PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 9/17/2015**
SECTION: DRUGS	**LAST REVIEW DATE: 2/17/2022**
	LAST CRITERIA REVISION DATE: 2/17/2022
	ARCHIVE DATE:

APTIOM® (eslicarbazepine acetate) oral
BANZEL® (rufinamide) oral
Rufinamide oral

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)

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

Criteria:

APTIOM (eslicarbazepine acetate)

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

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
2. Individual is 4 year of age or older
3. A confirmed diagnosis of partial-onset seizures
4. Individual has failure, contraindication or intolerance to **THREE** of the following preferred step therapy agents:
    a. Preferred step therapy agents include:
        i. Gabapentin
        ii. Lamotrigine
        iii. Levetiracetam
        iv. Oxcarbazepine
        v. Pregabalin
        vi. Topiramate
        vii. Zonisamide
5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Liver function tests
6. There are **NO** FDA-label contraindications, such as:
    a. Hypersensitivity to oxcarbazepine or eslicarbazepine
7. Individual does not have severe hepatic impairment (Child-Pugh Class C)
8. Will not be used as an adjunct therapy with oxcarbazepine (Oxtellar XR or Trileptal)
9. There are no significant interacting drugs

Initial approval duration: 6 months

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

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

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

  3. Individual has been adherent with the medication

  4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
     a. Contraindications as listed in the criteria for initial therapy section
     b. Significant adverse effect such as:
        i. Emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior
        ii. Stevens-Johnson syndrome or toxic epidermal necrolysis or other dermatologic reaction
        iii. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) or Multiorgan Hypersensitivity
        iv. Anaphylaxis or angioedema
        v. Clinically significant hyponatremia (sodium < 125 mEq/L) or Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)
        vi. Liver injury or jaundice
        vii. Bone marrow suppression (pancytopenia, agranulocytosis, or leukopenia)

  5. Individual does not have severe hepatic impairment (Child-Pugh Class C)

  6. Will not be used as an adjunct therapy with oxcarbazepine (Oxtellar XR or Trileptal)

  7. There are no significant interacting drugs

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-cancer Medications**

  2. **Off-Label Use of Cancer Medications**

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BANZEL® (rufinamide) oral
Rufinamide oral

BANZEL (rufinamide)
Rufinamide

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

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
  2. Individual is 1 year of age or older
  3. A confirmed diagnosis of adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome
  4. Individual has failure, contraindication or intolerance to **ALL** of the following preferred step therapy agents:
     a. Preferred step therapy agents include:
        i. Felbamate
        ii. Lamotrigine
        iii. Topiramate
  5. Request for brand Banzel, documented failure, contraindication per FDA label, intolerance to generic rufinamide
  6. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Liver function tests
  7. Individual does not have severe hepatic impairment (Child-Pugh Class C)
  8. There are **NO** FDA-label contraindications, such as:
     a. Familial Short QT Syndrome
  9. There are no significant interacting drugs

  Initial approval duration: 6 months

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

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. Documented evidence of efficacy, disease stability and/or improvement in the number of seizure episodes
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) or Multiorgan Hypersensitivity
        ii. Emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior

5. Individual does not have severe hepatic impairment (Child-Pugh Class C)

6. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Aptiom (eslicarbazepine acetate) is indicated as monotherapy or adjunctive treatment of partial-onset seizures. Rufinamide (generic or brand Banzel) 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.

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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.

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.

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Resources:

Aptiom (eslicarbazepine) product information, revised by Sunovion Pharmaceuticals Inc. 03-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 16, 2021.

Banzel (rufinamide) product information, revised by Eisai Inc. 04-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 16, 2021.

Rufinamide suspension product information, revised by Ascend Laboratories, LLC. 02-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 16, 2021.

Rufinamide tablet product information, revised by Mylan Pharmaceutical Inc. 05-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 16, 2021.

Karceski S. Initial treatment of epilepsy in adults. In: UpToDate, Garcia P, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated July 19, 2021. Accessed December 16, 2021.

Wilfong A. Seizures and epilepsy in children: Initial treatment and monitoring. In: UpToDate, Nordli DR, Dashe JF (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated September 20, 2021. Accessed December 16, 2021.