U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Peramivir. [Updated 2017 Mar 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Peramivir

Updated: March 15, 2017.

OVERVIEW

Introduction

Peramivir is an inhibitor of the influenza neuraminidase enzyme and is used as therapy of acute symptomatic influenza A and B. Peramivir has not been associated with serum enzyme elevations during therapy or with clinically apparent liver injury.

Background

Peramivir (per am' i vir) is a sialic acid analog and potent inhibitor of the virus-encoded neuraminidases of influenza A and B. In several prospective clinical trials, peramivir given as a single intravenous infusion [300 to 600 mg] within 2 days of symptomatic onset, shortened the period of symptoms and viral shedding. Peramivir was approved in the United States under an emergency use authorization during the influenza A (H1N1) epidemic in 2009. Peramivir received standard full approval in 2014. Current formal indications are for the treatment of acute, uncomplicated influenza A or B in adults within 2 days of symptom onset. It is not approved for, but is widely used in, patients with complicated, life-threatening influenza. Peramivir is used only for treatment of influenza and is not indicated for prophylaxis after a known exposure. Peramivir is available in single use vials of 200 mg in 20 mL [10 mg/mL] under the brand name Rapivab. The recommended dose is a single intravenous infusion of 600 mg administered over 15 minutes. Side effects from peramivir infusions are uncommon and generally mild, including headache, nausea and vomiting. Rare, but potentially severe adverse events include anaphylaxis and Stevens Johnson syndrome. Recommendations for treatment and prophylaxis of influenza in the United States change frequently in response to changes in the circulating influenza strains and antiviral resistance patterns. Regularly updated recommendations are available from the Centers for Disease Control and Prevention at: https://www.cdc.gov/flu/.

Hepatotoxicity

Despite widespread use, there is little evidence that peramivir, when given as recommended as a single intravenous infusion, is associated with liver injury, either in the form of serum enzyme elevations or clinically apparent liver disease. A proportion of patients with influenza may have minor serum enzyme elevations during the acute illness, but these appear to be independent of therapy and are not exacerbated by peramivir.

Mechanism of Injury

The mechanism by which peramivir might cause liver injury is unknown. Peramivir is not significantly metabolized in humans and 90% is excreted unchanged in the urine. Peramivir is not a substrate for the cytochrome P450 enzyme system and demonstrates no significant drug-drug interactions. Peramivir is typically

given as a single intravenous infusion, and the brief exposure and minimal hepatic metabolism may account for the absence of hepatotoxicity.

Drug Classes: Antiviral Agents

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

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Peramivir – Rapivab®

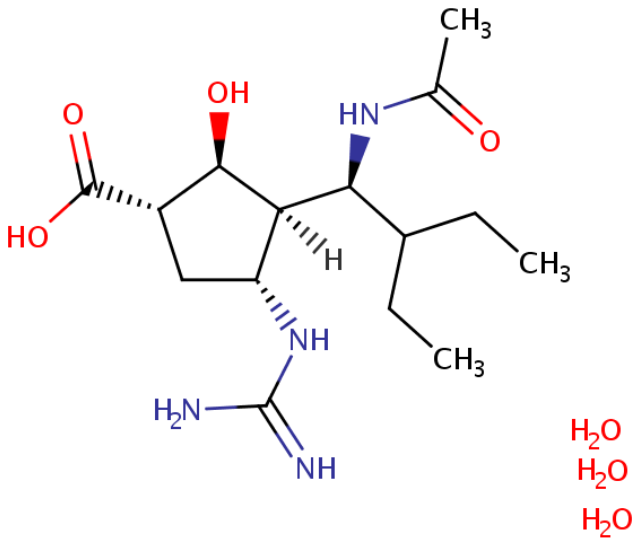
DRUG CLASS

Antiviral Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Peramivir	1041434-82-5	C15-H28-N4-O4.3H2-O	

ANNOTATED BIBLIOGRAPHY

References updated: 15 March 2017

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; amantadine and rimantadine have not caused "overt hepatic injury"; peramivir and other influenza neuraminidase inhibitors are not mentioned).

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; peramivir is not discussed).

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).

Birnkrant D, Cox E. The Emergency Use Authorization of peramivir for treatment of 2009 H1N1 influenza. N Engl J Med 2009; 361: 2204-7. PubMed PMID: 19884645.

(Announcement of the FDA's emergency use authorization of peramivir during the 2009 H1N1 epidemic of influenza A and the legal and scientific basis for the decision).

Kohno S, Kida H, Mizuguchi M, Shimada J; S-021812 Clinical Study Group. Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection. Antimicrob Agents Chemother 2010; 54: 4568-74. PubMed PMID: 20713668.

