VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

ATRIPLA

(efavirenz, tenofovir and emtricitabine)

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

Effective Date: 1/28/14

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

Atripla is a combination Antiretroviral consisting of efavirenz,tenofer and emtricitabine. **Efavirenz** has activity against HIV-1 by binding to reverse transcriptase. It consequently blocks the RNA-dependent and DNA-dependent DNA polymerase activities including HIV-1 replication. It does not require intracellular phosphorylation for antiviral activity. **Tenofovir** disoproxil fumarate (TDF), is an analog of adenosine 5'-monophosphate; it interferes with the HIV viral RNA dependent DNA polymerase resulting in inhibition of viral replication. TDF is first converted intracellularly by hydrolysis to tenofovir and subsequently phosphorylated to the active tenofovir diphosphate. Tenofovir inhibits replication of HBV by inhibiting HBV polymerase. **Emtricitabine** is a cytosine analogue which is phosphorylated intracellularly to emtricitabine 5'-triphosphate which interferes with HIV viral RNA dependent DNA polymerase resulting in inhibition of viral replication.

Authorization Criteria: treatment of HIV-1 infection

Dosing: Adult
HIV infection: Oral: One tablet once daily. (600mg/200mg/300mg tablets)

Dosing: Pediatric
HIV infection: Children ≥12 years and ≥40 kg and Adolescents: Oral: Refer to adult dosing. Consider premedication with antihistamine

Dosing: Geriatric
Refer to adult dosing.

Dosing: Renal Impairment
Moderate-to-severe renal impairment (Cl_{cr} <50 mL/minute): Use not recommended.

Dosing: Hepatic Impairment
Mild hepatic impairment (Child-Pugh class A): Use with caution.
Moderate or severe hepatic impairment (Child-Pugh class B, C): Not recommended.

Dosage Forms: U.S.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Tablet:
Atripla®: Efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg

Generic Equivalent Available: U.S.-No

Administration:
Should be taken on an empty stomach, normally at bedtime to increase gastrointestinal tolerance and decrease nervous system manifestations.

Contraindications:
History of clinically-significant hypersensitivity (eg, Stevens-Johnson syndrome, erythema multiforme, or toxic skin reactions) to efavirenz; concurrent use of bepridil, cisapride, midazolam, triazolam, voriconazole, ergot alkaloids (includes dihydroergotamine, ergotamine, ergonovine, methylergonovine), St. John's wort, pimozide.

Adverse Reactions:
>8%-Hypercholesterolemia, depression, fatigue, dizziness, rash, nausea, diarrhea, creatine increased, sinusitis, upper respiratory infection
Other Serious Less Common Reactions: decreased bone mineral density, fat redistribution, immune reconstitution syndrome, lactic acidosis, hepatomegaly, suicidality, renal toxicity, rhabdomyolysis, myopathy, pancreatitis, neutropenia, autoimmune disorders, exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, seizures, teratogenicity (1st trimester use).
Note: the complete adverse reaction profile of combination therapy has not been established. See individual agents.

U.S. BOXED WARNING:
Lactic acidosis and severe hepatomegaly with steatosis have been reported with nucleoside analogues, including fatal cases. Suspend treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity.
Safety and efficacy during co-infection of HIV and HBV have not been established; acute, severe exacerbations of HBV have been reported following discontinuation of antiretroviral therapy not indicated for treatment of chronic hepatitis B. Monitor hepatic function closely for at least several months in HBV/HIV co-infected patients who discontinue efavirenz/emtricitabine/tenofovir; initiate anti-HBV treatment if needed.

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References:

1. 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
2. Gallant JE, DeJesus E, Arribas JR, et al, "Tenofovir DF, Emtricitabine, and Efavirenz vs Zidovudine, Lamivudine, and Efavirenz for HIV," *N Engl J Med*, 2006, 354(3):251-60. [PubMed 16421366]
3. 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
4. UpToDate.com:Efavirenz, tenofovir, and emtricitabine: Drug information

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