Clinical Policy: Vigabatrin (Sabril)

Reference Number: PA.CP.PHAR.169
Effective Date: 01/18
Last Review Date: 07/17/19 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for vigabatrin (Sabril®).

FDA Approved Indication(s)
Sabril is indicated:

- For the treatment of refractory complex partial seizures as adjunctive therapy in patients ≥ 10 years of age who have responded inadequately to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss; Sabril is not indicated as a first line agent for complex partial seizures
- For the treatment of infantile spasms as monotherapy in infants 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss

Policy/Criteria
It is the policy Pennsylvania Health and Wellness 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;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 10 years;
4. Sabril will be used as adjunctive therapy;
5. Inadequate response to ≥ 2 alternative anticonvulsant drugs (*see Appendix B for examples*);
6. Dose does not exceed (a or b):
   - Pediatric members age 10 to 16 years: 2,000 mg/day (members > 60 kg should be dosed as adults);
   - Adults age ≥ 17 years: 3,000 mg/day; or

B. Member is currently receiving treatment with Sabril and exhibiting positive response to therapy.

Approval duration: 6 months

C. Infantile Spasms* (must meet all):

1. Diagnosis of infantile spasms;
2. Prescribed by or in consultation with a neurologist;
3. Age between 1 month to 2 years;
4. Dose does not exceed 150 mg/kg/day.

Approval duration: 3 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
    a. Pediatric members age 10 to 16 years: 2,000 mg/day (members > 60 kg should be dosed as adults);
    b. Adults (age ≥ 17 years): 3,000 mg/day.

Approval duration: 12 months

B. Infantile Spasms (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.;
2. Age between 1 month to 2 years;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 150 mg/kg/day.

Approval duration: 12 months or up to 2 years of age, whichever is less

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.; or
2. Refer to PA.CP.PMN.53

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.

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

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

- 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
3Q 2018 annual review: for infantile spasms: removed abnormal EEG requirement to confirm diagnosis and added specialist requirement, extended initial approval duration from 4 weeks to 3 months, added back age requirement on re-auth; added “or up to 2 years of age, whichever is less” to continued approval duration; modified continued therapy to allow for continuity of care for infantile spasms and complex partial seizures; for complex partial seizures: added specialist requirement; references reviewed and updated.	04.18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

References

a. Sabril Prescribing Information. Deerfield, IL: Lundbeck. March 2018. Available at https://www.sabril.net/prescribing-sabril. Accessed April 6, 2018.
b. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. Cochrane Epilepsy Group – Cochrane Database of Syst Rev. June 5, 2013; 6: CD001770. doi: 10.1002/14651858.CD001770.pub3.
c. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. Epilepsia. October 2010; 51(10): 2175-89. doi: 10.1111/j.1528-1167.2010.02657.x.
d. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms. Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. June 12, 2012; 78(24): 1974-80. doi: 10.1212/WNL.0b013e318259e2cf.
e. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed April 6, 2018.