



Therapeutic Class ReviewSM

emtricitabine plus tenofovir (Truvada[®])

November 2005

New Product for Review:

emtricitabine plus tenofovir (Truvada[®]) - Gilead

Dossier Provided by Manufacturer: No

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Preferred/Non-Formulary
Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs):	
delavirdine (Rescriptor [®]) [Pfizer]	
efavirenz (Sustiva [®]) [Bristol-Myers Squibb (BMS)]	
nevirapine (Viramune [®]) [Boehringer Ingelheim]	
Nucleoside Reverse Transcriptase Inhibitors (NRTIs):	
abacavir (Ziagen [®]) [GlaxoSmithKline (GSK)]	
abacavir/lamivudine (Epzicom [®]) [GSK]	
abacavir/lamivudine/zidovudine (Trizivir [®]) [GSK]	
didanosine (Videx [®]) [BMS]	
didanosine enteric coated (Videx [®] EC) (generics)	
emtricitabine (Emtriva [®]) [Gilead]	
lamivudine (Epivir [®]) [GSK]	
lamivudine/zidovudine (Combivir [®]) [GSK]	
stavudine (Zerit [®]) [BMS]	
tenofovir (Viread [®]) [Gilead]	
zalcitabine (Hivid [®]) [Roche]	
zidovudine (Retrovir [®]) [GSK]	
Protease Inhibitors (PIs):	
amprenavir (Agenerase [®]) [GSK/Vertex]	tipranavir (Aptivus [®]) [Boehringer Ingelheim]
atazanavir (Reyataz [®]) [BMS]	
fosamprenavir (Lexiva [®]) [GSK/Vertex]	
indinavir (Crixivan [®]) [Merck]	
lopinavir/ritonavir (Kaletra [®]) [Abbott]	
nelfinavir (Viracept [®]) [Pfizer]	
ritonavir (Norvir [®]) [Abbott]	
saquinavir (Fortovase [®] , Invirase [®]) [Roche]	
Fusion Inhibitors:	
enfuvirtide (Fuzeon [®]) [Roche/Trimeris]	

Executive Summary

- Truvada is a combination of two nucleoside reverse transcriptase inhibitors (NRTIs), emtricitabine and tenofovir.
- The manufacturer promotes this product as a convenient, one tablet once-a-day alternative to multiple-dose regimens.
- The cost of Truvada is greater than the combined cost of its individual components, which are each dosed as one tablet once-a-day.
- Current therapy recommendations include the combination of two NRTIs plus a nonnucleoside reverse transcriptase inhibitor (NNRTI) for the treatment of HIV-1 infection in treatment-naïve patients.
- Emtricitabine (Emtriva), one of the components of Truvada, and lamivudine (Epivir), another NRTI, have similar structures and pharmacology. Concomitant or sequential use of these two agents should be avoided due to their overlapping toxicity and resistance profiles.

Evidence

- There are no published studies that support the use of Truvada in the treatment of HIV infection.
- Truvada was approved under the FDA accelerated approval regulations. Efficacy of the product was based on the efficacy of its individual components.
- There are no studies that demonstrate improved adherence with Truvada over its individual components taken separately, or over other NRTI-based regimens.

Conclusion

- Emtricitabine/tenofovir (Truvada[®]) is non-preferred/ non-formulary because there is no evidence that it offers any additional benefit over current preferred/formulary options for its increased cost.

Products

Table 1:

