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Famciclovir

Updated: January 29, 2018.

OVERVIEW

Introduction

Famciclovir is a nucleoside analogue and antiviral agent used in therapy of herpes zoster and simplex virus infections. Famciclovir is associated with a low rate of mild-to-moderate serum ALT elevations during therapy, but has not been associated with instances of clinically apparent liver injury.

Background

Famciclovir (fam sye' kloe vir) is an acyclic purine nucleoside analogue with antiviral activity against many herpes viruses, including herpes simplex 1 and 2, cytomegalovirus, Ebstein-Barr virus and varicella-zoster. Famciclovir is a prodrug of penciclovir which is the active component. After absorption, famciclovir is converted in the liver to penciclovir which is phosphorylated intracellularly by viral kinases; the resultant triphosphate competes with guanosine for incorporation into viral DNA, blocking viral DNA polymerase activity. Famciclovir is indicated for therapy of varicella zoster and for mucocutaneous or genital herpes simplex infections, both type 1 and 2. Famciclovir was approved for use in the United States in 1994 and is widely used in treatment of herpes zoster and prophylaxis of genital and mucocutaneous herpes simplex infection. Famciclovir is available as tablets of 125, 250 and 500 mg, generically and under the brand name of Famvir. The recommended dose of famciclovir and duration of therapy varies by indication. The typical recommended oral dose for herpes zoster in adults is 500 three times daily for 7 days; a lower daily dose is recommended for prophylaxis. Side effects are uncommon but can include headache, dizziness, and gastrointestinal upset.

Hepatotoxicity

Famciclovir has been associated with a low rate of serum aminotransferase elevations during oral therapy. In pooled analyses of patients on long term suppressive therapy, 3.2% of famciclovir vs 1.5% of placebo recipients had ALT elevations above twice normal. The elevations were transient and asymptomatic and resolved even without dose modification. Since approval, cases of cholestatic jaundice have been reported to the sponsor, but there have been no published cases. Thus, clinically apparent liver disease due to famciclovir must be rare if it occurs at all.

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

Mechanism of Injury

After absorption, famciclovir is converted to penciclovir by the liver, which is metabolized intracellularly in viral infected cells. Hepatic metabolism of penciclovir is minimal and it is excreted largely unchanged by the kidneys, perhaps accounting for the absence or rarity of hepatic injury.

Drug Class: Antiviral Agents

Other Antiviral Agents for Herpes Virus Infections: Acyclovir, Cidofovir, Foscarnet, Ganciclovir, Letermovir, Valacyclovir, Valganciclovir

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Famciclovir – Famvir®

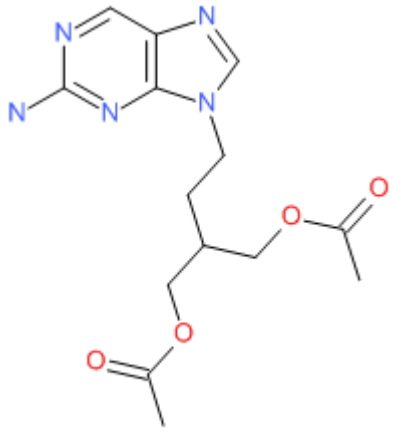
DRUG CLASS

Antiviral Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Famciclovir	104227-87-4	C14-H19-N5-O4	

ANNOTATED BIBLIOGRAPHY

References updated: 29 January 2018

Núñez M. Drugs used for herpes simplex and varicella-zoster viruses. Hepatic toxicity of antiviral agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 512-3.

(Review of hepatotoxicity of antiviral agents; famciclovir has been linked to ALT elevations in 3.2% of patients).

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).

Simpson D, Lyseng-Williamson KA. Famciclovir: a review of its use in herpes zoster and genital and orolabial herpes. Drugs 2006; 66: 2397-416. PubMed PMID: 17181386.

(Review of famciclovir, oral prodrug of penciclovir, used in herpes zoster and simplex virus infections for a limited period as therapy and extended use for suppression; in suppression studies, ALT elevations above twice ULN occurred in 3.2% of famciclovir vs 1.5% of placebo recipients; AST elevations in 2.3% of famciclovir vs 1.2% of placebo recipients; no hepatic serious adverse events were reported).

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 including one due to valacyclovir, but none to famciclovir).

Mubareka S, Leung V, Aoki FY, Vinh DC. Famciclovir: a focus on efficacy and safety. Expert Opin Drug Saf 2010; 9: 643-58. PubMed PMID: 20429777.

(Review of the safety and efficacy of famciclovir mentions that serum ALT elevations can occur during therapy, but are usually mild and transient, and rates of abnormalities are similar in frequency to that with placebo or comparator arms).

Gopal MG, Shannoma, Kumar BCS, Ramesh M R, Nandini AS, Manjunath NC. A comparative study to evaluate the efficacy and safety of acyclovir and famciclovir in the management of herpes zoster. J Clin Diagn Res 2013; 7: 2904-7. PubMed PMID: 24551671.

(Controlled trial of 7 day course of oral acyclovir vs famciclovir in 100 patients with herpes zoster found similar efficacy and no differences in laboratory test results between the two groups, and no serious adverse events).

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. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, none were attributed to famciclovir).