

Clinical Policy: Vigabatrin (Sabril)

Reference Number: CP.PHAR.169

Effective Date: 02/16

Last Review Date: 02/17

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene[®] clinical policy for vigabatrin (Sabril[®]).

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation[®] that Sabril is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria:

A. Refractory Complex Partial Seizures (must meet all):

1. Diagnosis of refractory complex partial seizures (see Appendix B for classification of seizures);
2. Age \geq 10 years;
3. Inadequate response to \geq 2 alternative anticonvulsant drugs (e.g., carbamazepine, phenytoin);
4. Prescribed as an add-on agent to anticonvulsant therapy;
5. Prescribed daily dose* does not exceed (a or b):
 - a. Pediatric members age 10 to 16 years: 1,000 mg twice daily (*if weight is > 60 kg, dosing should follow adult recommendations*);
 - b. Adults age \geq 17 years: 1,500 mg twice daily.

**The lowest dosage and shortest exposure to Sabril is used to achieve clinical objectives. Doses are titrated upward every week to max dose if needed; titration also is used upon discontinuation. The initial recommended total daily dose (renal dosing adjustment if necessary) for pediatric members age 10 to 16 years is 500 mg/day (250 mg twice daily) and 1,000 mg/day (500 mg twice daily) for adult members age \geq 17 years.*

Approval duration: 3 months

B. Infantile Spasms* (must meet all):

1. Diagnosis of infantile spasms;
2. Age \leq 2 years.

**The lowest dosage and shortest exposure to Sabril is used to achieve clinical objectives. Doses are titrated upward every 3 days to max dose (75 mg/kg twice daily) if needed; titration also is used upon discontinuation. The initial recommended total daily dose for pediatric members age \leq 2 years is 50 mg/kg/day given in two divided doses (25 mg/kg twice daily). Information regarding renal dose adjustments in this population is not provided by the PI. The powder for oral solution formulation is recommended for members with infantile spasms.¹*

Approval duration: 4 weeks

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy

II. Continued Approval

A. Refractory Complex Partial Seizures (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Since starting vigabatrin therapy, member has experienced a reduction in seizures;
3. Prescribed daily dose does not exceed (a or b):
 - a. Pediatric members age 10 to 16 years: 1,000 mg twice daily (*if weight is > 60 kg, dosing should follow adult recommendations*);
 - b. Adults age ≥ 17 years: 1,500 mg twice daily.

Approval duration: 6 months

B. Infantile Spasms (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Age ≤ 2 years;
3. Since starting vigabatrin therapy, member has experienced a reduction or cessation of spasms and/or a normalization of electroencephalogram (EEG) changes associated with spasms.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy

Background*Description/Mechanism of Action:*

Sabril (vigabatrin) is an oral antiepileptic drug. 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. This action results in increased levels of GABA in the central nervous system. No direct correlation between plasma concentration and efficacy has been established. The duration of drug effect is presumed to be dependent on the rate of enzyme re-synthesis rather than on the rate of elimination of the drug from the systemic circulation.

Formulations:

- Sabril 500 mg tablets supplied as bottles of 100.
- Sabril 500 mg packets contain a white to off-white granular powder (to be mixed with water). They are supplied in packages of 50.

Tablet and powder formulations are bioequivalent; powder is recommended for infants and young children with infantile spasms. Vigabatrin should be tapered upon discontinuation.

FDA Approved Indications:

Sabril is an antiepileptic drug/oral tablet or powder for oral solution indicated as:

- Refractory complex partial seizures (CPS)
 - Adjunctive therapy for adults and pediatric patients 10 years of age and older with refractory complex partial seizures who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss.

Limitation of use: Sabril is not indicated as a first line agent for complex partial seizures.
- Infantile spasms (IS)
 - Monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.

