Pharmacy Medical Necessity Guidelines: Anticonvulsants/Mood Stabilizers

Effective: November 12, 2024

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
These pharmacy medical necessity guidelines apply to the following: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FDA-APPROVED INDICATIONS

Aptiom (eslicarbazepine) is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.

Banzel (rufinamide) is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in pediatric patients 1 year or age and older and in adults.

Briviact (brivaracetam) is indicated for the treatment of partial-onset seizures in patients one month of age and older.

Diacomit (stiripentol) capsules and powder for oral suspension are indicated for the treatment of seizures associate with Drave syndrome in patients 6 months of age and older weighing 7 kilograms or more who are taking clobazam. There are no clinical data to support the use of Diacomit as monotherapy for the treatment of Dravet syndrome.

Epidiolex (cannabidiol) oral solution is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome, Drave syndrome, or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

Felbamate is not indicated as a first line antiepileptic treatment. Felbamate (Felbatol) is recommended for use only in those patients who respond inadequately to alternative treatments and whose epilepsy is so severe that a substantial risk of aplastic anemia and/or liver failure is deemed acceptable in light of the benefits conferred by its use. If these criteria are met and the patient has fully been advised of the risk and provided written acknowledgement, then felbamate can be considered as either monotherapy or adjunctive therapy in the treatment of partial seizures, with or without generalization, in adults with epilepsy. It can also be used as adjunctive therapy in the treatment of partial and generalized seizures associated with LGS in children.

Fintepla (fenfluramine) oral solution is indicated for the treatment of seizures associated with Dravet syndrome and LGS in patients who are 2 years of age and older.

Fycompa (perampanel) is indicated as adjunctive therapy or monotherapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older, and as adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in patients with epilepsy who are 12 years and older.

Lamotrigine extended-release is indicated as adjunctive therapy for primary generalized tonic-clonic seizures and partial-onset seizures with or without secondary generalization in patients aged 13 years and older. Lamotrigine extended-release is also indicated for the conversion to monotherapy in patients age 13 years and older with partial-onset seizures who are receiving treatment with a single anti-epileptic drug.

Levetiracetam extended-release (Keppra XR) is indicated for the treatment of partial onset seizures in patients 12 years of age and older. Elepsia XR (levetiracetam extended-release) is indicated as adjunctive therapy for the treatment of partial-onset seizures in patients 12 years of age and older.

Generic Keppra XR is available as 500 mg and 750 mg tablets, while Elepsia XR is available as 1,000 mg and 1,500 mg tablets.

Nayzilam (midazolam) nasal spray is indicated for acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

Onfi (clobazam) is indicated as adjunctive treatment of seizures associated with LGS in patients 2 years of age and older.

Oxtellar XR (oxcarbazepine) is indicated as adjunctive therapy of partial onset seizures in adults and in children 6 years of age and older

Spritam (levetiracetam) is indicated as adjunctive therapy in the treatment of partial onset seizures in patients with epilepsy 4 years of age and older weighing more than 20 kg, as adjunctive therapy in the treatment of myoclonic seizures in patients 12 years of age and older with juvenile myoclonic epilepsy, and as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy.

Sympazan (clobazam) is indicated as adjunctive treatment of seizures associated with LGS in children 2 years of age or older.

Topiramate extended-release capsule (Qudexy XR) is indicated as initial monotherapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures or seizures associated with LGS. Topiramate extended-release capsule (Qudexy XR) is also indicated for prophylaxis of migraine headache in adults and adolescents 12 years of age and older.

Trokendi XR (topiramate) is indicated as initial monotherapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures. Trokendi XR (topiramate) is also indicated as adjunctive therapy in patients 6 years of age and older with seizures associated with LGS as well as for prophylaxis of migraine in patients 12 years of age and older.

Valtoco (diazepam) nasal spray is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older.

Vimpat (lacosamide) tablet and oral solution are indicated for the treatment of partial-onset seizures in patients 1 month of age and older. It is also approved as adjunctive therapy in treatment of primary generalized tonic-clonic seizures in patients 4 years and older.

