

Vigabatrin (Sabril®)—A New Treatment Option for Infantile Spasms and Adults with Refractory Complex Partial Seizures

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Vigabatrin is an irreversible inhibitor of GABA transaminase first synthesized in 1975. It has been used outside the US to treat refractory partial epilepsy and infantile spasms since its first marketing approval in the UK in 1989. Vigabatrin received FDA approval for marketing in the US in August, 2009. Its efficacy for adults with complex partial seizures (CPS) and infantile spasms (IS) has been demonstrated in controlled trials, but its clinical use is primarily limited by the occurrence of retinal toxicity in over 30% of patients who take the drug chronically. The retinal effect is manifest as a characteristic bilateral constriction of the visual fields; central retinal effects, including mild decreases in visual acuity, have been reported by some investigators. These effects are generally asymptomatic, so formal testing of vision is required to detect them. In children treated for IS, vigabatrin can also cause reversible MRI signal abnormalities in deep brain structures including thalamus, globus pallidus, brain stem and cerebellum.

As a condition of marketing approval, the FDA has required several post-marketing studies be performed. These include a placebo-controlled, randomized trial of vigabatrin safety and efficacy in pediatric patients, age 10-16; a single and multiple dose pharmacokinetic study in infants; and a controlled study in children with IS to determine the minimum duration of therapy need to achieve durable cessation of spasms. In addition, to better elucidate the pathology underlying the MRI abnormalities in infants the FDA has required non-clinical studies of vigabatrin's effects on the brains of juvenile rats and a non-rodent species. To better study the retinal effects of vigabatrin, a non-clinical study of the ability of taurine to ameliorate the retinal toxicity in rodents is required.

To fill gaps in knowledge concerning the clinical effects of vigabatrin on the retina, Lundbeck Inc. is undertaking a prospective study of vision in adults newly started on vigabatrin for the treatment of CPS. The main objectives are to better define the effects of vigabatrin on vision after short durations of drug exposure and to assess the utility of optical coherence tomography (OCT) in detecting the effects of vigabatrin on the retina. To these ends, patients newly starting Sabril will undergo a standardized vision examination every 3 months, including visual acuity, color vision, static and kinetic perimetry and OCT.

As another condition of approval, the FDA has required a comprehensive REMS be employed. This includes distribution of the drug only through specialty pharmacies, enrolment of all patients taking vigabatrin and all prescribers in a registry (managed by the SHARE® program), a mandatory benefit-risk assessment, and mandatory ophthalmic testing at baseline, every 3 months on drug and 3-6 months after stopping Sabril. Results of the vision testing will be collected by SHARE.

Vigabatrin is a drug that addresses the needs of patients with 2 types of catastrophic epilepsy, but the retinal effects of the drug necessitate careful patient selection and ongoing benefit-risk assessments informed by periodic monitoring of vision.