Drug Product	Date of FDA Approval	FDA Approved Indication	Dose/Route	AWP Cost*	Potential Off-Label Uses
Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs):					
delavirdine (Rescriptor) ^{®1, 28}	4/1997	Treatment of HIV-1 infection in combination with at least two other active antiretroviral agents.	400 mg p.o. t.i.d	\$317	occupational HIV post-exposure prophylaxis
efavirenz (Sustiva) ^{®2, 28}	9/1998	Treatment of HIV-1 infection in combination with other antiretroviral medications (combine with a PI +/-or NRTI).	600 mg p.o. q.d. [empty stomach]	\$500	occupational HIV post-exposure prophylaxis
nevirapine (Viramune) ^{®3, 28}	6/1996	Treatment of HIV-1 infection in combination with other antiretroviral medications.	200 mg p.o. q.d. x 14 days, then b.i.d.	\$443	perinatal and postnatal transmission of HIV
Nucleoside Reverse Transcriptase Inhibitors (NRTIs):					
abacavir (Ziagen) ^{®4, 28}	12/1998	Treatment of HIV-1 infection in combination with other antiretroviral medications.	300 mg p.o. b.i.d. or 600 mg p.o. q.d.	\$467	occupational HIV post-exposure prophylaxis
abacavir/lamivudine (Epzicom) ^{®5, 28} [600 mg/300 mg]	8/2004	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1 tablet p.o. q.d.	\$814	occupational HIV post-exposure prophylaxis
abacavir/lamivudine/zidovudine (Trizivir) ^{®6, 28} [300 mg/150 mg/300 mg]	11/2000	Treatment of HIV-1 infection alone or in combination with other antiretroviral medications.	1 tablet p.o. b.i.d.	\$1220	occupational HIV post-exposure prophylaxis
didanosine (Videx) ^{®7, 28}	10/1991	Treatment of HIV-1 infection in combination with other antiretroviral medications.	≥ 60 kg: 200 mg b.i.d. < 60 kg: 125 mg b.i.d. [empty stomach]	\$307 \$192	occupational HIV post-exposure prophylaxis
didanosine (Videx EC) ^{®8, 28}	10/2000	Treatment of HIV-1 infection in combination with other antiretroviral medications.	≥ 60 kg: 400 mg q.d. < 60 kg: 250 mg q.d. [empty stomach]	\$237 † \$154 †	occupational HIV post-exposure prophylaxis
emtricitabine (Emtriva) ^{®9, 28}	7/2003	Treatment of HIV-1 infection in combination with other antiretroviral medications.	200 mg p.o. q.d.	\$304	Hepatitis B infection
emtricitabine/tenofovir (Truvada) ^{®10, 28} [200 mg/300 mg]	8/2004	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1 tablet p.o. q.d.	\$868	Hepatitis B infection
lamivudine (EpiVir) ^{®11, 28}	11/1995	1) Treatment of HIV-1 infection in combination with other antiretroviral medications. 2) Hepatitis B (EpiVir HBV)	150 mg p.o. b.i.d. or 300 mg p.o. q.d.	\$348	occupational HIV post-exposure prophylaxis; Perinatal and postnatal transmission of HIV
lamivudine/zidovudine (Combivir) ^{®12, 28} [150 mg/300 mg]	9/1997	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1 tablet p.o. b.i.d.	\$753	perinatal HIV transmission prevention
stavudine (Zerit) ^{®13, 28}	6/1994	Treatment of HIV-1 infection in combination with other antiretroviral medications.	≥ 60 kg: 40 mg b.i.d. < 60 kg: 30 mg b.i.d. (every 12 hours)	\$386 \$379	occupational HIV post-exposure prophylaxis

* AWP (average wholesale price) based on First Data Bank as of July 2005 for 30 days of therapy.

† MAC = maximum allowable cost as of July 2005 for 30 days of therapy.

Products (continued)

Table 1:

Drug Product	Date of FDA Approval	FDA Approved Indication	Dose/Route	AWP Cost*	Potential Off-Label Uses
Nucleoside Reverse Transcriptase Inhibitors (NRTIs): [continued]					
tenofovir (Viread [®]) ^{14, 28}	10/2001	Treatment of HIV-1 infection in combination with other antiretroviral medications.	300 mg p.o. q.d.	\$521	Hepatitis B
zalcitabine (Hivid [®]) ^{15, 28}	6/1992	Treatment of HIV-1 infection in combination with other antiretroviral medications.	0.75 mg p.o. q. 8 hrs	\$259	
zidovudine (Retrovir [®]) ^{16, 28}	3/1987	Treatment of HIV-1 infection in combination with other antiretroviral medications.	300 mg p.o. b.i.d. or 200 mg p.o. t.i.d.	\$406 \$406	occupational HIV post-exposure prophylaxis; Hepatitis B; perinatal HIV transmission prevention
Protease Inhibitors (PIs):					
amprenavir (Agenerase [®]) ^{17, 28}	4/1999	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1200 mg p.o. b.i.d. (decrease by 50% if given with ritonavir)	\$772	occupational HIV post-exposure prophylaxis
atazanavir (Reyataz [®]) ^{18, 28}	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. (with ritonavir) [take with food]	\$893 \$893	
fosamprenavir (Lexiva [®]) ^{19, 28}	10/2003	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1400 mg p.o. b.i.d. (decrease by 50% if given with ritonavir)	\$1318	
indinavir (Crixivan [®]) ^{20, 28}	3/1996	Treatment of HIV-1 infection in combination with other antiretroviral medications.	800 mg p.o. q. 8 hrs [empty stomach]	\$637	occupational HIV post-exposure prophylaxis
lopinavir/ritonavir (Kaletra [®]) ^{21, 28} [133.3 mg/33.3 mg]	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]	\$738 \$738	occupational HIV post-exposure prophylaxis
nelfinavir (Viracept [®]) ^{22, 28}	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]	\$801 \$690	occupational HIV post-exposure prophylaxis
ritonavir (Norvir [®]) ^{23, 28}	3/1996	Treatment of HIV-1 infection in combination with other antiretroviral medications.	600 mg p.o. b.i.d.	\$3858	occupational HIV post-exposure prophylaxis
saquinavir (Fortovase [®]) ^{24, 28}	11/1997	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1200 mg p.o. t.i.d. [with food]	\$791	occupational HIV post-exposure prophylaxis
saquinavir (Invirase [®]) ^{25, 28}	12/1995	Treatment of HIV-1 infection in combination with other antiretroviral medications.	1000 mg p.o. b.i.d. + ritonavir 100 mg b.i.d. [with food]	\$702 + \$643	occupational HIV post-exposure prophylaxis
tipranavir (Aptivus [®]) ^{26, 28}	6/2005	Treatment of HIV-1 infection in combination with ritonavir in patients with evidence of viral replication that are highly treatment-experienced or have HIV-1 strains resistant to multiple protease inhibitors.	500 mg p.o. b.i.d. co-administered with ritonavir 200 mg b.i.d. [with food]	\$2404 (includes cost of ritonavir)	

