

Prior Authorization DRUG Guidelines

EPIVIR/EPIVIR-HBV (Lamivudine)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Lamivudine is a cytosine analog. Its principle mode of action is inhibition of HIV reverse transcription via viral DNA chain termination and thus inhibits RNA- and DNA-dependent DNA polymerase activities of reverse transcriptase. In hepatitis B, lamivudine is incorporated into the viral DNA by hepatitis B virus polymerase, resulting in DNA chain termination.

Pre-Authorization Criteria: treatment of chronic hepatitis B associated with evidence of hepatitis B viral replication and active liver inflammation; HIV infection in combination with other antiretroviral agents

Note: Use only if other anti-HBV agents with more favorable resistance patterns have failed or cannot be used; has not been evaluated in patients with HBV-HIV-1 coinfection

NOTE: The formulation and dosage of Epivir-HBV® are not appropriate for patients infected with both HBV and HIV.

Off-Label: nonoccupational postexposure prophylaxis for HIV exposure (as a component of a multidrug regimen). Prevention of perinatal HIV transmission

Note: Use with caution; heightened risk of causing significant patient harm when used in error.

Dosing: Adult:

HIV: Oral (use with at least two other antiretroviral agents): 150 mg twice daily or 300 mg once daily; <50 kg: 4 mg/kg twice daily (maximum: 150 mg twice daily)

Postexposure prophylaxis for HIV exposure (unlabeled use [CDC, 2005]): Oral: 150 mg/dose twice daily or 300 mg/dose once daily (in combination with zidovudine, tenofovir, stavudine, or

didanosine, with or without a protease inhibitor depending on risk). Initiate therapy within 72 hours of exposure and continue for 28 days

Treatment of hepatitis B: Oral: 100 mg/day

Treatment duration (AASLD practice guidelines): Treatment duration for nucleos(t)ide analog-based therapy (eg, lamivudine) is variable and influenced by HBeAg status, duration of HBV suppression, and presence of cirrhosis/decompensation. Refer to current Guidelines.

Adverse Reactions:

>10%: Headache, fatigue, insomnia, nausea, diarrhea, pancreatitis, abdominal pain, vomiting, neutropenia, transaminases increased, myalgia, neuropathy, musculoskeletal pain, nasal signs and symptoms, cough, sore throat.

Other Severe Less Common Reactions: fat redistribution, immune reconstitution syndrome, lactic acidosis/hepatomegaly, HBV exacerbation, post treatment, peripheral neuropathy, rhabdomyolysis, anemia, severe, anaphylaxis, autoimmune disorders.

U.S. BOXED WARNING:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, associated with nucleoside analogue used alone or in combination; suspend treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.

Lamivudine dosage forms contain higher dose used to treat HIV compared to lamivudine-HBV dosage forms used to treat chronic HBV; ensure patients receive correct dosage form for indicated use.

Severe acute HBV exacerbations in HBV/HIV co-infected patients upon lamivudine discontinuation; monitor hepatic function closely for at least several months in HBV/HIV co-infected patients who discontinue abacavir/lamivudine; initiate anti-HBV treatment if needed. Lamivudine-HBV is not approved for the treatment of HIV-1 infection because the lamivudine dosage in lamivudine-HBV is subtherapeutic and monotherapy is inappropriate for the treatment of HIV-1 infection. HIV-1 resistance may emerge in chronic hepatitis B-infected patients with unrecognized or untreated HIV-1 infection. HIV counseling and testing should be offered to all patients before beginning treatment with lamivudine-HBV and periodically during treatment

References:

1. Centers for Disease Control and Prevention, "Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children: Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics," *MMWR Recomm Rep*, 2009,

