

Vigabatrin Products

Policy # 00244

Original Effective Date: 12/16/2009

Current Effective Date: 01/13/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Repository corticotropin Injection (ACTH Gel, H.P. Acthar Gel) is addressed separately in medical policy 00230.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member’s contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider brand or generic vigabatrin (Sabril[®], Vigadrone[™], Vigpoder[™], Vigafyde[™])[‡] for the treatment of infantile spasms or refractory complex partial seizures to be **eligible for coverage**.**

Infantile Spasms

Patient Selection Criteria

Coverage eligibility for brand or generic vigabatrin (Sabril, Vigadrone, Vigpoder, Vigafyde) for the treatment of infantile spasms (IS) will be considered when ALL of the following criteria are met:

- Patient has a diagnosis of infantile spasms; AND
- Patient is 1 month to 2 years of age; AND
- Vigabatrin is used as monotherapy; AND
- If the requested drug is Vigafyde, the patient has tried and failed (e.g., intolerance or inadequate response) at least one generic vigabatrin product unless there is clinical evidence or patient history that suggests the generic products will be ineffective or cause an adverse reaction to the patient.

*(Note: This specific patient selection criterion is an additional requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Refractory Complex Partial Seizures

Patient Selection Criteria

Coverage eligibility for brand or generic vigabatrin (Sabril, Vigadrone, Vigpoder) for the treatment of refractory complex partial seizures will be considered when all of the following criteria are met:

- Patient has a diagnosis of refractory complex partial seizures (CPS); AND

Vigabatrin Products

Policy # 00244

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- Patient is greater than or equal to 2 years of age; AND
- Vigabatrin is used as adjunctive therapy in patients who have inadequately responded to alternative treatments and not as a first line agent for CPS.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of vigabatrin (Vigafyde) for the treatment of infantile spasms when the patient has not tried and failed at least one generic vigabatrin product to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of brand or generic vigabatrin (Sabril, Vigadrone, Vigpoder, Vigafyde) when patient selection criteria are not met (except that noted above as **not medically necessary*****) to be **investigational**.*

Background/Overview

About vigabatrin Tablets and Oral Solution

Vigabatrin is an oral antiepileptic drug that is available in multiple formulations—500 mg tablets, 500 mg packets of powder for oral solution, and a 100 mg/mL oral solution (Vigafyde). There are generics available including Vigadrone and Vigpoder, which are generic versions of the 500 mg powder packets marketed under a brand name. Brand Sabril, generic vigabatrin, Vigadrone, and Vigpoder are indicated as add-on therapy for patients greater than or equal to 2 years of age with refractory complex partial seizures (CPS) and for infants with infantile spasms (IS). Vigafyde is a branded oral solution that is only indicated as monotherapy for the treatment of IS in pediatric patients 1 month to 2 years of age.

The precise mechanism of vigabatrin's antiseizure effect is unknown but is believed to be the result of its action as an irreversible inhibitor of gamma-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.

Because of the risk of permanent vision loss, vigabatrin is available only through a special restricted distribution program called the Vigabatrin REMS program. Only prescribers and pharmacies registered with the Vigabatrin REMS program may prescribe and distribute vigabatrin. In addition, vigabatrin may be dispensed only to patients who are authorized to receive vigabatrin.



Policy # 00244

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Infantile Spasms

Infantile spasms is a difficult-to-treat epilepsy syndrome that usually strikes infants between three to six months old. An estimated 8,500 infants in the U.S. have been diagnosed with IS, and each year approximately 2,500 new cases of IS are reported in the U.S. Vigabatrin may not be appropriate for use in all patients with IS.

Complex Partial Seizures

Of the three million Americans affected by epilepsy, approximately 35 percent have CPS, the single largest seizure type which originates from a single region of the brain and can cause impaired consciousness. Despite the availability of many antiepileptic drugs, approximately 30 to 36 percent of adults with CPS continue to have seizures. Vigabatrin provides an add-on treatment option for CPS patients greater than or equal to 2 years of age who have not responded to several alternative treatments and are considered 'refractory' to treatment. Given the potential benefit compared to the risk of permanent vision loss, it is expected that only a small percentage of refractory CPS patients will initiate and maintain treatment with vigabatrin as add-on therapy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

On August 21, 2009, the FDA approved vigabatrin (Sabril) oral solution and tablets for treatment of IS and refractory CPS in patients who have inadequately responded to other anti-epilepsy drugs (AEDs). Sabril was the first therapy approved for the treatment of IS. In October of 2013, the age for treatment of refractory CPS was changed to greater than or equal to 10 years of age. In February of 2020, the age for refractory CPS was again expanded to include patients greater than or equal to 2 years of age.