Xcopri (cenobamate) is indicated for the treatment of partial-onset seizures in adult patients.

Ztalmy (ganaxolone) oral suspension is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder in patients 2 years of age and older.

If the request is for Lyrica (pregabalin) or Sabril (vigabatrin), please see individual drug-specific medical necessity guidelines.

COVERAGE GUIDELINES

The plan may authorize coverage of a non-preferred anticonvulsant agent for Members, when **all** the following criteria are met:

1. Documentation the Member is stable on the requested medication

OR

2. The Member meets the medication-specific criteria below

Aptiom (eslicarbazepine), Briviact (brivaracetam)

1. Documented diagnosis of partial-onset seizures by a neurologist

AND

2. The Member has had an inadequate response, adverse reaction, or contraindication to at least two other anticonvulsants

Banzel (rufinamide)

1. The Member is diagnosed with Lennox-Gastaut syndrome (LGS) or an epileptic condition associated with LGS made by a neurologist

AND

2. The Member had an inadequate response, adverse reaction, or contraindication to two anticonvulsants

Diacomit (stiripentol)

1. The Member has a diagnosis of Dravet syndrome

AND

2. The Member is 6 months of age or older

AND

3. Diacomit is prescribed by or in consultation with a neurologist

AND

4. The Member will take clobazam in conjunction with Diacomit

AND

5. The Member had an inadequate response, intolerance, adverse reaction, or contraindication to one anticonvulsant

Epidiolex (cannabidiol)

1. Member is 1 year of age or older

AND

2. Epidiolex is prescribed by or in consultation with a neurologist

AND

3. The Member meets either a, b, or c:
   a) The Member has a diagnosis of Dravet Syndrome

   AND

   The Member will be using Epidiolex as adjunctive therapy

   AND

   The Member had an inadequate response, intolerance, adverse reaction, or contraindication to two anticonvulsants

   OR

   b) The Member has a diagnosis of Lennox-Gastaut Syndrome

   AND

   The Member will be using Epidiolex as adjunctive therapy

   AND

   The Member had an inadequate response, intolerance, adverse reaction, or contraindication to two anticonvulsants

   OR

   c) The Member has a diagnosis of Tuberous Sclerosis Complex (TSC)

Felbamate

1. The Member is diagnosed with epilepsy or a condition associated with a seizure disorder

AND

2. Documentation that the member has had an inadequate response, adverse reaction, or contraindication to therapy with two anticonvulsants

Fintepla (fenfluramine)

1. Member is 2 years of age or older

AND

2. Fintepla is prescribed by or in consultation with a neurologist

AND

3. The Member has one of the following diagnoses:
   a. Dravet Syndrome

   OR

   b. Lennox-Gastaut Syndrome (LGS)

   AND

4. The Member has had an inadequate response, intolerance, adverse reaction, or contraindication to two anticonvulsants

Fycompa (perampanel)

1. Documented diagnosis of partial-onset seizures or tonic-clonic seizures by a neurologist

AND

2. The Member has had an inadequate response, adverse reaction, or contraindication to two anticonvulsants

Lamotrigine extended-release

1. The Member is diagnosed with epilepsy, a condition associated with a seizure disorder, or bipolar disorder

AND

2. Documentation that therapy with immediate-release lamotrigine has been insufficient

Levetiracetam extended-release (Keppra XR, Elepsia XR)

1. The Member is diagnosed with epilepsy or a condition associated with a seizure disorder

AND

2. Documentation that therapy with immediate-release levetiracetam has been insufficient

AND

3. **Elepsia XR:** Documentation that Member has had an inadequate response or adverse reaction to generic Keppra XR