- 58(RR-11):1-166. Available at http://aidsinfo.nih.gov/contentfiles/Pediatric_OI.pdf. [PubMed 19730409]
2. Centers for Disease Control and Prevention, "Notice to Readers: Updated Information Regarding Antiretroviral Agents Used as HIV Postexposure Prophylaxis for Occupational HIV Exposures," *MMWR Morb Mortal Wkly Rep*, 2007, 56(49):1291-2. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5649a4.htm>
3. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, Department of Health and Human Services," February 12, 2013;1-267. Available at <http://www.aidsinfo.nih.gov>
4. Dienstag JL, Perrillo, RP, Schiff, ER, et al, "A Preliminary Trial of Lamivudine for Chronic Hepatitis B Infection," *N Engl J Med*, 1995, 333(25):1657-61. [PubMed 7477217]
5. Eron JJ, Benoit SL, Jemsek J, et al, "Treatment With Lamivudine, Zidovudine, or Both in HIV-Positive Patients With 200 to 500 CD4⁺ Cells Per Cubic Millimeter," *N Engl J Med*, 1995, 333(25):1662-9. [PubMed 7477218]
6. Hiltz AE and Fish DN, "Dosage Adjustment of Antiretroviral Agents in Patients With Organ Dysfunction," *Am J Health Syst Pharm*, 1998, 55:2528-33. [PubMed 9853641]
7. Johnson MA, Verpooten GA, Daniel MJ, et al, "Single Dose Pharmacokinetics of Lamivudine in Subjects With Impaired Renal Function and the Effect of Haemodialysis," *Br J Clin Pharmacol*, 1998, 46(1):21-7. [PubMed 9690945]
8. Kuhar DT, Henderson DK, Struble KA, et al, "Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis," *Infect Control Hosp Epidemiol*, 2013, 34(9): 875-92. [PubMed 23917901]
9. Lai CL, Chien RN, Leung NW, et al, "A One-Year Trial of Lamivudine for Chronic Hepatitis B," *N Engl J Med*, 1998, 339(2):61-8. [PubMed 9654535]
10. Lewis LL, Venzon D, Church J, et al, "Lamivudine in Children With Human Immunodeficiency Virus Infection: A Phase I/II Study," *J Infect Dis*, 1996, 174(1):16-25. [PubMed 8655986]
11. Lok AS and McMahon BJ, "Chronic Hepatitis B: Update 2009," *Hepatology*, 2009, 50(3):661-2. [PubMed 19714720]
12. Panlilio AL, Cardo DM, Grohskopf LA, et al, "Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis," *MMWR Recomm Rep*, 2005, 54(RR-9):1-17. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.htm> [PubMed 16195697]
13. Perry CM and Faulds D, "Lamivudine. A Review of Its Antiviral Activity, Pharmacokinetic Properties and Therapeutic Efficacy in the Management of HIV Infection," *Drugs*, 1997, 53(4):657-80. [PubMed 9098665]
14. Tremoulet AH, Capparelli EV, Patel P, et al, "Population Pharmacokinetics of Lamivudine in Human Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, "Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection," August 16, 2010. Available at <http://www.aidsinfo.nih.gov>
15. www.uptodate.com/contents/lamivudine-drug-information: Lamivudine: Drug Information

16. www.epocrates.com: Epivir Drug Information
17. Mounzer K, Brunet L, Wyatt CM, et al. To dose-adjust or not to dose-adjust: lamivudine dose in kidney impairment. AIDS. 2021;35(8):1201-1208.
18. Wood BR, Pozniak AL. Dosing lamivudine or emtricitabine in renal impairment: new data confirm it's time for updated guidance! AIDS. 2021;35(8):1305-1307.
19. US Department of Health and Human Services (HHS) Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Updated April 2023.
20. Perry CM and Faulds D, "Lamivudine. A Review of Its Antiviral Activity, Pharmacokinetic Properties and Therapeutic Efficacy in the Management of HIV Infection," Drugs, 1997, 53(4):657-80.
21. Epivir HBV (lamivudine) [prescribing information]. Research Triangle Park, NC; GlaxoSmithKline; December 2021

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2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Replaced Epivir background to Lamivudine. Added Note: Use only if other anti-HBV agents with more favorable resistance patterns have failed or cannot be used; has not been evaluated in patients with HBV-HIV-1 coinfection. NOTE: The formulation and dosage of Epivir-HBV® are not appropriate for patients infected with both HBV and HIV. "Updated dosing & US Boxed warning sections