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Rimantadine

Updated: May 28, 2018.

OVERVIEW

Introduction

Rimantadine is an antiviral agent used as therapy for influenza A. Rimantadine has not been associated with clinically apparent liver injury.

Background

Rimantadine (ri man' ta deen) is a cyclic primary amine that has antiviral and anti-Parkinsonian activities. The antiviral activity of rimantadine is attributed to inhibition of virion uncoating and release of viral RNA in the initial stages of viral replication. Rimantadine is active only against influenza A virus and has no activity against influenza B or other upper respiratory viruses. In addition, resistance to rimantadine with cross reactivity against amantadine can develop rapidly and is now common. The anti-Parkinsonian activity of rimantadine appears to be due to its effects on release of dopamine in the substantia nigra; however, it has not been developed or approved for this indication. Rimantadine is indicated for treatment or prevention of influenza A and was approved for this use in the United States in 1993. Rimantadine is available as tablets of 100 mg and as syrup (50 mg/5 mL) in generic forms and under the brand name of Flumadine. The recommended dose for influenza in adults is 100 mg twice daily for 5-7 days; rimantadine is also administered as prophylaxis starting as soon as possible after close personal exposure. Side effects may include anxiety, dizziness, ataxia, confusion, fatigue, headache, insomnia, dry mouth and gastrointestinal upset.

Hepatotoxicity

Despite widespread use, there is little evidence that rimantadine when given orally causes liver injury, either in the form of serum enzyme elevations or clinically apparent liver disease.

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

Mechanism of Injury

Rimantadine has minimal hepatic metabolism and is excreted largely unchanged in the urine, factors which perhaps explain the absence of significant hepatotoxicity.

Drug Class: Antiviral Agents

Other Drugs in the Class for Influenza: Amantadine, Baloxavir, Oseltamivir, Peramivir, Zanamivir

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Rimantadine – Generic, Flumadine®

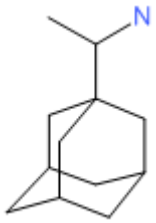
DRUG CLASS

Antiviral Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Rimantadine	13392-28-4	C12-H21-N	

ANNOTATED BIBLIOGRAPHY

References updated: 28 May 2018

Zimmerman HJ. Antiviral agents. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 621-3.

(Expert review of antiviral agents and liver injury published in 1999; both amantadine and rimantadine appear to have "no adverse effect on the liver").

Núñez M. Influenza virus treatments. Hepatic toxicity of antiviral agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 513.

(Review of hepatotoxicity of antiviral agents; amantadine has been linked to rare instances of liver enzyme elevations).

Acosta EP, Flexner C. Antiviral agents (nonretroviral). In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1593-1622.

(Textbook of pharmacology and therapeutics).

Jefferson T, Demicheli V, Di Pietrantonj C, Rivetti D. Amantadine and rimantadine for influenza A in adults. Cochrane Database Syst Rev 2006; (2): CD001169. PubMed PMID: 16625539.

(Systematic review of efficacy of amantadine and rimantadine in treatment and prevention of influenza A; side effects are frequent, but largely consist of dizziness, insomnia, lightheadedness and headache; no mention of liver test abnormalities or hepatitis).

Antiviral drugs for influenza. Med Lett Drugs Ther 2009; 51 (1325): 89-92. PubMed PMID: 20220738.

(Review of status of antiviral agents for prevention and treatment of influenza A and B; rates of resistance to amantadine and rimantadine are high, making these agents poorly effective; no mention of liver toxicity).

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, 8 were attributed to antiviral agents, but none to drugs used in therapy of influenza).

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, 16 [1.8%] were attributed to antiviral agents, but none to rimantadine or other drugs for influenza).

Antiviral drugs for seasonal influenza 2016-2017. Med Lett Drugs Ther 2017; 59 (1511): 1-3. PubMed PMID: 28026833.

(Review of status of antiviral agents for prevention and treatment of influenza A and B during the 2016-2017 season, discusses the neuraminidase inhibitors, but does not discuss or recommend amantadine or rimantadine).