Tiagabine approved for partial seizures

Tiagabine hydrochloride (Gabitril), an anti-epilepsy drug (AED) from Abbott Laboratories, has received marketing approval from FDA. Tiagabine is indicated for use as adjunctive therapy for partial seizures in adults and children age 12 or older.

The mechanism of action of tiagabine is thought to be related to its effects on γ-aminobutyric acid (GABA). In vitro studies have shown that tiagabine binds to recognition sites associated with the GABA uptake carrier. This is thought to block GABA uptake into presynaptic neurons, increasing the amount of GABA available for binding to postsynaptic receptors. Tiagabine is nearly completely absorbed after oral administration. It is 96% bound to plasma proteins. At least two metabolic pathways—oxidation and glucuronidation—have been identified. It appears that tiagabine is metabolized primarily by cytochrome P-450 3A isoenzymes. The elimination half-life is 7–9 hours in healthy volunteers but 4–7 hours in patients taking AEDs that induce hepatic enzymes.

The approval of tiagabine as adjunctive therapy was based on the results of three placebo-controlled, parallel-group studies involving 769 patients with refractory partial seizures and two placebo-controlled crossover studies involving 90 patients. The studies showed a reduction in seizure rates among patients treated with tiagabine.

The adverse events most commonly associated with tiagabine as “add-on” therapy include dizziness (27%), lack of energy (20%), somnolence (18%), nausea (11%), nervousness (10%), tremor (9%), abdominal pain (7%), and difficulty with concentration or attention (6%). In both adolescents and adults, tiagabine hydrochloride should be started at a dosage of 4 mg once daily. The dosage should be increased slowly until a clinical response is achieved or a maximum dosage of 32 mg/day in adolescents or 56 mg/day in adults is reached. The drug should be taken with food and the daily dosage administered in two to four divided doses.

Nearly all the patients in whom tiagabine was studied were taking enzyme-inducing drugs. Patients taking other AEDs may require lower dosages of tiagabine or slower dosage adjustment. Patients with impaired hepatic function may also require lower dosages.

Gabitril is available as 4-, 12-, 16-, and 20-mg tablets for oral administration. The product is packaged in bottles of 100 and 500 and unit dose packages of 100.