VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

STRIBILD (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil)

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

Stribild is an Antiretroviral Agent, Integrase strand transfer inhibitor, CYP3A enzyme inhibitor plus nucleoside and nucleotide reverse transcriptase inhibitor combination. The viral cDNA strand produced by reverse transcriptase is processed and inserted into the human genome by the enzyme HIV-1 integrase. Elvitegravir inhibits the catalytic activity of integrase, thus preventing integration of the proviral gene into human DNA. Cobicistat inhibits enzymes of the CYP3A subfamily and enhances systemic exposure to elvitegravir. Emtricitabine is a cytosine analogue and tenofovir disoproxil fumarate (TDF) is an analog of adenosine 5'-monophosphate. Emtricitabine and tenofovir interfere with HIV viral RNA dependent DNA polymerase activities resulting in inhibition of viral replication.

Pre-Authorization Criteria:
Stribild is used in the treatment of HIV-1 infections in antiretroviral treatment-naïve patients. The major recommendation is for use as an alternative regimen for antiretroviral-naïve patients with a creatinine clearance of >70mL/minute. Stribild is not recommended for use concomitantly with other antiretroviral drugs due to the potential for drug interactions and lack of dosing recommendations.

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

Dosing: Adult:
HIV-1: Oral: One tablet once daily. Note: Recommended as an alternative regimen for antiretroviral-naive patients with Cl_{cr} >70 mL/minute (DHHS, 2013).

Dosing: Pediatric:
Pediatric dosing is currently unavailable or not applicable for this drug.

Administration:
Administer with food.

Dosing: Geriatric:
Refer to adult dosing.

Dosing: Renal Impairment:

Cl_{cr} ≥70 mL/minute: No dosage adjustments are recommended.
Cl_{cr} <70 mL/minute at initiation of therapy: Initial use is not recommended.
Cl_{cr} <50 mL/minute during therapy: Continued use is not recommended.
ESRD requiring dialysis: Use is not recommended.

Dosing: Hepatic Impairment:
Mild-to-moderate hepatic impairment (Child-Pugh class A or B): No dosage adjustments are recommended.
Severe hepatic impairment (Child-Pugh class C): Use is not recommended (has not been studied).

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Tablet, oral:
Stribild™: Elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg

Generic Equivalent Available: U.S.-No

Contraindications:
Concurrent use of alfuzosin, cisapride, ergot derivatives (eg, dihydroergotamine, ergotamine, methylergonovine); lovastatin, midazolam (oral), pimozide, rifampin, sildenafil (when used for pulmonary arterial hypertension), simvastatin, St John's wort, triazolam

Exclusions:
Stribild is not to be used in treatment-experienced patients
Stribild is not to be used in patients with a creatinine clearance <70 mL/minute at initiation of therapy and is not to be continued in patients with a creatinine clearance of <50 mL/minute during therapy.
Stribild is not to be used in patients with ESRD requiring dialysis.

Adverse Reactions:
>10%: nausea, diarrhea, proteinuria
Other Severe Less Common Reactions: lactic acidosis, hepatomegaly, hepatotoxicity, HBV exacerbation, post-treatment, nephrotoxicity, rhabdomyolysis, myopathy, osteromalacia, fractures, pancreatitis, neutropenia, immune reconstitution syndrome, autoimmune disorders, hypersensitivity reaction, fat redistribution.

U.S.BOXED WARNING:
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.
Safety and efficacy not established in HIV/HBV co-infections; severe acute HBV exacerbations in HBV/HIV co-infected patients upon discontinuation of emtricitabine or tenofovir; monitor hepatic function closely for at least several months in HBV/HIV co-infected patient who discontinue elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil; initiate anti-HBV treatment if needed.

References:

1. DeJesus E, Rockstroh JK, Henry K, et al, "Co-Formulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Disoproxil Fumarate Versus Ritonavir-Boosted Atazanavir Plus Co-Formulated Emtricitabine and Tenofovir Disoproxil Fumarate for Initial Treatment of HIV-1 Infection: A Randomised, Double-Blind, Phase 3, Non-Inferiority Trial," *Lancet*, 2012, 379(9835):2429-38. [PubMed 22748590]
2. 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
3. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, Statement Update: "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, Department of Health and Human Services," September 18, 2012b. Available at http://www.aidsinfo.nih.gov
4. Sax PE, DeJesus E, Mills A, et al, "Co-Formulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Versus Co-Formulated Efavirenz, Emtricitabine, and Tenofovir for Initial Treatment of HIV-1 Infection: A Randomised, Double-Blind, Phase 3 Trial, Analysis of Results After 48 Weeks," *Lancet*, 2012, 379(9835):2439-48. [PubMed 22748591]
5. www.uptodate.com: Stribild :Drug Information
6. www epocrates.com: Elvitegravir, cobicistat, tenofovir and emtricitabine: 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: 1/24/17
Date Reviewed/No Updates: 1/23/18 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