Nayzilam (midazolam) nasal spray

1. The Member is diagnosed with a seizure disorder and needs acute treatment on hand for seizures

AND

2. The Member is 12 years of age or older

Onfi (clobazam) tablet and suspension, Sympazan (clobazam) film

1. The Member is diagnosed with Lennox-Gastaut syndrome (LGS), epilepsy, or a seizure disorder

AND

2. The Member has had an inadequate response, adverse reaction, or contraindication to two anticonvulsants

AND

3. **Sympazan only:** Documentation that member has difficulty swallowing

Oxtellar XR (oxcarbazepine extended-release)

1. The Member is diagnosed with epilepsy or a condition associated with a seizure disorder

AND

2. Documentation that the Member had an inadequate response or adverse reaction therapy with immediate-release oxcarbazepine and at least one additional anticonvulsant has been insufficient

Spritam (levetiracetam)

1. The member is diagnosed with epilepsy or a condition associated with a seizure disorder

AND

2. Documentation that the Member has had an inadequate response or adverse reaction to therapy with levetiracetam immediate-release tablet AND solution or that treatment with both formulations is clinically inappropriate for the member

Topiramate extended-release sprinkle capsule (Qudexy XR)

1. The Member is diagnosed with epilepsy or a seizure disorder and is at least 2 years of age

AND

2. Documentation that the Member has and an inadequate response or adverse reaction to topiramate immediate-release

OR

1. The Member is diagnosed with chronic migraine and requires migraine prophylaxis

AND

2. The Member has had an inadequate response or adverse reaction to topiramate immediate release

Trokendi XR (topiramate extended-release capsule)

1. The Member is diagnosed with epilepsy or a seizure disorder and is at least 6 years of age

AND

2. Documentation that the Member has had an inadequate response or adverse reaction go topiramate immediate-release

OR

1. The Member is diagnosed with chronic migraine and requires migraine prophylaxis

AND

2. The Member has had an inadequate response or adverse reaction to topiramate immediate release AND generic topiramate extended-release sprinkle capsule

Xcopri (cenobamate tablet)

1. The member has diagnosis of partial-onset seizures

AND

2. The prescribing physician is a neurologist or prescribed in consultation by a neurologist

AND

3. Member is 18 years of age or older

AND

4. Documentation that the Member has had an inadequate response, adverse reaction, or contraindication to two anticonvulsants

Valtoco (diazepam nasal spray)

1. The Member is diagnosed with a seizure disorder and needs acute treatment on hand for seizures

AND

2. The Member is 6 years of age or older

Vimpat (lacosamide)

1. Documented diagnosis by a neurologist of partial-onset seizures or primary generalized tonic-clonic seizure

AND

2. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to two anticonvulsants

Ztalmy (ganaxolone)

1. The Member has a diagnosis of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)

AND

2. The Member is 2 years of age or older

AND

3. Ztalmy is prescribed by or in consultation with a neurologist

LIMITATIONS

1. The following quantity limitations apply to coverage:

Nayzilam (midazolam) nasal spray	1 box (2 nasal spray units)/fill
Valtoco (diazepam) nasal spray	1 box per fill

2. Fintepla (fenfluramine) will not be approved for weight loss.
3. Requests for brand-name products, which have AB-rated generics, will be reviewed according to the Brand Name criteria.
4. Samples, free goods, or similar offerings of the requested medication do not qualify for an established clinical response or exception, but will be considered on an individual basis for prior authorization.

