Pharmacy Policy Bulletin: J-0252 Xcopri (cenobamate) – Commercial and Healthcare Reform	
Number: J-0252	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0252-007	**Original Date:** 01/29/2020
Effective Date: 12/20/2024	**Review Date:** 12/02/2024

Drugs Product(s):	• Xcopri (cenobamate)
FDA-Approved Indication(s):	• Treatment of partial-onset seizures in adult patients

Background:	• The precise mechanism of action in partial-onset seizures is unknown. Xcopri has been demonstrated to reduce repetitive neuronal firing by inhibiting voltage-gated sodium currents. Xcopri is also a positive allosteric modulator of the gamma-aminobutyric acid ($GABA_A$) ion channel.
	• Partial-onset seizures are also called focal seizures. In partial-onset seizures the electrical disturbance begins in one side of the brain. Partial seizures are subdivided into simple partial seizures (also called focal onset aware seizures) in which consciousness is retained and complex partial seizures (also called focal impaired awareness seizures) in which consciousness is impaired or lost.
	• In Xcopri clinical trials, patients not adequately controlled on 1 to 3 concomitant anti-epileptic drugs (AEDs) were administered Xcopri or placebo. More than 80% of patients were taking 2 or more concomitant AEDs.
	• The 2018 American Academy of Neurology (AAN) guidelines recommend first-line AED therapy for partial-onset seizures with carbamazepine, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, and/or zonisamide. Other AEDs indicated for the treatment of partial-onset seizures include eslicarbazepine, lacosamide, perampanel, phenytoin, pregabalin, tiagabine, topiramate, and valproic acid.
	• Prescribing Considerations:
	  ○ Xcopri is contraindicated in patients with familial short QT syndrome.
	  ○ Xcopri should be gradually withdrawn to minimize the potential of increased seizure frequency.
	  ○ The recommended initial dosage of Xcopri is 12.5 mg once daily, titrated to the recommended maintenance dosage of 200 mg once daily. The maximum dosage of Xcopri is 400 mg once daily.

	○ Xcopri decreases plasma concentrations for lamotrigine, carbamazepine, oral contraceptives, CYP2B6 substrates, and CYP3A substrates. Dosage increase may be necessary for these medications. For oral contraceptives, women should use additional or alternative non-hormonal birth control while taking Xcopri. ○ Xcopri increases plasma concentrations for phenytoin, phenobarbital, clobazam, and CYP2C19 substrates. Dosage decrease may be necessary in these medications.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Xcopri may be approved when all of the following criteria are met **(A., B., and C.):**

A. The member is 18 years of age or older.

B. The member has a diagnosis of partial-onset seizures (i.e. focal seizures) (ICD-10: G40.0-G40.2).

C. The member has experienced therapeutic failure or intolerance to at least two (2) other anti-epileptic drugs indicated for partial-onset seizures, or all are contraindicated.

II. Reauthorization

When a benefit, reauthorization of Xcopri may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced a reduction in seizure frequency from baseline.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Xcopri [package insert]. Paramus, NJ. SK Life Science, Inc.; April 2024.
2. Epilepsy Foundation. Partial Seizures. Available at: https://www.epilepsy.com/what-is-epilepsy/seizure-types/focal-onset-aware-seizures. Accessed November 4, 2024.
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 Jul 2018*;81:74-81.
4. Margolis JM, Chu BC, Wang ZJ, et al. Effectiveness of antiepileptic drug combination therapy for partial-onset seizures based on mechanisms of action. *JAMA Neurol 2014*;71:985.