



Therapeutic Class ReviewSM

tipranavir (Aptivus[®])

April 2006

New Product for Review:

tipranavir (Aptivus[®]) [Boehringer-Ingelheim]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: 3

1- dossier w/missing components

2- all components present, except pharmacoeconomic model

3- all components present (comprehensive)

Executive Summary

- Tipranavir (Aptivus):
 - is the 9th PI approved in the U.S.
 - is intended for use in combination with other antiretroviral medications for the treatment of HIV-1 infection.
- The PI class accounts for over \$4 million in costs (about 1300 patients) over the past year at Regence.
- Aptivus is likely to capture only a small fraction of the PI market due to its restricted indication and potential safety issues.
- Initial approval of Aptivus was based on preliminary results from two, pivotal, open-label trials under FDA accelerated approval regulations.
- Patients enrolled in these trials had received at least two previous PIs, had ongoing viremia on a PI-based antiretroviral (ARV) regimen, and 97% had isolates showing resistance to at least on PI.
- Labeling for Aptivus is limited to clinically advanced, highly treatment-experienced and multiple protease inhibitor resistant HIV-1 infected population who have limited treatment options and ongoing measurable viremia (desperate population).
- Aptivus must be co-administered with ritonavir (Norvir[®]) to boost serum drug levels to concentrations that will inhibit HIV replication.
- Aptivus carries Box Warnings that alert of the potential for liver failure and intracranial bleeding.

Evidence

- There is no useful evidence to show that tipranavir (Aptivus) is superior to existing ritonavir-boosted (Norvir-boosted) PI regimens based on its ability to suppress HIV-1 replication.
- There is no evidence that tipranavir (Aptivus) prevents the clinical progression of HIV-1 infection.
- There are no trials of adequate design or duration to verify that harms reported in patients treated with Aptivus were not due to chance. However, a dose-related elevation in liver function tests was

observed with tipranavir (Aptivus) in clinical trials which increases the likelihood that hepatotoxicity is a potential risk with tipranavir (Aptivus).

- There is no useful evidence to show any difference in harms between tipranavir (Aptivus) plus ritonavir (Norvir) and other ritonavir-boosted (Norvir-boosted) PI regimens.
- The risk versus benefit of tipranavir (Aptivus) has not been evaluated in treatment-naïve patients.

Decision

- Tipranavir (Aptivus) is non-preferred/non-formulary because:
 - Evidence provided from clinical trials is fatally flawed.
 - There are potentially serious safety issues with this product.

Products

| Drug Product | Date of FDA Approval | FDA Approved Indication | Dose/Route | Potential Off-Label Uses ^a |
|---|----------------------|---|--|--|
| amprenavir (Agenerase [®]) ² [50mg, and 150mg cap] | 4/1999 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 1200 mg p.o. b.i.d. 1200 mg p.o. q.d. plus ritonavir 200 mg q.d. | occupational HIV post-exposure prophylaxis |
| atazanavir (Reyataz [®]) ³ [100mg, 150mg, and 200 mg cap] | 6/2003 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 400 mg p.o. q.d. 300 mg p.o. q.d. plus ritonavir 100 mg q.d. [with food] | |
| fosamprenavir (Lexiva [®]) ⁴ [700mg tab] | 10/2003 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 1400 mg p.o. b.i.d. 1400 mg p.o. q.d. plus ritonavir 200 mg q.d. | |
| indinavir (Crixivan [®]) ⁵ [100mg, 200mg, 333mg, and 400 mg cap] | 3/1996 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 800 mg p.o. q. 8 hrs [empty stomach] | occupational HIV post-exposure prophylaxis |
| lopinavir/ritonavir (Kaletra [®]) ⁶ [133.3mg/33.3mg cap and 200mg/50mg tab] | 9/2000 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 3 caps p.o. b.i.d. or 6 caps p.o. q.d. [with food] | occupational HIV post-exposure prophylaxis |
| nelfinavir (Viracept [®]) ⁷ [250mg and 625mg tab] | 3/1997 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 1250 mg p.o. b.i.d. or 750 mg t.i.d. [with food] | occupational HIV post-exposure prophylaxis |
| ritonavir (Norvir [®]) ⁸ [100mg cap] | 3/1996 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 600 mg p.o. b.i.d. | occupational HIV post-exposure prophylaxis |
| saquinavir (Fortovase [®]) ⁹ [200mg cap] | 11/1997 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 1200 mg p.o. t.i.d. [with food] | occupational HIV post-exposure prophylaxis |
| saquinavir (Invirase [®]) ¹⁰ 250mg cap and 500mg tab] | 12/1995 | Treatment of HIV-1 infection in combination with other antiretroviral medications. | 1000 mg p.o. b.i.d. plus ritonavir 100 mg b.i.d. [with food] | occupational HIV post-exposure prophylaxis |
| tipranavir (Aptivus [®]) ¹¹ [250mg cap] | 6/2005 | Treatment of HIV-1 infection in combination with ritonavir in patients with evidence of viral | 500 mg p.o. b.i.d. plus ritonavir 200 mg b.i.d. [with food] | |

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| | | replication that are highly treatment-experienced or have HIV-1 strains resistant to multiple protease inhibitors. | | |
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^a As listed in © 1974 - 2005 Thomson MICROMEDEX database ^[12] or as referenced.

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