



Tiagabine

Updated: February 19, 2018.

OVERVIEW

Introduction

Tiagabine is a unique anticonvulsant used largely as an adjunctive agent in therapy of partial seizures in adults or children. Therapy with tiagabine is not associated with serum aminotransferase elevations, and clinically apparent liver injury from tiagabine has not been reported and must be rare if it occurs at all.

Background

Tiagabine (tye ag' a been) is a selective gamma aminobutyric acid (GABA) reuptake inhibitor that increases synactive concentrations of this major neuroinhibitory transmitter, thus decreasing spread of abnormal neuronal impulses that contribute to seizures. Tiagabine has been shown to be effective both as monotherapy and in combination with other anticonvulsants for partial seizures. Tiagabine was approved for use in epilepsy in the United States in 1997 and is currently used predominantly as adjunctive therapy with other major anticonvulsants for partial seizures. Tiagabine is occasionally used off-label to treat anxiety disorders and neuropathic pain. Tiagabine is available in tablets of 2, 4, 12 and 16 mg in generic formulations and under the brand name of Gabitril. The recommended initial dose in adults is 4 mg once daily, increasing by 4 to 8 mg at weekly intervals based upon clinical response, but not exceeding 56 mg daily. The dose should be increased and tapered gradually. The most common side effects of tiagabine are dose related and include dizziness, somnolence, impaired concentration, nervousness, nausea, weakness and tremor.

Hepatotoxicity

Limited data are available on the hepatotoxicity of tiagabine. In clinical trials, therapy with tiagabine was not associated with an increased frequency of serum aminotransferase elevations or liver toxicity. No individual case reports of liver injury from tiagabine have been published and its use has not been associated with hypersensitivity syndromes or autoimmunity. However, its overall use has been limited.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

The apparent absence of significant hepatotoxicity from tiagabine is despite the fact that it is metabolized by the liver and interacts with the CYP 450 system.

Drug Class: [Anticonvulsants](#)

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Tiagabine – Generic, Gabitril®

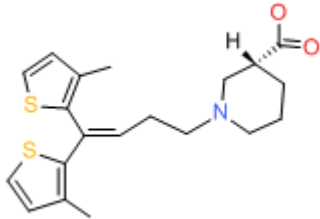
DRUG CLASS

Anticonvulsants

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Tiagabine	115103-54-3	C ₂₀ H ₂₅ N-O ₂ -S ₂	 The chemical structure of Tiagabine consists of a 2,5-dimethylthiophene ring system connected via a double bond to a propyl chain, which is further connected to a piperidine ring. The piperidine ring has a hydrogen atom on the nitrogen and a carbonyl group (C=O) attached to the adjacent carbon.

ANNOTATED BIBLIOGRAPHY

References updated: 19 February 2018

Zimmerman HJ. Anticonvulsants. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 498-516.

(Expert review of anticonvulsants and liver injury published in 1999; tiagabine is not discussed).

Pirmohamed M, Leeder SJ. Anticonvulsant agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013: pp 423-42.

(Review of anticonvulsant induced liver injury; tiagabine is not discussed).

McNamara JO. Pharmacology of the epilepsies. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 583-607.

(Textbook of pharmacology and therapeutics).

Wallace SJ. A comparative review of the adverse effects of anticonvulsants in children with epilepsy. Drug Saf 1996; 15: 378-93. PubMed PMID: 8968693.

(Systematic review; ALT elevations occur in 4% of children on phenytoin, 6% on valproate, 1% on carbamazepine but none reported in children on tiagabine or gabapentin).

Wilby J, Kainth A, Hawkins N, et al. Clinical effectiveness, tolerability and cost-effectiveness of newer drugs for epilepsy in adults: a systematic review and economic evaluation. Health Technol Assess 2005; 9: 1-157, iii-iv. PubMed PMID: 15842952.

(Extensive systematic review of anticonvulsant medications including assessment of serious, rare and long-term adverse events; tiagabine adverse events were limited to neurological effects; no mention of hepatotoxicity).

