**PHARMACY COVERAGE GUIDELINES**
**SECTION: DRUGS**

**ORIGINAL EFFECTIVE DATE: 9/17/15**
**LAST REVIEW DATE: 1/18/18**
**LAST CRITERIA REVISION DATE: 1/18/18**
**ARCHIVE DATE:**

# ANTIEPILEPTIC DRUGS:
# APTIOM® (eslicarbazepine acetate) oral tablet
# BANZEL® (rufinamide) oral film-coated tablet and oral suspension
# POTIGA®™ (ezogabine) oral tablet

**Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.**

**This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.**

**The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.**

**The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.**

**State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.**

**Pharmacy Coverage Guidelines are subject to change as new information becomes available.**

**For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.**



This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602)

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

**Description:**

Aptiom (eslicarbazepine acetate) is indicated as monotherapy or adjunctive treatment of partial-onset seizures. Potiga (ezogabine) is indicated as adjunctive treatment of partial-onset seizures in patients who have responded inadequately to several alternative treatments and for whom the benefits outweigh the risk of retinal abnormalities and potential decline in visual acuity. Banzel (rufinamide) is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS).

Epilepsy is a neurological disorder where brief disturbances in the electrical function of the brain result in seizures. These seizures may affect consciousness and bodily movements or sensations for a short time. There are several different types of seizure that occur in epilepsy including partial (affecting one area of the brain), generalized (affecting nerve cells throughout the brain), and unclassified.

Anti-epileptic drugs (AED) are effective in controlling seizures. There is insufficient evidence to conclude that one AED is superior to another in controlling partial and generalized seizures or in improving outcomes. The evidence is also insufficient to conclude that branded AED are more effective than generic AED in terms of reducing seizure frequency or improving outcomes. In addition, the evidence is insufficient to support any relevant negative outcomes (such as increased seizure frequency, hospitalizations, and mortality) when switching from a branded to a generic medication. However, switching between different manufacturers could lead to variations in serum concentrations and it is suggested that prescription refills should be from the same manufacturer. The FDA maintains that there is no convincing evidence that people with epilepsy have less seizure control when taking generic medications.

All AED are associated with an increased risk of suicidal ideation and suicidal behavior when used in patients with epilepsy. While there is a high degree of variability in tolerability to AED, no specific AED is considered to be the safest or best tolerated. Adverse events are common to all AED and include confusion, dizziness, somnolence, ataxia, nausea, and vomiting. Individual AED are associated with serious, but rare adverse events. Ezogabine (Potiga) has a boxed warning for risk of retinal abnormalities and vision loss.

Practice guidelines suggest that choice of treatment should be individualized based on several factors such as drug effectiveness for the seizure type, patient age, concomitant medications, tolerability, safety, response to previous therapy, potential adverse effects of the drug, interactions with other medications, comorbid medical conditions, gender, lifestyle, patient preferences, and cost. Treatment should begin with a single agent with dose titration to achieve control of seizures or development of unacceptable side effects. If seizures persist, another agent is used as monotherapy; some recommend attempting a second alternative before using multiple drugs to control seizures. Achieving a seizure-free state is difficult and many patients may have to try multiple regimens and combination therapies to achieve control of seizures.

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

Lennox–Gastaut Syndrome (LGS), also known as Lennox syndrome, is a severe and difficult-to-treat form of childhood-onset epilepsy that most often appears between the second and sixth year of life. It is characterized by frequent seizures and can include different seizure types, such as, tonic, atonic, atypical absence, and myoclonic seizures. There may be periods of frequent seizures mixed with brief, relatively seizure-free periods. Most children with LGS experience some degree of impaired intellectual functioning or information processing, along with developmental delays and behavioral disturbances.

Treatment for LGS includes AED such as Clobazam, Clonazepam, Felbamate, Lamotrigine, Rufinamide, or Topiramate. There is usually no single antiepileptic medication that will control seizures. Children who improve initially may later show tolerance to a drug or have uncontrollable seizures.

Aptiom (eslicarbazepine) is chemically related to Oxcarbazepine and Carbamazepine. Eslicarbazepine is the active metabolite of Oxcarbazepine.

