

Peramivir

Updated: June 22, 2020.

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 and received standard full approval in 2014. Current formal indications are for the treatment of acute, uncomplicated influenza A or B in adults or children above the age of 2 years who have been symptomatic for 2 days or less. 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 in adults is a single intravenous infusion of 600 mg administered over 15 to 30 minutes. Side effects from peramivir infusions are uncommon and generally mild, including headache, nausea and vomiting. Rare, but potentially severe adverse events include hypersensitivity reactions, anaphylaxis, Stevens Johnson syndrome and acute delirium and hallucination. 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.

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

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®

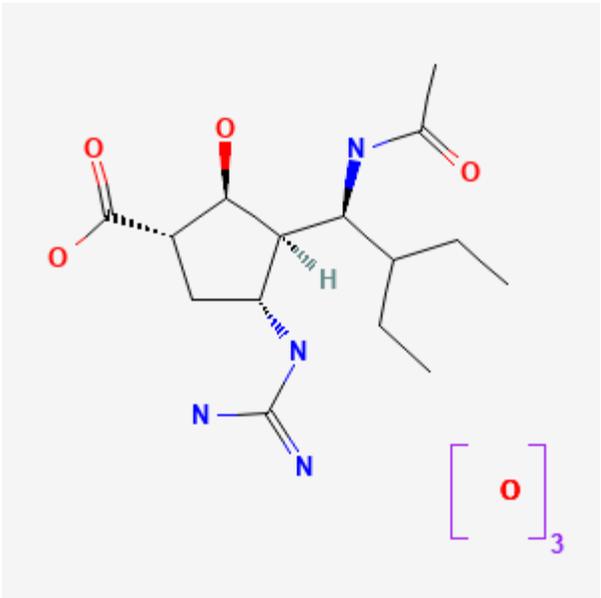
DRUG CLASS

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	C ₁₅ -H ₂₈ -N ₄ -O ₄ .3H ₂ -O	

ANNOTATED BIBLIOGRAPHY

References updated: 22 June 2020

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. Antiviral agents (nonretroviral). In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 1105-18.

(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).

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation and outcomes in patients with drug-induced liver injury in the general population of Iceland. *Gastroenterology*. 2013;144:1419–25. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, but none were attributed to a drug used to treat influenza).

Chalasan 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, 12 cases [1.3%] were attributed to antiviral agents, but none to antivirals used to treat influenza).

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 PMID: 27497712.

(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).

Nakamura S, Miyazaki T, Izumikawa K, Takeya H, Saisho Y, Yanagihara K, Miyazaki Y, et al. Efficacy and safety of intravenous peramivir compared With oseltamivir in high-risk patients infected with influenza A and B viruses: a multicenter randomized controlled study. *Open Forum Infect Dis*. 2017;4:ofx129. PubMed PMID: 28761899.

(Among 92 high risk Japanese adults with influenza who were treated with a single dose of intravenous peramivir [600 mg] or a 5 day course of oseltamivir [75 mg twice daily], clinical response rates were similar in the two groups but adverse events were less common with peramivir than oseltamivir [2% vs 13%], with “liver dysfunction” occurring in none vs 2 [4%].

Choi WS, Ryu SY, Lee J, Hong SB, Eom JS, Shin J, Park KH, et al. Safety and effectiveness of peramivir in Korean adult influenza patients: prospective observational study based on post-marketing surveillance data. *J Korean Med Sci.* 2018;33:e212. PubMed PMID: 30079005.

(Among 3024 Korean adults with influenza treated with intravenous peramivir in postmarketing surveillance studies, only 35 [1.2%] were reported as having an adverse event, which were mostly mild fevers, diarrhea and nausea, liver test abnormalities being reported in only 2 [<0.1%]).

Antiviral drugs for treatment and prophylaxis of seasonal influenza. *Med Lett Drugs Ther.* 2019;61(1563):1–4. PubMed PMID: 30681660.

(Concise review of the drug therapy of influenza mentions that there are no data suggesting the superiority of one drug over another, they are all approved for treatment of uncomplicated influenza, should be started as soon as possible, and have been shown to shorten the duration of symptoms by one day in adults; no mention of ALT elevations or hepatotoxicity of any of the neuraminidase inhibitors).

Antiviral drugs for influenza. *Med Lett Drugs Ther.* 2020;62(1589):1–4. PubMed PMID: 31999661.

(Concise review of the drug therapy of influenza mentions that there is no evidence that one drug is more effective than any other in treating uncomplicated influenza infections but that oseltamivir is preferred for treatment of pregnant women, hospitalized patients and those with severe, complicated or progressive illness; adverse events reported with peramivir include diarrhea and neutropenia; no mention of ALT elevations or hepatic adverse events).