In June 2024, the FDA approved vigabatrin oral solution (Vigafyde) as monotherapy for the treatment of infantile spasms in pediatric patients 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss. This approval was based upon a comparison of the compositional differences between vigabatrin for oral solution and Vigafyde oral solution.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Infantile Spasms

The effectiveness of vigabatrin as monotherapy was established for IS in two multicenter controlled studies. Both studies were similar in terms of disease characteristics and prior treatments of patients and all enrolled infants had a confirmed diagnosis of IS.



Vigabatrin Products

Policy # 00244

Original Effective Date: 12/16/2009

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Study 1 (N=221) was a multicenter, randomized, low-dose high-dose, parallel group, partially-blinded (caregivers knew the actual dose but not whether their child was classified as low or high dose; EEG reader was blinded but investigators were not blinded) study to evaluate the safety and efficacy of vigabatrin in patients < 2 years of age with new-onset IS. Patients with both symptomatic and cryptogenic etiologies were studied. The study was comprised of two phases. The first phase was a 14 to 21 day partially-blind phase in which patients were randomized to receive either low-dose (18-36 mg/kg/day) or high-dose (100-148 mg/kg/day) vigabatrin. Study drug was titrated over seven days, followed by a constant dose for seven days. If the patient became spasm-free on or before day 14, another seven days of constant dose was administered. The primary efficacy endpoint of this study was the proportion of patients who were spasm-free for seven consecutive days beginning within the first 14 days of vigabatrin therapy. Patients considered spasm-free were defined as those patients who remained free of spasms (evaluated according to caregiver response to direct questioning regarding spasm frequency) and who had no indication of spasms or hypsarrhythmia during eight hours of CCTV EEG recording (including at least one sleep-wake-sleep cycle) performed within three days of the seventh day of spasm freedom and interpreted by a blinded EEG reader. Seventeen patients in the high dose group achieved spasm freedom compared with eight patients in the low dose group.

Study 2 (N=40) was a multicenter, randomized, double-blind, placebo-controlled, parallel group study consisting of a pre-treatment (baseline) period of two to three days, followed by a five-day double-blind treatment phase during which patients were treated with vigabatrin (initial dose of 50 mg/kg/day with titration allowed to 150 mg/kg/day) or placebo. The primary efficacy endpoint in this study was the average percent change in daily spasm frequency, assessed during a pre-defined and consistent two-hour window of evaluation, comparing baseline to the final two days of the five-day double-blind treatment phase. No statistically significant differences were observed in the average frequency of spasms using the two-hour evaluation window. However, a post-hoc alternative efficacy analysis, using a 24-hour clinical evaluation window, found a statistically significant difference in the overall percentage of reductions in spasms between the vigabatrin group (68.9%) and the placebo group (17.0%) (p=0.030).

Complex Partial Seizures in Adults

The effectiveness of vigabatrin as adjunctive therapy in adult patients with CPS was established in two U.S. multicenter, double-blind, placebo-controlled, parallel-group clinical studies. A total of 357 adults (age 18 to 60 years) with CPS, with or without secondary generalization were enrolled (Studies 1 and 2). Patients were required to be on an adequate and stable dose of an anticonvulsant and have a history of failure on an adequate regimen of carbamazepine or phenytoin. Patients had a history of about eight seizures per month (median) for about 20 years (median) prior to entrance into the study. These studies were not capable by design of demonstrating direct superiority of vigabatrin over any other anticonvulsant added to a regimen to which the patient had not adequately responded. Further, in these studies patients had previously been treated with a limited range of anticonvulsants.



Vigabatrin Products

Policy # 00244

Original Effective Date: 12/16/2009

Current Effective Date: 01/13/2025

The primary measure of efficacy was the patient's reduction in mean monthly frequency of complex partial seizures plus partial seizures secondarily generalized at end of study compared to baseline.

Study 1 (N=174) was a randomized, double-blind, placebo-controlled, dose-response study consisting of an 8-week baseline period followed by an 18-week treatment period. Patients were randomized to receive placebo or 1, 3, or 6 g/day vigabatrin administered twice daily. During the first six weeks following randomization, the dose was titrated upward beginning with 1 g/day and increasing by 0.5 g/day on days 1 and 5 of each subsequent week in the 3 g/day and 6 g/day groups, until the assigned dose was reached. The 3 g/day and 6 g/day dose groups were statistically significantly superior to placebo, but the 6 g/day dose was not superior to the three g/day dose.

