VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

APTIVUS (tipranavir)

Effective Date: 1/28/14

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

Rev. 9/16/15 R. Sterling MD

Date Approved by P&T Committee: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Aptivus is an Antiretroviral Agent (Protease Inhibitor). It is the first nonpeptidic Protease Inhibitor and is active against strains of HIV that are resistant to other protease inhibitors. Aptivus binds to the site of HIV-1 protease activity and inhibits cleavage of viral Gag-Pol polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles.

Pre-Authorization Criteria: treatment of HIV infections in combination with ritonavir and other antiretroviral agents (limited to highly treatment-experienced or multi-protease inhibitor-resistant patients)

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

NOTE: Aptivus is not recommended for use in treatment-naïve patients.

Dosing: Adult
HIV infection: Oral: 500 mg twice daily; **Note:** Coadministration with ritonavir (200 mg twice daily) is required.

Dosing: Pediatric
HIV infection: Children ≥2 years: Oral: 14 mg/kg or 375 mg/m^2 (maximum: 500 mg/dose) twice daily.
Note: Coadministration with ritonavir (6 mg/kg or 150 mg/m^2 [maximum: 200 mg/dose] twice daily) is required.

If intolerance or toxicity develops and virus is not resistant to multiple protease inhibitors: May decrease dose to 12 mg/kg or 290 mg/m^2 twice daily.
Note: Coadministration with ritonavir (5 mg/kg or 115 mg/m^2 twice daily) is required.

How Supplied:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Capsule250 mg
Solution: 100 mg/mL (95 mL) [contains polyethylene glycol, propylene glycol, tocophersolan; buttermint-butter toffee flavor]
Precautions: may cause Cushingoid appearance; hypercholesterolemia; caution with sulfa allergy (contains a sulfonamide moiety);

Drug Interactions: Use caution with concurrent therapy of tipranavir/ritonavir with alfuzosin, amiodarone, bepridil, cisapride, ergot derivatives (eg, dihydroergotamine, ergonovine, ergotamine, methylergonovine), flecainide, lovastatin, midazolam (oral), pimozide, propafenone, quinidine, rifampin, sildenafil (for pulmonary arterial hypertension, simvastatin, St John's wort, and triazolam (see product literature)

U.S. BOXED WARNINGS:
1) Use in combination with ritonavir has been associated with rare reports of fatal and nonfatal **intracranial hemorrhage**; causal relationship not clearly established.
2) Use in combination with ritonavir, may cause **hepatitis** (including fatalities) and/or exacerbate pre-existing hepatic dysfunction (causal relationship not established); patients with chronic hepatitis B or C are at increased risk.

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. www.uptodate.com: HIV protease inhibitors
3. US Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available at: http://aidsinfo.nih.gov/Guidelines
4. Cooper D, Zajdenverg R, Ruxrungtham K, et al. Efficacy and safety of two doses of tipranavir/ritonavir versus lopinavir/ritonavir-based therapy in antiretroviral-naive patients: results of BI 1182.33 (Abstract PL13.4]. In: Program and abstracts of the 8th International Congress on Drug Therapy in HIV infection 2006.

5. HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Updated April 8, 2015.
6. Graff J, von Hentig N, Kuczka, K, et al, "Significant Effects of Tipranavir on Platelet Aggregation and Thromboxane B_2 Formation *in vitro* and *in vivo*," *J Antimicrob Chemother*, 2008, 61(2):394-9.

Revision History:

Date Developed: 1/28/14 by C. Sanders MD
Date Approved by P&T Committee: 1/28/14
Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
Date Approved by P&T Committee: 1/27/15
Date Reviewed/Updated: 9/6/15 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