

Prior Authorization DRUG Guidelines

TRIZIVIR

(Abacavir, lamivudine, and zidovudine)

Effective Date: 1/28/14

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

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Trizivir is an Antiretroviral Agent, Reverse Transcriptase Inhibitor (Nucleoside) used in the treatment of HIV-1 infections. The combination of abacavir, lamivudine, and zidovudine is believed to act synergistically to inhibit reverse transcriptase via DNA chain termination after incorporation of the nucleoside analogue as well as to delay the emergence of mutations conferring resistance.

Pre-Authorization Criteria:

Trizivir is used for the treatment of patients with HIV-1 infection either alone or in combination with other antiretroviral agents when the regimen would otherwise contain the components of Trizivir. Due to increased risk of hypersensitivity reactions in the presence of the HLA-B*5701 allele, screening for HLA-B*5701 allele status is recommended prior to initiating therapy or reinitiating therapy in patients of unknown genotype status, including patients who previously tolerated therapy.

VCHCP requires that Trizivir be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease.

Medication Guide:

An FDA-approved patient medication guide, which is available with the product information and at <http://www.fda.gov/downloads/Drugs/DrugSafety/ucm089807.pdf>, must be dispensed with this medication. A Warning Card (summarizing symptoms of hypersensitivity), which is available with the product information, must also be dispensed with this medication for each new outpatient prescription and refill.

Dosing: Adult:

HIV treatment: Oral:

U.S. labeling: Adolescents ≥ 40 kg and Adults: One tablet twice daily. Note: Not recommended for patients < 40 kg.

Dosing: Pediatric:

HIV treatment: Adolescents ≥ 40 kg: Refer to adult dosing.

Note: not recommended for children and adolescents < 40 kg as product is a fixed-dose combination.

Dosing: Geriatric:

Refer to adult dosing.

Dosing: Renal Impairment:

$Cl_{cr} < 50$ mL/minute: Avoid use.

Dosing: Hepatic Impairment:

Use is contraindicated.

Dosage Forms: U.S.:

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, oral:

Trizivir®: Abacavir sulfate 300 mg, lamivudine 150 mg, and zidovudine 300 mg

Generic Equivalent Available: U.S.-No

Exceptions:

Trizivir is not to be used in patients <40 kg.

Trizivir is not to be used in patients with a creatinine clearance <50 mL/minute or with hepatic impairment. Use individual agents to reduce dosage.

Trizivir is not to be prescribed with abacavir, lamivudine, or zidovudine-containing products (eg, Epivir®, Combivir®, Epzicom®, or Ziagen®) or emtricitabine-containing products (eg, Atripla®, Complera®, Emtriva®, Stribild®, or Truvada®).

Contraindications:

Hypersensitivity to abacavir, lamivudine, zidovudine, or any component; hepatic impairment. Do not rechallenge patients who have experienced hypersensitivity reactions to abacavir (regardless of *HLA-B*5701* status), potentially fatal hypersensitivity reactions may occur

Adverse Reactions:

Also see individual agents.

Severe Less Common Reactions: hypersensitivity reaction, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, MI, lactic acidosis, hepatomegaly, pancreatitis, HBV exacerbation post-treatment, myopathy, rhabdomyolysis, fat redistribution, peripheral neuropathy, anemia, severe, neutropenia, pancytopenia, immune reconstitution syndrome, autoimmune disorders,

U.S. BOXED WARNING:

Severe or fatal hypersensitivity reaction/multi-organ clinical syndrome with signs or symptoms from >2 of the following groups: 1) fever, 2) rash, 3) GI (nausea, vomiting, diarrhea, or abdominal pain), 4) constitutional (malaise, fatigue, or achiness), and 5) respiratory. (dyspnea, cough, or pharyngitis); carriers of *HLA-B*5701* allele are at higher risk of hypersensitivity reactions; *HLA-B*5701* allele screening recommended prior to treatment or reinitiation of treatment in pts of unknown *HLA-B*5701* status who have previously tolerated abacavir; permanently discontinue if hypersensitivity reaction suspected or cannot be ruled out, regardless of *HLA-B*5701* status; NEVER restart after hypersensitivity reaction as more severe symptoms may occur within hours, including life-threatening hypotension or death; reaction may occur within hours of restarting even in patients without hypersensitivity reaction history. Zidovudine-associated neutropenia and severe anemia, especially in patients with advanced HIV Symptomatic myopathy associated with prolonged zidovudine use

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

Severe acute HBV exacerbations in HBV/HIV co-infected pts upon lamivudine discontinuation; monitor hepatic function closely for at least several months in HBV/HIV co-infected pts who discontinue abacavir/lamivudine; initiate anti-HBV treatment if needed

References:

1. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, "Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents," February 12, 2013. Available at <http://www.aidsinfo.nih.gov>
2. DHHS Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children, "Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection," November 5, 2012. Available at <http://aidsinfo.nih.gov>
3. Hetherington S, Hughes AR, Mosteller M, et al, "Genetic Variations in HLA-B Region and Hypersensitivity Reactions to Abacavir," *Lancet*, 2002, 359(9312):1121-2. [PubMed [11943262](#)]
4. Lucas A, Nolan D, and Mallal S, "HLA-B*5701 Screening for Susceptibility to Abacavir Hypersensitivity," *J Antimicrob Chemother*, 2007, 59(4):591-3. [PubMed [17317695](#)]
5. Mallal S, Nolan D, Witt C, et al, "Association Between Presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and Hypersensitivity to HIV-1 Reverse-Transcriptase Inhibitor Abacavir," *Lancet*, 2002, 359(9308):727-32. [PubMed [11888582](#)]
6. Peyrière H, Nicolas J, Siffert M, et al, "Hypersensitivity Related to Abacavir in Two Members of a Family," *Ann Pharmacother*, 2001, 35(10):1291-2.
7. Saez-Llorens X, Nelson RP, Emmanuel P, et al, "A Randomized, Double-Blind Study of Triple Nucleoside Therapy of Abacavir, Lamivudine, and Zidovudine Versus Lamivudine and Zidovudine in Previously Treated Human Immunodeficiency Virus Type 1-Infected Children," *Pediatrics*, 2001, 107(1). Available at <http://www.pediatrics.org/cgi/content/full/107/1/e4> [PubMed [11134468](#)]
8. www.uptodate.com: Abacavir, lamivudine, and zidovudine: Drug Information.
9. www.epocrates.com: Trizivir Drug Information

Revision History:

Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD

Date Approved by P&T Committee: 1/27/15

Date Reviewed/No Updates: 1/26/16 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/26/16

Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/24/18

Date Reviewed/No Updates: 1/23/17 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/23/18

Date Reviewed/No Updates: 1/22/19 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/22/19

Date Reviewed/No Updates: 2/18/20 by H. Taekman, MD; R. Sterling, MD

Date Approved by P&T Committee: 2/18/20

Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review

1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review