Pharmacy Medical Necessity Guidelines: Anticonvulsants/Mood Stabilizers

Effective: December 14, 2020

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:

Commercial Products

☐ Tufts Health Plan Commercial products – large group plans
☐ Tufts Health Plan Commercial products – small group and individual plans
☐ Tufts Health Freedom Plan products – large group plans
☐ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:
RXUM: 617.673.0988

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 LGS in pediatric patients 1 year or age and older and in adults.

Briviact (brivaracetam) tablets and solution are indicated for the treatment of partial-onset seizures in patients 4 years of age and older. Briviact injection is indicated for the treatment of partial-onset seizures in patients 16 years 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 2 years of age and older 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-Gestaut 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.

Fintepla (fenfluramine) oral solution is indicated for the treatment of seizures associated with Dravet syndrome 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 is indicated as adjunctive therapy in the treatment of partial onset seizures in patients 12 years of age and older with epilepsy.

Nazyzilam (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.

Oxtellar XR (oxcarbazepine) is indicated as adjunctive therapy of partial onset seizures in adults and in children 6 years to 17 years.

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

Peganone (ethotoin) is indicated for the control of tonic-clonic and complex partial (psychomotor) seizures.

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 Lennox-Gestault Syndrome 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. Topiramate extended-release capsule (Qudexy XR) is also indicated as adjunctive therapy in patients 2 years of age and older with seizures associated with LGS as well as 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.

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

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 patter in patients with epilepsy 6 years of age and older.

Vimpat (lacosamide) tablet and oral solution are indicated for the treatment of partial-onset symptoms in patients 4 years and older. Vimpat (lacosamide) injection for intravenous use is indicated for the treatment of partial-onset seizures only in adult patients (17 years of age and older) and is an alternative when oral administration is temporarily not feasible.

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:

Aptiom (eslicarbazepine), Briviact (brivaracetam), Vimpat (lacosamide)

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

AND

2. One of the following:
   a) The Member is stable on the medication

   OR

   b) The Member has had an insufficient response or intolerance to at least two other medications indicated for adjunct partial seizures*

Examples of alternative medications indicated for adjunct partial seizures:

a) Felbatol (felbamate)
b) Gabitril (tiagabine)
c) Lamictal (lamotrigine)
d) Lyrica (pregabalin)
e) Keppra/Keppra XR (levetiracetam)
f) Neurontin (gabapentin)
g) Tegretol (carbamazepine)
h) Topamax (topiramate)
i) Trileptal (oxcarbazepine)
j) Zonegran (zonisamide)

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. One of the following:
   a) The Member is currently stable on the medication

   OR

   b) The Member tried and failed therapy with, or has a contraindication or an intolerance to at least two of the following alternative anticonvulsant agents: valproic acid derivative (Depakene, Depakote), Topamax (topiramate), Lamictal (lamotrigine), Felbatol (felbamate), or Onfi (clobazam)

Diacomit (stiripentol)

1. The Member has a diagnosis of Dravet syndrome

AND

2. The Member is two years 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 of the following anticonvulsants: clonazepam, divalproex, ethosuximide, levetiracetam, topiramate, valproic acid, and zonisamide.

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 of the following anticonvulsants: clobazam, clonazepam, ethosuximide, levetiracetam, stiripentol, topiramate, valproic acid, and zonisamide

   OR

   b) The Member has a diagnosis of Lennox-Gestaut 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 of the following anticonvulsants: clobazam, felbamate, lamotrigine, rufinamide, topiramate, and valproic acid.