Study 2 (N=183 randomized, 182 evaluated for efficacy) was a randomized, double blind, placebo-controlled, parallel study consisting of an eight-week baseline period and a 16-week treatment period. During the first four weeks following randomization, the dose of vigabatrin was titrated upward beginning with 1 g/day and increased by 0.5 g/day on a weekly basis to the maintenance dose of 3 g/day. Vigabatrin 3 g/day was statistically significantly superior to placebo in reducing seizure frequency.

Complex Partial Seizures in Patients 3 to 16 Years of Age

Vigabatrin was studied in three double-blind, placebo-controlled, parallel-group studies in 269 patients who received Sabril and 104 patients who received placebo. No individual study was considered adequately powered to determine efficacy in pediatric patients age 3 years and above. The data from all three pediatric studies were pooled and used in a pharmacometric bridging analysis using weight-normalized doses to establish efficacy and determine appropriate dosing. All three studies were randomized, double-blind, placebo-controlled, parallel-group, adjunctive-treatment studies in patients aged 3-16 years with uncontrolled complex partial seizures with or without secondary generalization. The study period included a 6 to 10 week baseline phase and a 14 to 17 week treatment phase (composed of a titration and maintenance period). The pharmacometric bridging approach consisted of defining a weight-normalized dose-response, and showing that a similar dose-response relationship exists between pediatric patients and adult patients when vigabatrin was given as adjunctive therapy for complex partial seizures. Dosing recommendations in pediatric patients 2 to 16 years of age were derived from simulations utilizing these pharmacometric dose-response analyses.

References

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2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *New England Journal of Medicine*. February 3, 2000;342:314-319.
3. Devinsky O. Patients with refractory seizures. *New England Journal of Medicine*. May 20, 1999; 340:1565-70.
4. Epilepsy and Seizure Statistics. Epilepsy Foundation.org.
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Vigabatrin Products

Policy # 00244

Original Effective Date: 12/16/2009

Current Effective Date: 01/13/2025

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9. Vermes K. REMS for Sabril Modified. Pharmacy Times. June 2016.
10. Vigadrone (vigabatrin) Full Prescribing Information. Updated Feb 2020.
11. Vigpoder (vigabatrin) Full Prescribing Information. Updated March 2024.
12. Vigafyde (vigabatrin solution). Full prescribing information. Updated November 2024.

Policy History

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12/04/2009	Medical Policy Committee approval
12/16/2009	Medical Policy Implementation Committee approval. New policy.
12/01/2010	Medical Policy Committee approval
12/15/2010	Medical Policy Implementation Committee approval. No change to coverage.
12/08/2011	Medical Policy Committee approval
12/21/2011	Medical Policy Implementation Committee approval. No change to coverage.
12/06/2012	Medical Policy Committee approval
12/19/2012	Medical Policy Implementation Committee approval. No change to coverage.
12/12/2013	Medical Policy Committee approval
12/18/2013	Medical Policy Implementation Committee approval. No change to coverage. FDA has combined the indications for both formulations of Sabril. Also extended the age for complex partial seizures to match new FDA expanded indication.
12/04/2014	Medical Policy Committee approval
12/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
12/03/2015	Medical Policy Committee approval
12/16/2015	Medical Policy Implementation Committee approval. No change to coverage.
12/01/2016	Medical Policy Committee approval
12/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
12/07/2017	Medical Policy Committee approval
12/20/2017	Medical Policy Implementation Committee approval. No change to coverage.
02/07/2019	Medical Policy Committee approval
02/20/2019	Medical Policy Implementation Committee approval. Title changed from “vigabatrin (Sabril)” to “Vigabatrin Products”. Added generic formulation and updated background information to reflect the generic availability and changes to the REMS program.



Vigabatrin Products

Policy # 00244

Original Effective Date: 12/16/2009

Current Effective Date: 01/13/2025

02/06/2020 Medical Policy Committee approval
02/12/2020 Medical Policy Implementation Committee approval. No change to coverage.
02/04/2021 Medical Policy Committee review
02/10/2021 Medical Policy Implementation Committee approval. Updated criteria to extend the age for complex partial seizures to ≥ 2 years to match the expanded FDA indication.
02/03/2022 Medical Policy Committee review
02/09/2022 Medical Policy Implementation Committee approval. No change to coverage.
02/02/2023 Medical Policy Committee review
02/08/2023 Medical Policy Implementation Committee approval. No change to coverage.
04/04/2024 Medical Policy Committee review
04/10/2024 Medical Policy Implementation Committee approval. Added new generic, Vigpoder, to policy. No change to coverage criteria.
12/05/2024 Medical Policy Committee review
12/11/2024 Medical Policy Implementation Committee approval. Added new product, Vigafyde, to the policy with relevant criteria and background information.

Next Scheduled Review Date: 12/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and



Vigabatrin Products

Policy # 00244

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- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

