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ARV Therapy in Adults & Adolescents

December 2011

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Florida/Caribbean AETC — AIDS Education and Training Center
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This convenient pocket-sized guide summarizes information from the referenced guidelines below. Critical information regarding antiretroviral agents currently approved for use in adults and adolescents is included. Information summarized includes adult dosing (including renal and hepatic dosing recommendations), available dosage forms, side effects, and important pt counseling points.

Unless otherwise indicated, content adapted from 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. October 14, 2011; 1–167. Available at *http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.*

The information contained in this publication is intended for medical professionals. If a serious adverse event occurs, please report the event to the FDA (*www.fda.gov/Safety/MedWatch/HowToReport/default.htm*), to help increase pt safety. Recognizing the rapid changes that occur in this field, clinicians are encouraged to consult with their local experts or research the literature for the most up-to-date information to assist in individual treatment decisions for their pt.

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Regimens for Treatment of HIV-1 in Antiretroviral-Naïve Patients

Regimens below assume no baseline resistance. Resistance testing recommended for all pts upon entry into care and prior to starting ARVs.
Note: (/r) Indicates low-dose ritonavir (Norvir®) for boosting

PREFERRED REGIMENS (ALL AI[1]): *Optimal/durable efficacy, favorable tolerability/toxicity, ease of use*

NNRTI-based:		
Efavirenz[2] + tenofovir[3] + emtricitabine[4] (Available as Atripla®)		
PI-based (alphabetical):		
Atazanavir (Reyataz®)/r[5] **or** Darunavir (Prezista®)/r once daily	+	tenofovir[3] + emtricitabine[4] (Truvada®)

Integrase Inhibitor-based:		
Raltegravir (Isentress®)	+	tenofovir[3] + emtricitabine[4]
Preferred Regimen in Pregnancy		
Lopinavir/r (Kaletra®) twice daily	+	zidovudine[6] + lamivudine[4] (available as Combivir®)

ALTERNATIVE REGIMENS: *Effective/tolerable but have potential disadvantages compared to preferred*

NNRTI-based (alphabetical):			
Efavirenz[2] (Sustiva®)	+	(abacavir[7] + lamivudine[4]), available as Epzicom®	BI[1]
Rilpivirine[8] + tenofovir[3] + emtricitabine[4] (Available as Complera™)			BI[1]
Rilpivirine[8] (Edurant™)	+	abacavir[7] + lamivudine[4]	BII[1]

PI-based (alphabetical):			
Atazanavir/r[5]	+	abacavir[7] + lamivudine[4]	BI[1]
Darunavir/r	+	abacavir[7] + lamivudine[4]	BIII[1]
Fosamprenavir (Lexiva®)/r[9] **or** Lopinavir/r[10] once or twice daily	+	(abacavir[7] + lamivudine[4]) **or** (tenofovir[3] + emtricitabine[4])	BI[1]
Integrase Inhibitor-based:			
Raltegravir	+	abacavir[7] + lamivudine[4]	BIII[1]

ACCEPTABLE REGIMENS (CI[1]): *May be selected for some patients but less satisfactory than preferred or alternative*

NNRTI-based:		
Efavirenz[2]	+	zidovudine[6] + lamivudine[4]
Nevirapine[11] (Viramune®, Viramune XR®)	+	(tenofovir[3] + emtricitabine[4]) **or** (zidovudine[6] + lamivudine[4])

PI-based:		
Atazanavir[5]	+	(abacavir[7] + lamivudine[4]) **or** (zidovudine[6] + lamivudine[4])
Atazanavir/r[5] **or** Fosamprenavir/r[9] **or** Lopinavir/r[10]	+	zidovudine[6] + lamivudine[4]
CCR5 Inhibitor-based:		
Maraviroc[12] (Selzentry®)	+	zidovudine[6] + lamivudine[4]

REGIMENS THAT MAY BE ACCEPTABLE (ALL CIII[1]): *May be acceptable but more definitive data needed*

NNRTI-Based:		
Nevirapine[11,13]	+	abacavir[7] + lamivudine[4]
Rilpivirine[8]	+	zidovudine[6] + lamivudine[4]
PI-based:		
Darunavir/r	+	zidovudine[6] + lamivudine[4]

Integrase Inhibitor-based:		
Raltegravir	+	zidovudine[6] + lamivudine[4]
CCR5 Inhibitor-based:		
Maraviroc[12]	+	(abacavir[7] + lamivudine[4]) **or** (tenofovir[3] + emtricitabine[4])