   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 therapy with two alternative anticonvulsant agents has been insufficient

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 will be using Fintepla as adjunctive therapy

AND

4. The Member has a diagnosis of Dravet Syndrome

AND

5. The Member had an inadequate response, intolerance, adverse reaction, or contraindication to two of the following anticonvulsants: clobazam, clonazepam, ethosuximide, levetiracetam, stiripentol, topiramate, valproic acid, and zonisamide

Fycompa (perampanel)

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

AND

2. One of the following:
   a) The Member is stable on the medication

   OR

   b) Documentation the Member has had an insufficient response or intolerance to at least two alternative anticonvulsant agents

Levetiracetam extended-release

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

Lamotrigine extended-release

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

AND

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

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. One of the following:
   a) The Member is currently stable on the medication

   OR

   b) **For the diagnosis of LGS:** The Member tried and failed therapy with, or has a contraindication or an intolerance to at least two of the following alternative anticonvulsant agents: valproic acid derivative (e.g., Depakene, Depakote), Topamax (topiramate), Lamictal (lamotrigine), Felbatol (felbamate), or Banzel (rufinamide)
   c) **For the diagnosis of epilepsy or seizure disorder:** Member has tried and failed therapy with, or has a contraindication or intolerance to any 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 therapy with immediate-release oxcarbazepine and at least one additional anticonvulsant has been insufficient

Peganone (ethotoin)

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

AND

2. Documentation that therapy with phenytoin and at least one other 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 therapy with levetiracetam immediate-release tablet AND solution has been insufficient or inappropriate

Topiramate extended-release spinkle capsule (Qudexy XR)

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

AND

2. One of the following:
   a) The Member is new to our health plan and is already stable on the medication

   OR

   b) Therapy with immediate-release topiramate has been insufficient

OR

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

AND

2. The Member has had an inadequate response, intolerance, or adverse effect 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. One of the following:
   a) The Member is new to our health plan and is already stable on the medication

   OR

   b) Therapy with immediate-release topiramate has been insufficient

OR

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

AND

2. The Member has had an inadequate response, intolerance, or adverse effect 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's condition was not adequately controlled with at least 2 concomitant antiepileptic drugs at stable doses for ≥ 4 weeks

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

LIMITATIONS

1. The following quantity limitations apply to coverage:

Levetiracetam extended-release	500 mg: six tablets per day
	750 mg: four tablets per day
Lamotrigine extended-release	Three tablets per day
Nayzilam (midazolam) nasal spray	1 box (2 nasal spray units)/fill
Onfi (clobazam)	Two tablets per day
Oxtellar XR (carbamazepine)	150 mg and 300 mg: one tablet per day
	600 mg: four tablets per day
Qudexy XR (topiramate extended release spinkle capsule)	25 mg, 50 mg, 100 mg: one capsule per day
	150 mg, 200 mg: two capsules per day
Spritam (levetiracetam)	250 mg, 500 mg, 750 mg, 1,000 mg tablet: two tablets per day
Trokendi XR (topiramate)	25 mg, 50 mg, 100 mg: one capsule per day
	200 mg: two capsules per day
Valtoco (diazepam) nasal spray	1 box per fill
Vimpat (lacosamide)	Two tablets (or 40 ml) per day

2. Epidiolox (cannabidiol) will only be approved for the following diagnoses: Dravet Syndrome, Lennox Gestaut Syndrome.
3. Fintepla (fenfluramine) will not be approved for weight loss.
4. Requests for brand-name products, which have AB-rated generics, will be reviewed according to the Brand Name criteria.
5. 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. Aptiom (eslicarbazepine) [prescribing information]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; March 2019.
2. Banzel (rufinamide) [prescribing information]. Woodcliff Lake, NJ: Eisai Co., Ltd.; November 2019.
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7. Epidiolex (cannabidiol) [prescribing information]. Carlsbad, CA; Greenwich Biosciences, Inc.; October 2020.
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9. Fintepla (fenfluramine) [prescribing information]. Emeryville, CA: Zogenix, Inc.; June 2020.
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12. 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

