Alert for Healthcare Professionals

Tiagabine hydrochloride (marketed as Gabitril)

FDA Alert [02/18/2005]: Seizures in Patients Without Epilepsy

Today the Food and Drug Administration announced that a bolded Warning will be added to the labeling for Gabitril (tiagabine) to warn prescribers of the risk of seizures in patients without epilepsy being treated with this drug. Although Gabitril has been shown to reduce the frequency of seizures in patients with epilepsy, paradoxically, Gabitril's use has been associated with the occurrence of seizures in patients without epilepsy. Gabitril is approved for use only as adjunctive therapy in adults and children 12 years and older in the treatment of partial seizures. Because Gabitril has not been systematically evaluated in adequate and well-controlled trials for any other indication, its safety and effectiveness have not been established for any other use.

Cephalon will undertake an educational campaign to discourage off-label use of Gabitril.

This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

Recommendations

Prescribers with patients taking Gabitril or who are considering prescribing the drug should consider the following:

- The off-label use of Gabitril is strongly discouraged.
- The use of Gabitril for any indication other than for partial seizures in patents with epilepsy who are least 12 years old is an *off-label* use, meaning the evidence to support safety and effectiveness for those uses has not been approved by the FDA .
- In non-epileptic patients who develop seizures while on Gabitril treatment, Gabitril should be discontinued and patients should be evaluated for an underlying seizure disorder.
- The Gabitril dosing recommendations in current labeling for treatment of epilepsy were based on use in patients with partial seizures 12 years of age and older, most of whom were taking enzyme-inducing antiepileptic drugs (AEDs; e.g., carbamazepine, phenytoin, primidone and phenobarbital),

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which lower plasma levels of Gabitril by inducing its metabolism. Use of Gabitril without enzyme-inducing antiepileptic drugs results in blood levels about twice those attained in the studies on which current dosing recommendations are based. Use in non-induced patients requires lower doses of Gabitril. These patients may also require a slower titration of Gabitril compared to that of induced patients (see full Prescribing Information).

Data Summary

There have been more than 30 postmarketing reports of new onset seizures and status epilepticus in patients without epilepsy in association with Gabitril use. In most of these cases, Gabitril was used as an *off-label* treatment for a psychiatric illness. In some cases, the prescriber had continued to treat with, or increased the dose of, Gabitril, presumably unaware of the possibility that Gabitril could cause seizures. Dose may be an important predisposing factor in the development of seizures, although seizures have been reported in patients taking daily doses of Gabitril as low as 4 mg/day. In most cases, patients were using concomitant medications (antidepressants, antipsychotics, stimulants, narcotics) that are thought to lower the seizure threshold. Some seizures occurred near the time of a dose increase, even after periods of prior stable dosing.