Appendices

Appendix A: Abbreviation Key

- CPS: Complex partial seizures
- EEG: Electroencephalogram
- GABA: Gamma-aminobutyric acid
- IS: Infantile spasms

Appendix B: International League Against Epilepsy (ILAE) 2010 Seizure Classification

- | | |
|-------------------------------------|--|
| • Generalized seizures | • Myoclonic tonic |
| • Tonic-clonic (in any combination) | • Clonic |
| • Absence | • Tonic |
| • Typical | • Atonic |
| • Atypical | • Focal seizures (<i>limited to one hemisphere; includes complex partial seizures</i>) |
| • Absence with special features | • Unknown |
| • Myoclonic absence | • Epileptic spasms (<i>includes infantile spasms</i>) |
| • Eyelid myoclonia | |
| • Myoclonic | |
| • Myoclonic atonic | |

ILAE 2010 descriptors of focal seizures according to degree of impairment during seizure:

- Without impairment of consciousness or awareness.
- With observable motor or autonomic components. This roughly corresponds to the concept of “simple partial seizure. “Focal motor” and “autonomic” are terms that may adequately convey this concept depending on the seizure manifestations).
- Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura.
- With impairment of consciousness or awareness. ***This roughly corresponds to the concept of complex partial seizure.*** “Dyscognitive” is a term that has been proposed for this concept.
- Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components). This expression replaces the term “secondarily generalized seizure.”

Appendix C: Black Box Warning – Permanent Vision Loss

CLINICAL POLICY

Vigabatrin

- Sabril can cause permanent bilateral concentric visual field constriction, including tunnel vision that can result in disability. In some cases, Sabril also can damage the central retina and may decrease visual acuity.
- The onset of vision loss from Sabril is unpredictable, and can occur within weeks of starting treatment or sooner, or at any time after starting treatment, even after months or years.
- Symptoms of vision loss from Sabril are unlikely to be recognized by patients or caregivers before vision loss is severe.
- Vision loss of milder severity, while often unrecognized by the patient or caregiver, can still adversely affect function.
- The risk of vision loss increases with increasing dose and cumulative exposure, but there is no dose or exposure known to be free of risk of vision loss.
- Vision assessment is recommended at baseline (no later than 4 weeks after starting Sabril), at least every 3 months during therapy, and about 3 to 6 months after the discontinuation of therapy.
- Once detected, vision loss due to Sabril is not reversible. It is expected that, even with frequent monitoring, some patients will develop severe vision loss.
- Consider drug discontinuation, balancing benefit and risk, if vision loss is documented.
- Risk of new or worsening vision loss continues as long as Sabril is used. It is possible that vision loss can worsen despite discontinuation of Sabril.
- Because of the risk of vision loss, Sabril should be withdrawn from patients with refractory complex partial seizures who fail to show substantial clinical benefit within 3 months of initiation and within 2-4 weeks of initiation for patients with infantile spasms, or sooner if treatment failure becomes obvious. Patient response to and continued need for Sabril should be periodically reassessed.
- Sabril should not be used in patients with, or at high risk of, other types of irreversible vision loss unless the benefits of treatment clearly outweigh the risks.
- Sabril should not be used with other drugs associated with serious adverse ophthalmic effects such as retinopathy or glaucoma unless the benefits clearly outweigh the risks.
- Use the lowest dosage and shortest exposure to Sabril consistent with clinical objectives.

Because of the risk of permanent vision loss, Sabril is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Sabril REMS Program.^{1,2} Further information is available at www.SabrilREMS.com or 1-888-457-4273.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.56.HP Acthar and Sabril. Criteria: added maximum dose. Substituted participation in SHARE program for vision assessment criteria. Background: limited to Description/MOA, FDA approved indications and safety information	02/16	2/16

Reviews, Revisions, and Approvals	Date	Approval Date
<p>Appendices: removed Appendix F and incorporated pertinent information about the SHARE program into the criteria.</p>		
<p>Infantile spasms: Lower age limit of one month is removed and left to provider discretion; dosing is removed given verification challenges around weight-based dosing; monotherapy is removed since other seizure medications are available without a PA making verification problematic. Complex partial seizures: Adjunctive therapy is defined and examples of anticonvulsant therapies are added per the PI; dosing is added to the continued approval section.</p> <p>Informational footnotes regarding dosing are added to both initial approval sections.</p> <p>Efficacy criteria are added to both continued approval sections.</p> <p>Classification of seizures per ILAE is added at Appendix B.</p> <p>PI black box warning is restated verbatim at Appendix C.</p> <p>Periodic visual monitoring is required under the REMS program and so is not stated separately in the criteria; documentation of REMS enrollment also is removed from criteria sets since it is required separately under the REMS program for both members and providers.</p> <p>Classification and guideline/consensus documentation is added to reference section.</p>	02/17	02/17

References

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Neurology. June 12, 2012; 78(24): 1974-80. doi: 10.1212/WNL.0b013e318259e2cf.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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