Pollack MH, Tiller J, Xie F, Trivedi MH. Tiagabine in adult patients with generalized anxiety disorder: results from 3 randomized, double-blind, placebo-controlled, parallel-group studies. *J Clin Psychopharmacol* 2008; 28: 308-16. PubMed PMID: 18480688.

(Summary of 3 randomized controlled trials of tiagabine vs placebo for 10 weeks; little or no evidence of efficacy for generalized anxiety disorder found; side effects included headache, dizziness, nausea, fatigue and somnolence but no mention of liver toxicity or ALT elevations).

Forbes RA, Kalra H, Hackett LP, Daly FF. Deliberate self-poisoning with tiagabine: an unusual toxidrome. *Emerg Med Australas* 2007; 19: 556-8. PubMed PMID: 18021110.

(Overdose of tiagabine associated with vomiting, coma, myoclonus, hypertension and priapism, but no mention of liver injury or jaundice).

Winhusen T, Somoza E, Ciraulo DA, et al. A double-blind, placebo-controlled trial of tiagabine for the treatment of cocaine dependence. *Drug Alcohol Depend* 2007; 91: 141-8. PubMed PMID: 17629631.

(Randomized controlled trial [n=141] of tiagabine vs placebo for cocaine dependence found no evidence of efficacy, but also “no pattern of physical or laboratory abnormality” attributable to tiagabine).

LaRoche SM. A new look at the second-generation antiepileptic drugs: a decade of experience. *Neurologist* 2007; 13: 133-9. PubMed PMID: 17495757.

(Review of second generation anticonvulsants approved since 1994 including felbamate, gabapentin, lamotrigine, topiramate, tiagabine, levetiracetam, oxcarbazepine, zonisamide and pregabalin: no mention of liver toxicity from tiagabine).

Bauer J, Cooper-Mahkorn D. Tiagabine: efficacy and safety in partial seizures—current status. *Neuropsychiatr Dis Treat* 2008; 4: 731-6. PubMed PMID: 19043517.

(Review of pharmacology, clinical efficacy and side effects of tiagabine; no mention of liver toxicity or ALT elevations).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. *Gastroenterology* 2008; 135: 1924-34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, valproate accounted for 6 cases, lamotrigine 5, phenytoin 5, gabapentin and topiramate 1 each; none were due to tiagabine).

Knowles SR, Dewhurst N, Shear NH. Anticonvulsant hypersensitivity syndrome: an update. *Expert Opin Drug Saf* 2012; 11: 767-78. PubMed PMID: 22794330.

(Updated review of anticonvulsant hypersensitivity syndrome; associated with phenytoin, phenobarbital, lamotrigine and carbamazepine and rarely with zonisamide, valproate and oxcarbazepine; tiagabine is not mentioned).

Drugs for epilepsy. *Treat Guidel Med Lett* 2013; 11: 9-18. PubMed PMID: 23348233.

(Concise review of indications and side effects of anticonvulsants; tiagabine is approved only for treatment of partial seizures and has prominent gastrointestinal and CNS side effects; no mention of hepatotoxicity).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. *Gastroenterology* 2015; 148: 1340-52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 40 [4.5%] were attributed to anticonvulsants, but none specifically to tiagabine).

Zaccara G, Giovannelli F, Giorgi FS, Franco V, Gasparini S, Benedetto U. Tolerability of new antiepileptic drugs: a network meta-analysis. *Eur J Clin Pharmacol* 2017; 73: 811-7. PubMed PMID: 28378057.

(Metaanalysis of the comparative tolerability of 18 new anticonvulsant agents, found best tolerability [lowest rates of withdrawal for adverse events] with levetiracetam, brivaracetam and gabapentin and lowest scores for tolerability from eslicarbazepine, oxcarbazepine, lacosamide and topiramate; tiagabine had an intermediate level of tolerability).

Drugs for epilepsy. *Med Lett Drugs Ther* 2017; 59 (1526): 121-30. PubMed PMID: 28746301.

(Concise review of the drugs available for therapy of epilepsy does not list tiagabine as either a first or second line drug for epilepsy and mentions that it is approved for adjunctive treatment of partial seizures, but has gastrointestinal and neurologic side effects and is associated with de novo seizures in patients treated off label for bipolar illness or neuropathic pain).