



Vigabatrin REMS Program

Healthcare Providers/Prescribers and Pharmacies must be certified in the Vigabatrin REMS Program in order to prescribe or dispense vigabatrin and Patients must be enrolled in the Vigabatrin REMS Program in order to receive vigabatrin. If you were previously certified or enrolled in the Sabril REMS Program or have certified or enrolled in the new shared Vigabatrin REMS Program, you DO NOT need to re-certify or re-enroll. If you have NOT certified or enrolled, please visit www.vigabatrinREMS.com for more information and to download the forms.

Sabril® is a registered trademark of Lundbeck LLC.

About Par Pharmaceutical

Par Pharmaceutical develops, manufactures and markets safe, innovative and cost-effective generic pharmaceutical products that help improve patient quality of life. Par, among the top four leaders in the U.S. generics industry, possesses a portfolio that includes sterile injectables, alternative dosage forms and many other differentiated products. We are proud to provide patients and customers with uncompromising quality and value for almost 40 years.

IMPORTANT SAFETY INFORMATION about vigabatrin for oral solution (continued)

- Suppression of alanine transaminase (ALT) and aspartate transaminase (AST) activity by vigabatrin may preclude the use of these markers, especially ALT, to detect early hepatic injury. Vigabatrin may increase the amount of amino acids in the urine, possibly leading to a false positive test for certain rare genetic metabolic diseases (e.g., alpha aminoacidic aciduria).
- Do not use vigabatrin during pregnancy unless the potential benefit justifies the potential risk to the fetus. **Pregnancy Registry:** To provide information regarding the effects of *in utero* exposure to vigabatrin, physicians should recommend that pregnant patients taking vigabatrin enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. Patients must call the toll-free number 1-888-233-2334 to enroll. Registry information can be found at <http://www.aedpregnancyregistry.org/>.
- Vigabatrin is excreted in human milk and may cause serious adverse events in nursing infants. Discontinue nursing or discontinue vigabatrin, taking into account the importance of the drug to the mother.
- Dose adjustment, including initiating treatment with a lower dose, is necessary in pediatric patients 10 years of age and older and adults with mild (creatinine clearance >50 to 80 mL/min), moderate (creatinine clearance >30 to 50 mL/min) and severe (creatinine clearance >10 to 30 mL/min) renal impairment.

Please see accompanying full Prescribing Information, including Boxed Warning and Medication Guide.



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Vigabatrin for Oral Solution AA-Rated Generic Version of Sabril®



For more information, please call 833-PAR-HELP (833-727-4357).

INDICATIONS

Vigabatrin for oral solution is indicated as 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. Vigabatrin for oral solution is not indicated as a first line agent for complex partial seizures.

Vigabatrin for oral solution is indicated as 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.

IMPORTANT SAFETY INFORMATION about vigabatrin for oral solution

WARNING: PERMANENT VISION LOSS

- Vigabatrin can cause permanent bilateral concentric visual field constriction, including tunnel vision that can result in disability. In some cases, vigabatrin also can damage the central retina and may decrease visual acuity.
- The onset of vision loss from vigabatrin 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 vigabatrin 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 vigabatrin), at least every 3 months during therapy, and about 3 to 6 months after the discontinuation of therapy.
- Once detected, vision loss due to vigabatrin 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 vigabatrin is used. It is possible that vision loss can worsen despite discontinuation of vigabatrin.

Please see additional Important Safety Information inside.

Please see accompanying full Prescribing Information, including Boxed Warning and Medication Guide.

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Par's Vigabatrin is AA-Rated What is an AA-rated drug?

Drug products are considered to be therapeutic equivalents only if they are pharmaceutical equivalents for which bioequivalence (BE) has been demonstrated, and they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling. AA-rated drugs are drugs (like vigabatrin) that meet these necessary approval standards established by the US Food and Drug Administration (FDA).

A generic drug is considered bioequivalent to a brand-name drug if it contains the same active pharmaceutical ingredient as the branded drug, and if there is no significant difference in the formulation, quality, and effectiveness of the two drugs. Products coded as AA contain active ingredients and dosage forms that are not regarded as presenting either actual or potential BE problems or drug quality or standards issues. However, all oral dosage forms must meet an appropriate *in vitro* BE standard that is acceptable to the FDA in order to be approved.

A pharmaceutical company seeking to market a generic version of a branded drug may file an Abbreviated New Drug Application (ANDA) with the FDA. FDA will determine whether or not the generic version meets approval standards. FDA has stated that it believes that products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product.

At the pharmacy, generic substitution is when a generic drug is dispensed rather than the brand-name drug, and many third party payers encourage the substitution of lower-priced therapeutically-equivalent generic drugs (such as AA-rated drugs) for higher-priced branded drugs.



We Can Help!

Par Pharmaceutical has established a dedicated **Patient Assistance Resource** to help vigabatrin patients and their families. We can help answer any questions or see if you may qualify for financial assistance. Please call **833-PAR-HELP (833-727-4357)** for help with any of the following:

- Insurance Authorization
- Patient Assistance Program*
- Copay Assistance*
- REMS Enrollment
- General Product Questions

*For eligible patients only

IMPORTANT SAFETY INFORMATION about vigabatrin for oral solution (continued)

- Because of the risk of vision loss, vigabatrin 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 vigabatrin should be periodically reassessed.
- Vigabatrin 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.
- Vigabatrin 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 vigabatrin consistent with clinical objectives.