*AWP (average wholesale price) based on First Data Bank as of July 2005 for 30 days of therapy.

Products (continued)

Table 1:

Drug Product	Date of FDA Approval	FDA Approved Indication	Dose/Route	AWP Cost*	Potential Off-Label Uses
Fusion Inhibitors:					
enfuvirtide (Fuzeon [®]) ^{27, 28}	3/2003	Treatment of HIV-1 infection in combination with other antiretroviral medications in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.	90 mg (1 ml) subcutaneously b.i.d.	\$2206	

*AWP (average wholesale price) based on First Data Bank as of July 2005 for 30 days of therapy.

Table 2:

Drug Product	Approval in pediatric patients	Minimum age of approval [#]	Pregnancy category
NNRTIs:			
delavirdine (Rescriptor [®]) ¹			Category C
efavirenz (Sustiva [®]) ²	X	≥ 3 years	Category D
nevirapine (Viramune [®]) ³	X	≥ 2 months	Category C
NRTIs:			
abacavir (Ziagen [®]) ⁴	X	≥ 3 months	Category C
abacavir/lamivudine (Epzicom [®]) ⁵			Category C
abacavir/lamivudine/zidovudine (Trizivir [®]) ⁶			Category C
didanosine (Videx [®]) ⁷	X	≥ 2 weeks	Category B
didanosine enteric coated (Videx [®] EC) ⁸			Category B
emtricitabine (Emtriva [®]) ⁹			Category B
emtricitabine/tenofovir (Truvada [®]) ¹⁰			Category B
lamivudine (Epivir [®]) ¹¹	X	≥ 3 months	Category C
lamivudine/zidovudine (Combivir [®]) ¹²			Category C
stavudine (Zerit [®]) ¹³	X	from birth	Category C
tenofovir (Viread [®]) ¹⁴			Category B
zalcitabine (Hivid [®]) ¹⁵	X	≥ 13 years	Category C
zidovudine (Retrovir [®]) ¹⁶	X	≥ 6 weeks	Category C
Protease Inhibitors (PIs):			
amprenavir (Agenerase [®]) ¹⁷	X	≥ 4 years	Category C
atazanavir (Reyataz [®]) ¹⁸			Category B
fosamprenavir (Lexiva [®]) ¹⁹			Category C
indinavir (Crixivan [®]) ²⁰			Category C
lopinavir/ritonavir (Kaletra [®]) ²¹	X	≥ 6 months	Category C
nelfinavir (Viracept [®]) ²²	X	≥ 2 years	Category B
ritonavir (Norvir [®]) ²³	X	≥ 2 years	Category B
saquinavir (Fortovase [®]) ²⁴			Category B
saquinavir (Invirase [®]) ²⁵			Category B
tipranavir (Aptivus [®]) ²⁶			Category C
Fusion Inhibitors:			
enfuvirtide (Fuzeon [®]) ²⁷	X	≥ 6 years	Category B

see prescribing information for pediatric dosing of individual products.

