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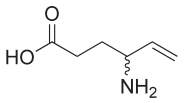
ACS Chemical Neuroscience Molecule Spotlight on Sabril

Corey R. Hopkins

Vanderbilt University, Vanderbilt University Medical Center, Department of Pharmacology and Vanderbilt Program in Drug Discovery, Nashville, Tennessee 37232-6600

Abstract



Sabril® (vigabatrin)
Irreversible inhibitor of GABA transaminase

Sabril (vigabatrin) oral solution was approved by the FDA on August 21st, 2009 for treatment of infantile spasms in children ages 1 month to 2 years and complex partial seizures in adults (tablets).

Sabril (vigabatrin) is a recently approved antiepileptic from H. Lundbeck A/S for the treatment of infantile spasms and complex partial seizures in adults. This represents the first therapy approved by the FDA for the treatment of infantile spasms (IS) (*1*). Infantile spasms (also known as West syndrome) are characterized by a sudden bending forward of the body followed by stiffening. Each seizure usually only last for a second or two; however, the spasms occur in clusters (up to 100) and usually occur upon awakening or after feeding (*2*). Even though it is thought that underlying disorders such as birth injury and genetic disorders can give rise to the spasms, thus making the identification of the underlying cause important, in some children no underlying cause can be found. Sabril was designated as an orphan drug (a drug that is intended to treat a disease affecting less than 200,000 people in the US) by the FDA and was also given priority review status.

Epilepsy is a neurological condition that produces disturbances in the normal electrical function of the brain (*3*). Complex partial seizures usually start in a small area of the temporal or frontal lobe and usually involve other areas of the brain that affect alertness and awareness. Some people that experience these seizures do so unknowingly since this type wipes out memories of events just before and just after. However, some complex partial seizures can turn into secondary generalized seizures.

Sabril's (vigabatrin) mechanism of action is unknown but is thought to be due to the irreversible inhibition of γ-aminobutyric acid transaminase (GABA-T). This enzyme is responsible for the catabolism of GABA, an inhibitory neurotransmitter in the brain. Thus, inhibition of GABA-T leads to increased levels of GABA. Sabril is a racemic compound, with its (*S*)-enantiomer being pharmacologically active.

The FDA approval of Sabril for the treatment of infantile spasms was based on two, multicentered clinical trials (one being partially blinded and the second being double-blinded, placebo controlled). In the first study, the primary efficacy end point was the proportion of patients that were spasm free for 7 consecutive days (after 14 days post-treatment). In this study, vigabatrin was statistically significant. In the second study, vigabatrin was statistically significant in reducing spasms compared to the placebo. The FDA approval of Sabril for the treatment of complex partial seizures was based on two clinical studies. In both trials (randomized and double-blind, placebo-controlled), vigabatrin was shown to be statistically significant in reducing seizure frequency when compared to that with the placebo (*4*).

The major side-effect concern with Sabril is irreversible damage to the peripheral vision (an event that was seen in ~25% of adults). Because of this, the drug will have a boxed warning regarding the progressive loss of peripheral vision and potential loss of vision acuity. The drug will thus only be available through a restricted distribution program (*2*).

References

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