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15. Keppra XR (levetiracetam) [prescribing information]. Smyrna, GA: UCB, Inc.; October 2019.
16. Lamictal XR (lamotrigine) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; September 2019.
17. Nayzilam (midazolam) nasal spray [prescribing information]. Plymouth, MN: Proximagen, LLC; May 2019.
18. Onfi (clobazam) [prescribing information]. Deerfield, IL: Lundbeck; June 2018.
19. Oxtellar XR (oxcarbazepine) [prescribing information]. Rockville, MD: Supernus Pharmaceuticals, Inc.; December 2018.
20. Peganone (ethotoin) [prescribing information]. North Chicago, IL: Abbott Laboratories; May 2010.
21. Qudexy (topiramate extended-release capsules) [prescribing information]. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; February 2019.
22. Spritam (levetiracetam) [prescribing information]. East Windsor, NJ: Aprecia Pharmaceuticals Company; September 2018.
23. Trokendi XR (topiramate extended-release capsules) [prescribing information]. Winchester, Kentucky: Catalent Pharma Solutions; February 2019.
24. Vimpat (lacosamide) [prescribing information]. Smyrna, GA: UCB, Inc.; June 2019.
25. Sympazan (clobazam) [prescribing information]. Warren, NJ: Aquestive Therapeutics; November 2018.
26. Valtoco (diazepam nasal spray) [prescribing information]. San Diego, CA: Neurelis; January 2020.

APPROVAL HISTORY

June 12, 2014: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
1. November 4, 2014: Changes include: approval durations changed to 1 year; renewal criteria added; individual criteria consolidated to a single document.
2. August 11, 2015: Modified Fycompa criteria to accommodate new indication of tonic-clonic seizures; approval duration extended to life of plan.
3. January 1, 2016: Administrative change to rebranded template.
4. May 10, 2016: Removed criteria for lamotrigine orally disintegrating tablets. Added approval criteria for Spritam.
5. July 12, 2016: Added Briviact to the criteria.
6. September 13, 2016: Renamed policy "Anticonvulsants/Mood Stabilizers". Added approval criteria for members less than six years of age. Added lithium to the criteria. Added language to limitations regarding requests for brand-name products with AB-rated generics and quantities exceeding the quantity limits.
7. May 9, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether. Removed Pediatric Behavioral Health Medication Initiative (PBHMI) from criteria. Updated criteria for Oxtellar XR, Peganone, and Trokendi XR to require a trial with at least two anticonvulsants.
8. December 12, 2017: Administrative update, removed Potiga from Medical Necessity Guideline due to product discontinuation.
9. October 16, 2018: Effective 11/1/18, updated Spritam criteria to specify that treatment with levetiracetam oral suspension and tablet has either been insufficient or inappropriate. Added approval criteria for the treatment of chronic migraine to topiramate ER and Trokendi XR. Administrative changes made to template.
10. November 13, 2018: Clarified generic name of Qudexy XR.
11. January 8, 2019: Effective 2/1/19, added criteria for Sympazan film.
12. February 12, 2019: Added Epidiolex (cannabadiol) to the Medical Necessity Guideline.
13. August 13, 2019: Added Diacomit (stiripentol) to the Medical Necessity Guideline. Updated Epidiolex approval criteria to include stiripentol as a trial option. Updated clobazam criteria to include diagnoses of epilepsy and seizure disorders.
14. October 15, 2019: Added Nayzilam (midazolam) nasal spray to the MNG.
15. March 10, 2020: Effective March 16, 2020, added Valtoco (diazepam) nasal spray criteria and quantity limit to the MNG.
16. June 9, 2020: Added criteria for Xcopri to the MNG.
17. July 14, 2020: Administrative update, added language regarding samples to the limitations section of the MNG.

18. September 15, 2020: Added criteria for Fintepla (fenfluramine) to the MNG. Updated the limitations section to indicate that Fintepla will not be approved for weight loss.
19. December 8, 2020: Updated Epidiolex criteria to include diagnosis of tuberous sclerosis complex (TSC) and decreased age minimum approvable age from two years of age to one year of age.

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.