

MEDICAL POLICY STATEMENT		
Effective Date	Next Annual Review Date	Last Review / Revision Date
06/15/2011	06/15/2012	06/15/2011
Author		
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CSMG Medical Policy Statements are derived from literature based and supported clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services are those health care services or supplies which are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative and are not provided mainly for the convenience of the member or provider.

A. SUBJECT

Vigabatrin (Sabril) Oral Solution and Tablets

B. BACKGROUND

Vigabatrin (Sabril) is an oral gamma aminobutyric acid transaminase inhibitor. The precise mechanism of vigabatrin's (Sabril'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. The creation of Sabril (vigabatrin) was the result of a deliberate search for a molecule to increase gamma-aminobutyric acid (GABA) levels in the central nervous system (CNS).

The patient selection criteria outlined was derived from the FDA-approved prescribing information for vigabatrin (Sabril), the studies that were presented to the FDA in support of the pre-market approval application, and studies in the peer-reviewed published medical literature. The FDA label indications that are found in the manufacturer prescribing information and are described below are infantile spasms and refractory complex partial seizures in adults. Coverage decisions for conditions other than the above FDA approved indication will be reviewed on a case-by-case basis if proven effective through research documentation. The requesting provider will need to support his exception request with the appropriate literature.

C. POLICY

CareSource will approve the use of vigabatrin (Sabril) and consider its use as medically necessary when the following criteria have been met for:

- Infantile Spasms
- Refractory Complex Partial Seizures

All other uses of vigabatrin (Sabril) are considered experimental/investigational, and therefore, not covered.

Infantile Spasms

Vigabatrin (Sabril) is indicated as monotherapy for pediatric patients 1 month to 2 years of age with infantile spasms (IS) for whom the potential benefits outweigh the potential risk of vision loss.

Prior Authorization Criteria:

- Documented diagnosis of Infantile Spasms
- Age 1 month to 2 years of age
- Prescribed by a pediatric neurologist or under recommendation of pediatric neurologist
- Prescribing physician is registered with SHARE (special restricted distribution plan)

NOTE: Sabril should be withdrawn from a pediatric patient treated for infantile spasms who fails to show substantial clinical benefit within 2-4 weeks of treatment initiation, or sooner if treatment failure becomes obvious.

Refractory Complex Partial Seizures (CPS)

Sabril is indicated as adjunctive therapy for **adult** patients with refractory complex partial seizures (CPS) who have inadequately responded 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.

Prior Authorization Criteria:

- Documented diagnosis of refractory complex partial seizures
- Prescribed by a neurologist or under recommendation of neurologist
- Prescribing physician is registered with SHARE (special restricted distribution plan)
- Patient has failed alternative treatments for control of the complex partial seizures.

NOTE: Sabril should be withdrawn from an adult patient treated for refractory complex partial seizures who fails to show substantial clinical benefit within 3 months of treatment initiation, or sooner if treatment failure becomes obvious.

Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to, test reports, chart notes from provider's office or hospital admission notes.

For Special Needs Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

For Medicare

NCD for vigabatrin (Sabril)

Medicare does not have a National Coverage Determination (NCD) for vigabatrin (Sabril). In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them.

Refer to the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, section 50 Drugs and Biologicals at: <http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf>.
Local Coverage Determinations (LCDs) for vigabatrin (Sabril) do not exist at this time.
(Accessed March 14, 2011)

Safety

CareSource will only review requests for **vigabatrin (Sabril)** if the patient has **none** of the following contraindications:

- Hypersensitivity to vigabatrin
- Sabril should not be used in patients with, or at high risk of, other types of irreversible vision loss or with other drugs associated with serious adverse ophthalmic effects, such as retinopathy or glaucoma unless the benefits clearly outweigh the risks

Precautions:

