PHARMACY COVERAGE GUIDELINE

SABRIL® (vigabatrin) oral
Vigabatrin oral
VIGADRONE™ (vigabatrin) oral

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Sabril (vigabatrin), Vigadrone (vigabatrin) or generic vigabatrin are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Individual is 2 years of age or older with a confirmed diagnosis of refractory complex partial seizures, who has not responded adequately to several alternative treatments **AND** where Sabril, Vigadrone, or Vigabatrin will be used as adjunctive therapy

    b. Individual is an infant 1 month to 2 years of age with a confirmed diagnosis of infantile spasms **AND** where Sabril, Vigadrone, or Vigabatrin will be used as monotherapy

2. **Additional criteria for refractory partial complex seizures**, individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **THREE** of the following preferred step therapy agents for complex partial seizures:
    a. Gabapentin
    b. Lamotrigine
    c. Levetiracetam
    d. Oxcarbazepine
    e. Topiramate

3. The individual has received and completed a **baseline** vision assessment before initiation of treatment and with continued monitoring of the individual as clinically appropriate: [Note: This is waved if it is verified that Provider, Patient, and Pharmacy are enrolled in the REMS program]

4. Creatinine clearance is > 10 mL/min.

Initial approval duration: 3 months. Continuation requires documentation of significant clinical benefit

- **Criteria for continuation of coverage (renewal request):** Sabril (vigabatrin), Vigadrone (vigabatrin) or generic vigabatrin are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual's condition has responded while on therapy as follows:
    a. **For refractory partial complex seizures**, response is defined as **ONE** of the following:
        i. Achieved and maintains at least a 50% reduction in frequency of complex partial seizures
        ii. Achieved and maintains at least a 50% reduction in secondary generalized seizures

    b. **For infantile spasms**, response is defined as **ONE** of the following:
        i. Achieved and maintains spasm freedom as assessed by caregiver
        ii. Achieved and maintains no spasms or hypsarrhythmia during closed circuit television electroencephalography (CCTV EEG)

2. Individual has been adherent with the medication.

3. Verification that Prescriber, Patient, and Pharmacy are enrolled in the REMS program.

4. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Vision loss
    b. Neurotoxicity
    c. Suicide thoughts or behaviors
    d. Emerging or worsening depression
    e. Any unusual change in mood or behavior
    f. Peripheral neuropathy

Renewal duration: 12 months. Continuation requires documentation of significant clinical benefit.

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- 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:

Sabril (vigabatrin), Vigadrone (vigabatrin) and vigabatrin are indicated as adjunctive therapy for adults and pediatric patients 2 years of age or older with refractory complex partial seizures who have inadequately responded to several alternative treatments, they are not indicated as a first line agent for complex partial seizures. They are also indicated as monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age.

Epilepsy is a neurological disorder where brief disturbances in the electrical function of the brain result in seizures. These seizures may affect consciousness, 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 outcome (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 AEDs, 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 AEDs are associated with serious, but rare adverse events. Sabril (vigabatrin) carries a boxed warning and has a REMS program for risk of irreversible vision loss.

Practice guidelines for 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.

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Partial seizures are divided into simple partial, complex partial, and partial seizures that evolve into secondary generalized seizures. The difference between simple and complex seizures is that during simple partial seizures, patients retain awareness; during complex partial seizures, they lose awareness.

Infantile spasms (also known as West's syndrome) is a rare epileptic disorder with main characteristics of infantile spasms, mental retardation, and hypsarrhythmia, a specific abnormal pattern detected by an electroencephalogram (EEG) that is described as slow waves of high voltage and random pattern of spikes that vary in duration and location. Infantile spasms are characterized by sudden jerking and bending forward of the body, followed by stiffening of the body. Spasms usually last around 1-5 seconds but can range from 2-500 spasms at any given time.

Use of Sabril (vigabatrin), Vigadrone (vigabatrin) and vigabatrin are subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

The precise mechanism of vigabatrin's anti-seizure effect is unknown, but it is believed to be the result of its action as an irreversible inhibitor of γ-aminobutyric acid transaminase (GABA-T), the enzyme responsible for the metabolism of the inhibitory neurotransmitter GABA. Inhibition of GABA-T results in increased levels of GABA in the central nervous system.

Definitions:

Sabril (vigabatrin), Vigadrone (vigabatrin), vigabatrin REMS items:

Enrollment and agreement information
Ophthalmologic assessment requirements
Treatment initiation information
Treatment maintenance information
Pharmacy requirements and responsibilities

Resources:

Sabril (vigabatrin) product information, revised by Lundbeck Pharmaceuticals, LLC. 10-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 13, 2022.

Vigabatrin product information, revised by Actavis Pharma, Inc. 02-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 13, 2022.

Vigadrone (vigabatrin) product information, revised by Upsher-Smith Laboratories, LLC. 02-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 13, 2022.

Takacs DS, Katyayan A. Infantile spasms: Clinical features and diagnosis. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on May 16, 2022. Accessed July 13, 2022.

Takacs DS, Katyayan A. Infantile spams: Management and prognosis. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on June 28, 2022. Accessed July 13, 2022.

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