EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Antiepileptics – Vigabatrin (Sabril) [vigabatrin tablets and powder for solution, generics]

DATE REVIEWED: 09/18/2019; selected revision 03/25/2020

OVERVIEW

Vigabatrin is indicated as adjunctive therapy for adults and pediatric patients ≥ 2 years of age 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.[1] Vigabatrin is not indicated as a first line agent for complex partial seizures. Vigabatrin is also 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.

According to the vigabatrin prescribing information, use the lowest dosage and shortest exposure to vigabatrin consistent with clinical objectives.[1] For infantile spasms, vigabatrin is titrated to a maximum dose of 150 mg/kg/day given in two divided doses (75 mg/kg twice daily). In patients with infantile spasms, vigabatrin should be withdrawn if a substantial clinical benefit is not observed within 2 to 4 weeks. If, in the clinical judgment of the prescriber, evidence of treatment failure becomes obvious earlier than 2 to 4 weeks, treatment should be discontinued at that time. In a controlled clinical study in patients with infantile spasms, vigabatrin was tapered by decreasing the daily dose at a rate of 25 mg/kg to 50 mg/kg every 3 to 4 days. For refractory complex partial seizures, vigabatrin is titrated to 3,000 mg/day (1,500 mg twice daily) for patients ≥ 17 years of age and to 2,000 mg/day (1,000 mg twice daily) for pediatric patients 10 years to 16 years of age. In patients with refractory complex partial seizures, vigabatrin should be withdrawn if a substantial clinical benefit is not observed within 3 months of initiating treatment. If, in the clinical judgment of the prescriber, evidence of treatment failure becomes obvious earlier than 3 months, treatment should be discontinued at that time. In a controlled study in pediatric patients with complex partial seizures, vigabatrin was tapered by decreasing the daily dose by one third every week for 3 weeks.

The incidence of infantile spasms ranges from 2 to 3.5 per 10,000 live births and most patients present between the ages of 3 months to 7 months; 90% of patients present in the first year of life. Onset after 18 months of age is rare, although onset up to 4 years of age has been reported.[2] Infantile spasms are a catastrophic form of epilepsy in children and poor developmental outcome may result. The recommended duration therapy for Acthar is short-term (2 weeks of treatment followed by a gradual taper and discontinuation over a 2-week period).

Safety

Vigabatrin has a Boxed Warning with regard to permanent vision loss.[1] 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. 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. Risk of new or worsening vision loss continues as long as vigabatrin is used. 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 to 4 weeks of initiation for patients with infantile spasms, or sooner if treatment failure becomes obvious. 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. Under the Vigabatrin REMS Program, prescribers must be certified by enrolling in the program, agreeing to counsel patients on the risk of vision loss and the need for periodic monitoring of vision, and reporting any event suggestive of vision loss to Lundbeck. Patients must also enroll in the program, and pharmacies must be certified and must only dispense to patients authorized to receive vigabatrin.

Guidelines/Recommendations

In 2012 the American Academy of Neurology (AAN) and the Child Neurology Society updated the evidence-based guideline for the medical treatment of infantile spasms.[2] The guidelines note that low-dose adrenocorticotropic hormone (ACTH) is a first-line agent for the short-term treatment of infantile spasms. ACTH or vigabatrin may be useful for short-term treatment of infantile spasms, with ACTH considered preferentially over vigabatrin. Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to vigabatrin in infants with cryptogenic infantile spasms, to possibly improve developmental outcome. A shorter lag time to treatment of infantile spasms with either hormonal therapy or vigabatrin possibly improves long-term developmental outcomes. The Infantile Spasms Working Group (ISWG) published a US consensus report on infantile spasms in 2010.[3] Data regarding ACTH use and vigabatrin use in infantile spasms were detailed.[3] ACTH is an effective first-line therapy for infantile spasms. Vigabatrin is considered a drug of first choice for infantile spasms comorbid with tuberous sclerosis complex, and it is the drug of second or third choice for children with other symptomatic or cryptogenic infantile spasms.

The American Academy of Neurology (AAN) and the American Epilepsy Society published a guideline update for treatment-resistant epilspsy (2018) that clobazam is probably effective as add-on therapy for LGS and is possibly effective as add-on therapy for treatment-resistant adult focal epilepsy.[4] Vigabatrin is effective as add-on therapy in treatment-resistant adult focal epilepsy based on two Class I studies, but it should not be used as a first-line treatment. The benefits of vigabatrin should be weighed against the risks, particularly the risk of irreversible retinopathy.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of vigabatrin. Because of the specialized skills required for evaluation and diagnosis of patients treated with vigabatrin as well as the monitoring required for adverse events and long-term efficacy, initial approval requires vigabatrin to be prescribed by, or in consultation with, a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of vigabatrin is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Infantile Spasms.** Approve for 6 months if the patient meets the following criteria (A, B and C):
   A) The patient is ≤ 2 years of age; AND
   B) Vigabatrin is being used as monotherapy; AND
   C) Vigabatrin is prescribed by, or in consultation with, a neurologist.

2. **Treatment-Refractory Complex Partial Seizures.** Approve for the duration noted below if the patient meets ONE of the following criteria (A or B):
   A) Initial Therapy: Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
      i. The patient is ≥ 2 years of age; AND
      ii. The patient has tried and/or is concomitantly receiving at least three other antiepileptic drugs; AND
      iii. Vigabatrin is prescribed by, or in consultation with, a neurologist.

      Note: Examples of antiepileptic drugs include valproic acid, gabapentin, phenytoin, carbamazepine, oxcarbazepine, lacosamide, levetiracetam, zonisamide, Fycompa, lamotrigine, topiramate, rufinamide, tiagabine, felbamate, Diacomit, and clobazam.
   B) Patient is Currently Receiving Vigabatrin: Approve for 1 year if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Vigabatrin has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

References

1. Sabril® tablets and oral solution [prescribing information]. Deerfield, IL: Lundbeck; January 2020.
2. 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*. 2012;78:1974-1980.
3. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: a US consensus report. *Epilepsia*. 2010;51(10):2175-2189.
4. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment-resistant epilepsy. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2018;91:82-90.
5. Treiman DM. Management of refractory complex partial seizures: current state of the art. *Neuropsychiatr Dis Treat*. 2010;6:297-308.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	--	09/18/2019
Selected revision	For the approval condition of treatment-refractory complex partial seizures, the age criterion was changed from ≥ 10 years of age to ≥ 2 years of age based on a change to the approved indication.	03/25/2020