CODES

None

REFERENCES

1. Andrade DM, Nascimento FA. Dravet syndrome: management and prognosis. UpToDate. Available at: www.uptodate.com. Accessed 1 November 2023.
2. Aptiom (eslicarbazepine) [prescribing information]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; November 2023.
3. Banzel (rufinamide) [prescribing information]. Nutley, NJ: Eisai Inc.; December 2022.
4. Biton V, Berkovic SF, Abou-Khalil B, et al. Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: a phase III randomized, double-blind, placebo-controlled trial. *Epilepsia*. 2014 Jan;55(1):57-66.
5. Briviact (brivaracetam) [prescribing information]. Smyrna, GA: UCB, Inc.; May 2023.
6. Brodie MJ, Lerche H, Gil-Nagel A, et al. Efficacy and safety of adjunctive ezogabine (retigabine) in refractory partial epilepsy. *Neurology*. 2010; 75(20):1817-24.
7. Diacomit (stripipentol) [prescribing information]. Beauvais, France: Biocodex; June 2024.
8. Elepsia XR (levetiracetam extended-release) [prescribing information]. Westfield, NJ: Tripoint Therapeutics, LLC; December 2020.
9. Epidiolex (cannabidiol) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2024.
10. Felbamate [prescribing information]. Somerset, NJ: Wallace Pharmaceuticals, Inc.; February 2018.
11. Fintepla (fenfluramine) [prescribing information]. Smyrna, GA: UCB, Inc.; September 2023.
12. French JA, Abou-Khalil BW, Leroy RF, et al. Randomized, double-blind, placebo-controlled trial of ezogabine (retigabine) in partial epilepsy. *Neurology*. 2011;76(18):1555-63.
13. French JA, Kanner AM, Bautista J, et al. Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy. Report of the therapeutics and technology assessment subcommittee and quality standards subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004b;62:1261-73.
14. French JA, Kanner AM, Bautista J, et al. Efficacy and tolerability of the new antiepileptic drugs I: treatment of new onset epilepsy. Report of the therapeutics and technology assessment subcommittee and quality standards subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004a;62:1252-60.
15. Fycompa (perampanel) [prescribing information]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc.; June 2023.
16. Keppra (levetiracetam) [prescribing information]. Smyrna, GA: UCB, Inc.; August 2023.
17. Keppra XR (levetiracetam) [prescribing information]. Smyrna, GA: UCB, Inc.; August 2023.
18. Lamictal XR (lamotrigine) [prescribing information]. Durham, NC: GlaxoSmithKline; May 2023.
19. Nayzilam (midazolam) nasal spray [prescribing information]. Smyrna, GA: UCB, Inc.,; January 2023.
20. Onfi (clobazam) [prescribing information]. Deerfield, IL: Lundbeck; January 2023.
21. Oxtellar XR (oxcarbazepine) [prescribing information]. Rockville, MD: Supernus Pharmaceuticals, Inc.; October 2024.
22. Qudexy (topiramate extended-release capsules) [prescribing information]. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; March 2023.
23. Spritam (levetiracetam) [prescribing information]. Blue Ash, OH: Aprecia Pharmaceuticals LLC; June 2024.
24. Sympazan (clobazam) [prescribing information]. Warren, NJ: Aquestive Therapeutics; March 2024.
25. Trokendi XR (topiramate extended-release capsules) [prescribing information]. Winchester, KY: Catalent Pharma Solutions; October 2022.
26. Valtoco (diazepam nasal spray) [prescribing information]. San Diego, CA: Neurelis; August 2023.
27. Vimpat (lacosamide) [prescribing information]. Smyrna, GA: UCB, Inc.; September 2024.
28. Xcopri (cenobamate) [prescribing information]. Paramus, NJ: SK Life Science, Inc.; August 2024.

29. Ztalmy (ganaxolone) oral suspension [prescribing information]. Marinus Pharmaceuticals, Inc: Radnor, PA; June 2023.

APPROVAL HISTORY

September 13, 2022: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. November 14, 2023: Effective December 1, 2023, added stability criteria for all agents, allowing for approval if the member is stable on the medication, thus removing the specific allowance from the criteria for Aptiom, Briviact, Banzel, Fycompa, Onfi, Sympazan, Qudexy XR, Trokendi XR, and Vimpat. Updated criteria for Aptiom, Briviact, Banzel, Epidiolex, Fintepla to update step through requirement with any two anticonvulsants. Updated criteria for Diacomit to remove specific step through anticonvulsants and allow trial and failure with any anticonvulsant. Removed Peganone from the MNG due to product discontinuation. Removed from the Limitations section the stipulation that Epidiolex will only be approved for FDA-approved indications. Updated previous trial language throughout the MNG. Updated fax number for RxUM.
2. November 12, 2024: No changes

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services