References

1. Rescriptor[®] (delavirdine) Product Information. La Jolla, CA: Pfizer, 2001.
2. Sustiva[®] (efavirenz) Product Information. Princeton, NJ: Bristol-Myers Squibb, 2005.
3. Viramune[®] (nevirapine) Product Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc., 2005.
4. Ziagen[®] (abacavir) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2004.
5. Epzicom[®] (abacavir/lamivudine) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2004.
6. Trizivir[®] (abacavir/lamivudine/zidovudine) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2005.
7. Videx[®] (didanosine) Product Information. Princeton, NJ: Bristol-Myers Squibb, 2003.
8. Videx[®] EC (didanosine) Product Information. Princeton, NJ: Bristol-Myers Squibb, 2005.
9. Emtriva[®] (emtricitabine) Product Information. Foster City, CA: Gilead Sciences, Inc., 2004.
10. Truvada[®] (emtricitabine/tenofovir) Product Information. Foster City, CA: Gilead Sciences, Inc., 2005.
11. Epivir[®] (lamivudine) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2004.
12. Combivir[®] (lamivudine/zidovudine) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2004.
13. Zerit[®] (stavudine) Product Information. Princeton, NJ: Bristol-Myers Squibb, 2004.
14. Viread[®] (tenofovir) Product Information. Foster City, CA: Gilead Sciences, Inc., 2005.
15. Hivid[®] (zalcitabine) Product Information. Nutley, NJ: Roche Laboratories, Inc., 2002.
16. Retrovir[®] (zidovudine) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2003.
17. Agenerase[®] (amprenavir) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2005.
18. Reyataz[®] (atazanavir) Product Information. Princeton, NJ: Bristol-Myers Squibb, 2005.
19. Lexiva[®] (fosamprenavir) Product Information. Research Triangle Park, NC: GlaxoSmithKline, 2005.
20. Crixivan[®] (indinavir) Product Information. Whitehouse Station, NJ: Merck & Co. Inc., 2005.
21. Kaletra[®] (lopinavir/ritonavir) Product Information. North Chicago, IL: Abbott Laboratories, 2005.
22. Viracept[®] (nelfinavir) Product Information. La Jolla, CA: Pfizer, 2004.
23. Norvir[®] (ritonavir) Product Information. North Chicago, IL: Abbott Laboratories, 2005.
24. Fortovase[®] (saquinavir) Product Information. Nutley, NJ: Roche Laboratories, Inc., 2003.
25. Invirase[®] (saquinavir) Product Information. Nutley, NJ: Roche Laboratories, Inc., 2004.
26. Aptivus[®] (tipranavir) Product Information. Ridgefield, CN: Boehringer Ingelheim Pharmaceuticals, Inc., 2005.
27. Fuzeon[®] (enfuvirtide) Product Information. Nutley, NJ: Roche Laboratories, Inc., 2005.
28. Thomson Micromedex © 1974-2005. Micromedex Healthcare Series, Vol 120.
29. Department of Health and Human Services; U.S. Food and Drug Administration. Approval letter for NDA 21-752 (Truvada); dated August 2, 2004. Available at: <http://www.fda.gov/cder/foi/appletter/2004/21752ltr.pdf>. Accessed 7/29/2005.
30. Combination of fixed dose tenofovir/emtricitabine plus efavirenz has significantly greater responses vs fixed dose zidovudine/lamivudine plus efavirenz in treatment-naïve patients: an interim analysis. Preliminary results presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Washington, D.C., October 30 to November 2, 2004. Available at: http://www.hivandhepatitis.com/2004icr/icaac2004/docs/1101/1101_b.html.
31. Center for Drug Evaluation and Research. Approval package for application number NDA 21-500 (Emtriva); Medical Review. Available at: http://www.fda.gov/cder/foi/nda/2003/021500_emtriva_toc.htm. Accessed 7/29/2005.
32. Department of Health and Human Services (DHHS) Panel on Clinical Practices for the Treatment of HIV Infection: Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents, April 7, 2005. Available at: http://www.aidsinfo.nih.gov/guidelines/adult/AA_040705.pdf. Accessed on July 26, 2005.
33. Center for Drug Evaluation and Research. Approval package for application number NDA 21-356 (Viread); Medical Review. Available at: http://www.fda.gov/cder/foi/nda/2001/21-356_Viread.htm. Accessed 7/29/2005.
34. Division of AIDS. Division of AIDS table for grading the severity of adult and pediatric adverse events, Version 1.0. Published December 2004. Accessed August 1, 2005. Available at: http://rcc.tech-res-intl.com/DAIDS%20RCC%20Forms/TB_ToxicityTables_D AIDS_AE_GradingTable_FinalDec2004.pdf
35. Lacy CF, Armstrong LL, Goldman MP, Lance LL, editors. Drug Information Handbook, 2004-2005. Hudson, OH: Lexi-Comp; 2004.