# Aptiom (eslicarbazepine acetate)

**Medication class:**
Anticonvulsant, miscellaneous

**FDA-approved indication(s):**
- Treatment of partial-onset seizures in adults and pediatric patients 4 years of age and older

**Recommended Dose:**
- Adult:
  - 400 mg once daily initially then increase by 400-600 mg weekly, regular maintenance dose ranges 800-1,600 mg once daily
- 4 years of age or older:
  - Weight based dosing once daily

| Body Weight | Initial & Titration Dose (mg/day) | Maintenance (mg/day) |
|---|---|---|
| 11-21 kg | 200 | 400-600 |
| 22-31 kg | 300 | 500-800 |
| 32-38 kg | 300 | 600-900 |
| > 38 kg | 400 | 800-1,200 |

***Maximum dosage***
- Not stated

**Available Dosage Forms:**
- 200 mg, 400 mg, 600 mg, 800 mg tabs

**Warnings, Precautions, and other Clinical Information:**
- Aptiom should not be taken as an adjunctive therapy with oxcarbazepine

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

- In patients with moderate and severe renal impairment (creatinine clearance < 50 mL/min), the initial, titration, and maintenance dosages should generally be reduced by 50%
- Use of Aptiom in patients with severe hepatic impairment is not recommended
- Avoid abrupt discontinuation in order to minimize risk of increased seizure frequency and status epilepticus
- Monitor for emergence or worsening depression, suicidal thoughts or behaviors and/or any unusual changes in mood or behavior
- Serious dermatologic reactions including Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported, discontinue if either develop
- Patients with a prior dermatologic reaction with oxcarbazepine, carbamazepine, or Aptiom should ordinarily not be treated with Aptiom
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as Multi-organ Hypersensitivity, has been reported, discontinue use if this develops
- Patients with a prior DRESS reaction with either oxcarbazepine or Aptiom should not be treated with Aptiom
- Anaphylaxis and angioedema have been reported, discontinue use if these occur, patients with a prior anaphylactic-type reaction with either oxcarbazepine or Aptiom should not be treated with Aptiom
- SIADH and hyponatremia may occur
- Discontinue Aptiom in patients with jaundice or other evidence of significant liver injury
- Discontinue Aptiom in patients who develop pancytopenia, agranulocytosis, or leukopenia
- Aptiom decreases ethinylestradiol and levonorgestrel levels
- Woman of child bearing potential should use effective contraception by using either additional contraception or alternative non-hormonal contraception

**Criteria:**

- **Criteria for initial therapy:** Aptiom (eslicarbazepine acetate) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is 4 years of age or older

2. A confirmed diagnosis of partial-onset seizures

3. Individual has failure, contraindication or intolerance to **THREE** of the following preferred step therapy agents:
    - Preferred step therapy agents include:
        - Gabapentin
        - Lamotrigine
        - Levetiracetam
        - Oxcarbazepine
        - Pregabalin

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

- Topiramate
- Zonisamide

4. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Liver function test

5. There are **NO** contraindications:
   - Contraindications include:
     - Hypersensitivity to Oxcarbazepine
     - Hypersensitivity to Eslicarbazepine

**Initial approval duration**: 12 months

- **Criteria for continuation of coverage (renewal request):** Aptiom (eslicarbazepine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition responded while on therapy
   - Response is defined as:
     - Reduction in the number of seizure episodes

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Stevens-Johnson syndrome or toxic epidermal necrolysis
       - Signs and symptoms may include: progressive skin rash, hives, blistering, oral ulcers
     - DRESS
       - Signs and symptoms may include: fever, rash, and/or lymphadenopathy, in association with other organ system involvement, such as hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis sometimes resembling an acute viral infection, eosinophilia is often present
     - Anaphylaxis or angioedema
       - Signs and symptoms may include: swelling of lips, mouth, tongue, or throat, severe skin reactions
     - Liver injury
       - Signs and symptoms may include: right sided abdominal pain, bruising, yellow skin or eyes, dark brown urine, severe nausea or vomiting, fatigue
     - Bone marrow suppression

- Signs and symptoms may include: : fever, chills, infection, unexplained bleeding or bruising, or unexplained weakness or shortness of breath

4. There are no significant interacting drugs

**Renewal duration**: 12 months

# Banzel (rufinamide)

**Medication class:**
Anticonvulsant, Triazole Derivative

**FDA-approved indication(s):**
- Adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in adults and pediatric patients 1 year and older

