Elvucitabine

Drug Class: **Nucleoside Reverse Transcriptase Inhibitors**

Drug Description

Elvucitabine, or ELV, is an L-cytosine nucleoside analogue of stavudine with potent activity against HIV. [1] [2]

HIV/AIDS-Related Uses

Elvucitabine is a nucleoside reverse transcriptase inhibitor (NRTI) currently under investigation in Phase II/III trials for the treatment of chronic HIV infection and infection by lamivudine-resistant HIV.[3]

Non-HIV/AIDS-Related Uses

Elvucitabine exhibits potent activity against hepatitis B virus (HBV). A Phase I/II study of elvucitabine in patients with chronic HBV infection demonstrated acceptable pharmacokinetics and safety profiles. Phase II studies of elvucitabine in chronically HBV infected patients are underway.[4]

Pharmacology

Elvucitabine is a beta-L-(-) nucleoside analogue developed to improve upon the antiviral activity of lamivudine, an FDA-approved beta-L-(-) nucleoside analogue. Compared with lamivudine, elvucitabine may allow for less frequent dosing and less escalation of dosage to overcome viral resistance.[5] Elvucitabine, a stavudine-substituted NRTI, has potent antiretroviral activity, even at doses low enough to avoid bone marrow toxicity.[6] [7] Elvucitabine inhibits wild-type HIV and HIV expressing the M184V mutation associated with lamivudine resistance.[8]

Elvucitabine has excellent oral bioavailability and a prolonged half-life of more than 100 hours.[9] [10] [11]

When elvucitabine dosages of 5 or 10 mg once daily or 20 mg once every other day were tested in 24 HIV infected patients for 21 days with concomitant lopinavir/ritonavir (LPV/r) every 12 hours, viral load decreased 1.8, 1.9, and 2.0 log, respectively. Elvucitabine's extended half-life required continuation of LPV/r doses for 35 days total in the 10 and 20 mg cohorts. Concentrations of elvucitabine remained above the 50% inhibitory concentration (IC50) at Day 28, supporting weekly or twice-weekly dosing. The every-other-day cohort appeared most efficacious and minimized resistance and adherence concerns.[12]

Adverse Events/Toxicity

Elvucitabine induces bone marrow toxicity when used at dosages higher than elvucitabine 50 mg daily. Preliminary study results reported at the 12th International HIV Drug Resistance Workshop in June 2003 indicated that elvucitabine induced reversible bone marrow suppression. Six of 56 patients experienced myelosuppression while taking elvucitabine; of these six patients, four received 100 mg daily and two received 50 mg daily. Mild to moderate macropapular rash occurred with the 50 and 100 mg doses but resolved with drug discontinuation. Mild headache and gastrointestinal distress were also reported.[13] [14]

For 21 days at dosages of elvucitabine 5 and 10 mg once daily and 20 mg once every other day, no bone marrow suppression was observed, and elvucitabine was generally nontoxic.[15]

Drug and Food Interactions

The half-life of elvucitabine was approximately 150 hours when administered with LPV/r. Elvucitabine exhibited decreased bioavailability and slower absorption rates with concomitant LPV/r but was otherwise unchanged.[16]

Clinical Trials

For information on clinical trials that involve Elvucitabine, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Elvucitabine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[17]

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Dosing Information (cont.)

Dosage Form: In clinical trials, dosages studied include 5 and 10 mg once daily and 20 mg once every other day.[18] [19]

Chemistry

CAS Name: 2(1H)-Pyrimidinone, 4-amino-1-((2S,5R)-2,5-dihydro-5-[20]

CAS Number: 181785-84-2[21]

Molecular formula: C9-H10-F-N3-O3[22]

C47.8%, H4.4%, F8.0%, N18.6%, O21.2%[23]

Molecular weight: 226[24]

Other Names

ACH-126443[25]

Further Reading

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Manufacturer Information

Elvucitabine
Achillion Pharmaceuticals
300 George Street
New Haven, CT 06511
(202) 624-7000

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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