to reduce seizure frequency

References

1. Xcopri (cenobamate) [prescribing information]. Paramus, NJ: SK Life Science Inc; August 2020. Available at: https://www.xcopri.com/wp-content/uploads/2020/09/SK_Prescribing_Information_Med_Guide_Combined.pdf. Accessed February 03, 2021.
2. Kanner, A. M., Ashman, E., Gloss, D., Harden, C., Bourgeois, B., Bautista, J. F., … French, J. (2018). Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment-resistant epilepsy. Epilepsy Currents, 18(4), 269–278. https://doi.org/10.5698/1535-7597.18.4.269.

3. Xocopri. Lexi-Drugs. Hudson, OH: Lexicomp, 2020. http://online.lexi.com/. Updated May 2, 2020. Accessed February 04, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	05/10/2020	05/21/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Line of business was updated to all lines of business. 3. Updated Dosage forms. 4. Initial approval criteria's language was changed, to maintain consistency. 5. Commercial & Medicaid approval duration was added in both initial as well as continued therapy approval criteria. 6. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication…" 7. Appendix A was updated: added FDA & $GABA_A$. 8. Appendix B & D was updated. 9. References were reviewed and updated.	02/04/2021	03/09/2021