**Recommended Dose:**
- Adult:
  - 400-800 mg/day, in two equally divided doses, increase dose by 400-800 mg every other day
- Age 1-17 years:
  - 10 mg/kg/day, in two equally divided doses, increase dose by 10 mg/kg every other day

***Maximum dosage***
- Adult: Daily dose of 3,200 mg, in two equally divided doses
- Age 1-17 years: Daily dose of 45 mg/kg (not to exceed 3,200 mg), in two equally divided doses

**Available Dosage Forms:**
- 200 mg, 400 mg scored tabs, and 40 mg/mL oral suspension
  - The oral suspension is bioequivalent on a mg per mg basis to the tablets

**Warnings, Precautions, and other Clinical Information:**
- Monitor for emergence or worsening depression, suicidal thoughts or behaviors and/or any unusual changes in mood or behavior
- Use caution when using Banzel with other drugs that shorten QT interval
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as Multi-organ Hypersensitivity, has been reported, discontinue use if this develops
- Avoid abrupt discontinuation in order to minimize risk of increased seizure frequency and status epilepticus
- Hormonal contraceptives may be less effective with Banzel; use additional non-hormonal forms of contraception
- Not recommended in patients with severe hepatic impairment (Child-Pugh score > 9)
- Woman who is breast feeding an infant or child should stop breast feeding

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

- Banzel tablets display decreasing bioavailability with increasing dose after single and multiple dose administration

**Criteria:**

- **Criteria for initial therapy:** Banzel (rufinamide) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 1 year of age or older

  2. A confirmed diagnosis of adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome

  3. Individual has failure, contraindication or intolerance to **ALL** of the following preferred step therapy agents:
     - Preferred step therapy agents include:
       - Felbamate
       - Lamotrigine
       - Topiramate

  4. There are **NO** contraindications:
     - Contraindications include:
       - Familial Short QT Syndrome

  **Initial approval duration**: 12 months

- **Criteria for continuation of coverage (renewal request):** Banzel (rufinamide) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined as:
       - Reduction in the number of seizure episodes

  2. Individual has been adherent with the medication

  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:
       - DRESS

- Signs and symptoms may include: fever, rash, and/or lymphadenopathy, in association with other organ system involvement, such as hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis sometimes resembling an acute viral infection, eosinophilia is often present

4. There are no significant interacting drugs

**Renewal duration**: 12 months

# Potiga (ezogabine)

**Medication class:**
Anticonvulsant, Neuronal Potassium Channel Opener

**FDA-approved indication(s):**
- As adjunctive treatment for partial-onset seizures in patients 18 years and older who have responded inadequately to several alternative treatments and for whom the benefits outweigh the risk of retinal abnormalities and potential decline in visual acuity

**Recommended Dose:**
- 100 mg three times daily, increase at weekly intervals by no more than 50 mg three times daily
  - Usual maintenance dosage is 200-400 mg three times daily

***Maximum dosage***
- 400 mg three times daily, safety and efficacy above this dose have not been examined in clinical trials

**Available Dosage Forms:**
- 50 mg, 200 mg, 300 mg, and 400 mg tabs

**Warnings, Precautions, and other Clinical Information:**
- Patients who fail to show substantial clinical benefit after titration, Potiga should be discontinued
- Patients who cannot have routine testing of visual function should not be treated with Potiga
- If retinal pigmentary abnormalities or vision changes are detected, Potiga should be discontinued, unless there are no other treatment options
- The rate of progression of retinal abnormalities and their reversibility are unknown
- Potiga causes urinary retention, monitor for retention in those at risk which includes patients with BPH, concurrent use of anticholinergics, and use with drugs that impair cognitive junction
- Potiga can cause a blue, grey-blue, or brown discoloration of the nails, lips, skin, palate, and parts of the eye; the consequence and reversibility are not fully described, if the patient develops skin discoloration, consider alternative medication