Because of the risk of permanent vision loss, vigabatrin is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Vigabatrin REMS Program. Further information is available at www.vigabatrinREMS.com or call 1-866-244-8175.

- Abnormal magnetic resonance imaging (MRI) signal changes have been observed in some infants treated for infantile spasms with vigabatrin. These changes generally resolved with discontinuation of treatment, and resolved in a few patients despite continued use.
- Antiepileptic drugs (AEDs), including vigabatrin, increase the risk of suicidal thoughts and behavior. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- As with all AEDs, discontinue vigabatrin gradually to avoid withdrawal seizures. However, if withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered. Patients and caregivers should be told not to suddenly discontinue vigabatrin therapy.
- Vigabatrin can cause anemia, peripheral neuropathy, weight gain, and edema. Vigabatrin can cause somnolence and fatigue. Advise patients not to drive or operate machinery until they know how vigabatrin will affect them.

Please see additional Important Safety Information on next page.

Please see accompanying full Prescribing Information, including Boxed Warning and Medication Guide.

Frequently Asked Questions

About Par's Vigabatrin product (generic version of Sabril®)



Is Par's Vigabatrin product interchangeable with Sabril®?

- Yes, the US Food and Drug Administration (FDA) gives drugs therapeutic equivalency ratings. AA-rated drugs are drugs that meet the necessary bioequivalence standards established by the FDA. An AA-rating designation means drugs are therapeutically equivalent and therefore are substitutable. **Par's Vigabatrin product is AA-rated to Sabril®.**

What does it mean that the Par Vigabatrin is the bioequivalent of Sabril®?

- Bioequivalence is a term in pharmacokinetics used to assess the expected *in vivo* (in humans) biological equivalence of two drug preparations. If two products are said to be bioequivalent, it means that they would be expected to have the same clinical effects and safety profile.

What dosage forms are available for Par's Vigabatrin product?

- Par is currently approved for the powder for oral solution dosage form of vigabatrin.

Does Par offer patient support services?

- Yes, Par does offer patient support services to help with insurance verification and financial assistance to qualifying patients. Please contact Par's Patient Assistance Resource program at **833-PAR-HELP (833-727-4357)**.

Will I need to manage two separate REMS programs?

- No, all vigabatrin products will be covered under a single shared REMS program called the Vigabatrin REMS Program. If you have previously certified in the Sabril REMS Program or have certified in the new shared Vigabatrin REMS Program, there is no need to re-certify when prescribing Par's AA-rated product. For more information, visit <https://www.vigabatrinREMS.com>.

Will hospital pharmacies be able to buy Par's Vigabatrin product through their normal wholesalers?

- Par's Vigabatrin product will be available direct from Par. For more information on setting up a direct purchase account, please see enclosed information or contact Par Customer Service at **833-PAR-HELP (833-727-4357)**.

Is Par making their vigabatrin available to both my inpatient and outpatient hospital pharmacy?

- At this time Par vigabatrin is available on a direct basis for inpatient dispensing only. Outpatient dispensing is available through specialty pharmacies. Please call **833-PAR-HELP (833-727-4357)** for more information.

Are there retail pharmacies that will carry Par's Vigabatrin product for patients being discharged?

- No, at this time this is a limited specialty pharmacy drug. For more information on availability at approved specialty pharmacies, contact **833-PAR-HELP (833-727-4357)**.

Will both commercial and government payers cover Par's Vigabatrin?

- Yes, Par's Vigabatrin product will be covered by both commercial and government payers.

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IMPORTANT SAFETY INFORMATION about vigabatrin for oral solution (continued)

- In clinical studies of 4,079 vigabatrin-treated patients, the most common ($\geq 5\%$) adverse reactions associated with the use of vigabatrin in combination with other AEDs were headache, somnolence, fatigue, dizziness, convulsion, nasopharyngitis, weight gain, upper respiratory tract infection, visual field defect, depression, tremor, nystagmus, nausea, diarrhea, memory impairment, insomnia, irritability, abnormal coordination, blurred vision, diplopia, vomiting, influenza, pyrexia, and rash.
- The adverse reactions most commonly associated with vigabatrin treatment discontinuation in $\geq 1\%$ of patients were convulsion and depression.
- In patients with infantile spasms, the adverse reactions most commonly associated with vigabatrin treatment discontinuation in $\geq 1\%$ of patients were infections, status epilepticus, developmental coordination disorder, dystonia, hypotonia, hypertonia, weight gain, and insomnia.
- Dose adjustment of phenytoin should be considered if clinically indicated, since vigabatrin may cause a moderate reduction in total phenytoin plasma levels. Vigabatrin may moderately increase the C_{max} of clonazepam resulting in an increase of clonazepam-associated adverse reactions.

Please see additional Important Safety Information on back page.

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