(Among 296 adults with acute influenza treated with a single intravenous infusion of peramivir [300 or 600 mg] vs placebo within 48 hours of clinical onset, symptoms and viral titers decreased faster with active treatment and adverse event rates were similar, ALT elevations occurring in 4% [300 mg], 7% [600 mg] and 8% [placebo] of subjects).

Yingying C. Abnormal liver chemistry in patients with influenza A H1N1. Liver Int 2011; 31: 902. PubMed PMID: 21645222.

(Among 131 patients admitted to a hospital for influenza A H1N1, 13% had abnormal ALT and 5% abnormal Alk P elevations, but the range of values was not provided).

Kohno S, Kida H, Mizuguchi M, Hirotsu N, Ishida T, Kadota J, Shimada J; S-021812 Clinical Study Group. Intravenous peramivir for treatment of influenza A and B virus infection in high-risk patients. Antimicrob Agents Chemother 2011; 55: 2803-12. PubMed PMID: 21464252.

(Among 37 patients with acute influenza who were considered at high risk for complications who were treated with peramivir [300 or 600 mg] for 1-5 days, resolution of symptoms was faster with the higher dose and adverse events arose in 74% of patients; no mention of ALT elevations or hepatotoxicity).

Sorbello A, Jones SC, Carter W, Struble K, Boucher R, Truffa M, Birnkrant D, et al. Emergency use authorization for intravenous peramivir: evaluation of safety in the treatment of hospitalized patients infected with 2009 H1N1 influenza A virus. Clin Infect Dis 2012; 55: 1-7. PubMed PMID: 22491501.

(Analysis of adverse event reports to the FDA from 344 patients with influenza who were treated with peramivir during the emergency use authorization period revealed 8 cases of hepatitis [ALT elevations only] and 1 case of hepatic failure; however, no details were provided, and the authors concluded that the only adverse event reasonably attributable to peramivir was rash [4% of events]).

Sugaya N, Kohno S, Ishibashi T, Wajima T, Takahashi T. Efficacy, safety, and pharmacokinetics of intravenous peramivir in children with 2009 pandemic H1N1 influenza A virus infection. Antimicrob Agents Chemother 2012; 56: 369-77 PubMed PMID: 22024821.

(Among 106 children with H1N1 influenza A treated within 2 days of onset with peramivir [10 mg/kg] once daily, 64% developed adverse events, most commonly diarrhea [16%] and vomiting [9%]; no mention of ALT elevations or hepatotoxicity).

Louie JK, Yang S, Yen C, Acosta M, Schechter R, Uyeki TM. Use of intravenous peramivir for treatment of severe influenza A(H1N1)pdm09. PLoS One 2012; 7: e40261. PubMed PMID: 22768265.

(During a 16 month period in 2009, 1962 California residents were hospitalized for influenza, of whom 57 were critically ill and were treated with intravenous peramivir starting 2-38 days after onset: 55 [96%] with pneumonia, 54 [95%] on mechanical ventilation of whom 29 [51%] died; no mention of ALT elevations or hepatotoxicity).

Komeda T, Ishii S, Itoh Y, Ariyasu Y, Sanekata M, Yoshikawa T, Shimada J. Post-marketing safety and effectiveness evaluation of the intravenous anti-influenza neuraminidase inhibitor peramivir. II: a pediatric drug use investigation. J Infect Chemother 2015; 21: 194-201. PubMed PMID: 25523716.

(Among 1199 children with influenza treated with intravenous peramivir at 161 centers in Japan, there were 245 adverse events in 161 children [14%], most commonly diarrhea, abnormal behavior, with serious events in 23 children [2%], but no mention of ALT elevations or hepatotoxicity).

Peramivir (Rapivab): an IV neuraminidase inhibitor for treatment of influenza. Med Lett Drugs Ther 2015; 57 (1461): 17-9. PubMed PMID: 25629811.

(Concise summary of the mechanism of action, clinical efficacy, safety and costs of peramivir shortly after its formal approval in the US; mentions side effects of gastrointestinal symptoms, behavioral disorders and rash [including rare cases of erythema multiforme and Stevens Johnson syndrome], but does not mention ALT elevations or hepatotoxicity).

Komeda T, Ishii S, Itoh Y, Sanekata M, Yoshikawa T, Shimada J. Post-marketing safety evaluation of the intravenous anti-influenza neuraminidase inhibitor peramivir: A drug-use investigation in patients with high risk factors. J Infect Chemother 2016; 22: 677-84. PubMed Citation

(Among 770 Japanese patients with influenza at high risk for complications who were treated with peramivir, adverse events were reported in 219 [28%], including elevations of ALT in 29 [4%], but the liver test abnormalities were considered due to the influenza infection rather than peramivir and there was no mention of clinically apparent liver injury).

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

(Concise summary of safety and efficacy of medications for influenza appropriate for the 2016-17 season; mentions that adverse effects of peramivir include nausea, vomiting and headache; no mention of liver injury).