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

- Potiga can prolong QT interval, the QT interval should be monitored when Potiga is prescribed with medicines known to increase QT interval and in patients with known prolonged QT interval, congestive heart failure, ventricular hypertrophy, hypokalemia, or hypomagnesemia
- Monitor for emergence or worsening depression, suicidal thoughts or behaviors and/or any unusual changes in mood or behavior
- Avoid abrupt discontinuation in order to minimize risk of increased seizure frequency and status epilepticus, reduce dose gradually over at least 3 weeks
- Woman who is breast feeding an infant or child should stop breast feeding

**Criteria:**

- **Criteria for initial therapy:** Potiga (ezogabine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older

  2. A confirmed diagnosis of adjunctive treatment of partial-onset seizures

  3. Individual has failure, contraindication or intolerance to **FOUR** of the following preferred step therapy agents:
     - Preferred step therapy agents include:
       - Gabapentin
       - Lamotrigine
       - Levetiracetam
       - Oxcarbazepine
       - Pregabalin
       - Topiramate
       - Zonisamide

  4. **ALL** of the following baseline tests have been completed before initiation of treatment:
     - Eye exam

  **Initial approval duration**: 12 months

- **Criteria for continuation of coverage (renewal request):** Potiga (ezogabine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined as:
       - Reduction in the number of seizure episodes

## ANTIEPILEPTIC DRUGS:
## APTIOM® (eslicarbazepine acetate) oral tablet
## BANZEL® (rufinamide) oral film-coated tablet and oral suspension
## POTIGA®™ (ezogabine) oral tablet (cont.)

2. Individual has been adherent with the medication

3. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effect such as:
     - Urinary retention
       - Signs and symptoms may include: unable to start urination, trouble emptying bladder, weak urine stream, painful urination
     - Skin discoloration
       - Signs and symptoms may include: : blue, grey-blue, or brown discoloration of the nails, lips, skin, palate, and parts of the eye (whites of the eye or eye lid)

4. There are no significant interacting drugs

**Renewal duration**: 12 months

**Resources:**

Aptiom. Package Insert. Revised by manufacturer 11/2013. Accessed 07/22/2015.

Aptiom. Package Insert. Revised by manufacturer 08/2015. Accessed 07/22/2016.

Aptiom. Package Insert. Revised by manufacturer 09/2016. Accessed 11/30/2016.

Aptiom. Package Insert. Revised by manufacturer 09/2017. Accessed 12/20/2017.

Banzel. Package Insert. Revised by manufacturer 06/2015. Accessed 07/22/2015, 12/20/2017.

Potiga. Package Insert. Revised by manufacturer 05/2015. Accessed 07/22/2015.

Potiga. Package Insert. Revised by manufacturer 05/2016. Accessed 07/22/2016, 12/20/2017.

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**Fax completed prior authorization request form to 602-864-3126** or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

# Pharmacy Prior Authorization Request Form

**Do not copy for future use. Forms are updated frequently.**
**REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.**

## Member Information

| Member Name (first & last): | Date of Birth: | Gender: | BCBSAZ ID#: |
|---|---|---|---|
| Address: | City: | State: | Zip Code: |

## Prescribing Provider Information

| Provider Name (first & last): | Specialty: | NPI#: | DEA#: |
|---|---|---|---|
| Office Address: | City: | State: | Zip Code: |
| Office Contact: | Office Phone: | Office Fax: | |

## Dispensing Pharmacy Information

| Pharmacy Name: | Pharmacy Phone: | Pharmacy Fax: |
|---|---|---|

## Requested Medication Information

| Medication Name: | Strength: | Dosage Form: |
|---|---|---|
| Directions for Use: | Quantity: / Refills: | Duration of Therapy/Use: |

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

## Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

## Clinical Information

1. **What is the diagnosis? Please specify below.**

   **ICD-10 Code:** _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

| Medication Name, Strength, Frequency | Dates started and stopped or Approximate Duration | Describe response, reason for failure, or allergy |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
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| | | |

5. **Are there any supporting labs or test results? Please specify below.**

| Date | Test | Value |
|---|---|---|
| | | |
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# Pharmacy Prior Authorization Request Form

**6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.**
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

**Signature affirms that information given on this form is true and accurate and reflects office notes**

Prescribing Provider's Signature: Date:

**Please note**: Some medications may require completion of a drug-specific request form.

**Incomplete forms or forms without the chart notes will be returned.**

Office notes, labs, and medical testing relevant to the request that show medical justification are required.