- Monitoring of vision by an ophthalmic professional with expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina, must be performed at baseline (no later than 4 weeks after starting vigabatrin (Sabril)) and at least every 3 months while on therapy. Vision testing is also required about 3 to 6 months after the discontinuation of vigabatrin (Sabril) therapy. This assessment should include visual acuity and visual field whenever possible.
- Attempts to monitor vision periodically must be documented under the SHARE program. In patients where vision testing is not possible, treatment may continue according to clinical judgment, with appropriate caregiver(s) counseling, and with documentation in the SHARE program of the inability to test vision. Because of variability, results from ophthalmic monitoring must be interpreted with caution, and repeat testing is recommended if results are abnormal or uninterpretable.
- The onset and progression of vision loss from Sabril is unpredictable. **Once detected, vision loss due to Sabril is not reversible.**
- Sabril should be discontinued gradually to avoid withdrawal seizures.
- In adults, dose adjustment, including initiating treatment with a lower dose, is necessary in patients with mild (creatinine clearance >50-80 mL/min), moderate (creatinine clearance >30-50 mL/min) and severe (creatinine clearance >10-30 mL/min) renal impairment
- Due to the risk of permanent vision loss, the FDA is requiring a Risk Evaluation and Mitigation Strategy (REMS) program for this product. This program, called the SHARE program, includes periodic vision testing and a restricted distribution program.

Pregnancy Risk Factor = C

There are no adequate and well-controlled studies in pregnant women. SABRIL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. To provide information regarding the effects of *in utero* exposure to SABRIL, physicians are advised to recommend that pregnant patients taking SABRIL enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry (1-888-233-2334) and must be done by patients themselves. Information on the registry can also be found by visiting <http://www.aedpregnancyregistry.org/>.

Vigabatrin is excreted in human milk. Because of the potential for serious adverse reactions from vigabatrin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Conditions of Coverage

Quantity Limitations	Infantile Spasms: Initial dosing is 50 mg/kg/day given in two divided doses and can be titrated by 25-50 mg/kg/day increments every 3 days up to a maximum of 150 mg/kg/day Refractory Complex Partial Seizures in Adults: Initiate therapy at 500 mg twice daily, increasing total daily dose per instructions. The recommended dose is 1.5 grams twice daily NOTE: Dose needs to be adjusted in patients with renal impairment. The lowest dose and shortest exposure to SABRIL should be used that is consistent with clinical objectives. Reduce dose gradually upon discontinuation.
J-Code	J3490
NDC	67386011101
Applicable ICD-9 Code	345.60-345.61 - Infantile Spasms 345.4 - Refractory Complex Partial Seizures
Place Of Service	Office, Outpatient, Home **Preferred place of service is the home
Authorization Period	Approved initial authorizations are valid for 3 months. Continued treatment may be considered when the member has shown biological response to treatment. All authorizations are subject to continued eligibility.

NOTE: Because of the risk of permanent vision loss, SABRIL is available only through a special restricted distribution program called SHARE, by calling 1-888-45-SHARE. Only prescribers and pharmacies registered with SHARE may prescribe and distribute SABRIL. In addition, SABRIL may be dispensed only to patients who are enrolled in and meet all conditions of SHARE.

D. REVIEW / REVISION HISTORY

6 /15 /11

E. REFERENCES

Sabril [package insert] for Oral Solution. Deerfield, IL: Lundbeck Inc.; 2010.

Sabril [package insert] Tablets. Deerfield, IL: Lundbeck Inc.; 2010.

French JA, Kanner AM, Bautista J et al. Efficacy and tolerability of the new antiepileptic drugs II: Treatment of refractory epilepsy: Report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004;62:1261-1273.

French JA, Mosier M, Walker S, et al. [A double-blind, placebo-controlled study of vigabatrin \(3 g/day\) in patients with uncontrolled complex partial seizures](#). Vigabatrin Protocol 024 Investigative Cohort. *Neurology* 1996;46(1):54-61. PMID: 8559421.

Dean C, Mosier M, Penry K. [Dose-response study of vigabatrin as add-on therapy in patients with uncontrolled complex partial seizures](#). *Epilepsia*. 1999;40(1):74-82. PMID: 9924905.

Kwan P, Brodie M. Early identification of refractory epilepsy. *N Engl J Med*. 2000;342(5):314-319.

U.S. Food and Drug Administration Drug Safety Data. www.fda.gov/downloads/Drugs/DrugSafety/UCM180720.pdf (March 15, 2011)

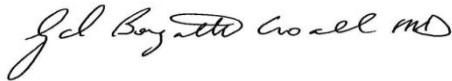
The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.



Chief Medical Officer

May 31, 2011

Date



Senior Medical Director

May 31, 2011

Date