REGIMENS THAT MAY BE ACCEPTABLE BUT SHOULD BE USED WITH CAUTION:
Virologic efficacy demonstrated in some studies but safety, resistance, and/or efficacy concerns exist

PI-based (alphabetical)			
Saquinavir (Invirase®)/r[14]	+	tenofovir[3] + emtricitabine[4]	CI[1]
Saquinavir/r[14]	+	(abacavir[7] + lamivudine[4]) **or** (zidovudine[6] + lamivudine[4])	CIII[1]

1. See Table 2 of DHHS guidelines for Rating Scheme for strength of recommendations/quality of evidence. *www.aidsinfo.nih.gov/contentfiles/AA_Tables.pdf#page=3*
2. Do not use EFV in 1st trimester of pregnancy or in sexually active ♀ with child-bearing potential not using adequate contraception. Caution with unstable psychiatric disease.
3. Tenofovir should be used with caution in pts with renal insufficiency.
4. FTC may replace 3TC and vice versa (co-formulation is major determining factor).
5. Significant interaction with proton pump inhibitors and other acid-reducing agents. See table under the Atazanavir section.
6. Zidovudine available in generic formulation. ZDV can cause bone marrow suppression, lipoatrophy, and rarely lactic acidosis with hepatic steatosis.
7. Do not use ABC in pts who test (+) for HLA-B*5701; use caution in pts with high CVD risk or with pre-ART viral load > 100,000 copies/mL.
8. Use rilpivirine with caution in pts with pretreatment HIV RNA > 100,000 copies/mL. Use of proton pump inhibitors with rilpivirine is contraindicated.
9. Ritonavir-boosted FPV preferred. Virologic failure with unboosted FPV may → cross-resistance with DRV.
10. LPV/r (twice daily) + ZDV + 3TC preferred regimen for pregnant women. Once daily lopinavir/r not recommended in pregnant ♀. See Perinatal Guidelines for detailed recommendations for treating HIV in pregnancy. *www.aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf*
11. Do not initiate NVP in pts with moderate-severe hepatic impairment or in ART-naïve ♀ or ♂ with pre-ART CD4 > 250 or > 400 cells/mm³, respectively.
12. Tropism test prior to use and use if CCR5-tropic only virus (i.e. no CXCR4)
13. Use NVP and ABC together with caution since both can cause HSR; early virologic failure and ↑ resistance with TDF/FTC (or 3TC).
14. Risk of PR and QT prolongation, baseline ECG before start. Do not use if pre ART QT > 450 milliseconds (msec), refractory ↓ K⁺ or ↓ Mg⁺⁺, tx with other drugs that prolong QT, complete AV block w/o pacemaker, risk of complete AV block.

Ⓡ Renal Dose Adjustments[14]

AGENT(S)	DOSE ADJUSTMENT
NRTIs	
Zidovudine	CrCl < 15 or HD[15]: 100 mg tid or 300 mg q24h
Didanosine	≥ 60 kg: CrCl 30-59: (EC) 200 mg q24h; CrCl 10-29: (EC) 125 mg q24h; CrCl < 10, HD[15] or CAPD: (EC) 125 mg q24h; < 60 kg: CrCl 30-59: (EC) 125 mg q24h; CrCl 10-29: (EC) 125 mg q24h; CrCl < 10, HD[15] or CAPD: 75 mg q24h (oral soln)
Emtricitabine	CrCl 30-49: 200 mg cap q48h or 120 mg soln q24h; CrCl 15-29: 200 mg cap q72h or 80 mg soln q24h; CrCl < 15 or HD[15]: 200 mg cap q96h or 60 mg soln q24h
Lamivudine	CrCl 30-49: 150 mg q24h; CrCl 15-29: 150 mg x 1 then 100 mg q24h; CrCl 5-14: 150 mg x 1 then 50 mg q24h; CrCl < 5 or HD[15]: 50 mg x 1 then 25 mg q24h
Stavudine	≥ 60 kg: CrCl 26-50: 20 mg q12h, CrCl ≤ 25 or HD[15]: 20 mg q24h; < 60 kg: CrCl 26-50: 15 mg q12h, CrCl ≤ 25 or HD[15]: 15 mg q24h
Tenofovir[16]	CrCl 30-49: 300 mg q48h; CrCl 10-29: 300 mg twice weekly; CrCl < 10, not on HD: no recommendation; HD[15]: 300 mg qweek
Combo Products	
AZT/3TC (Combivir®)	CrCl < 50: Combo product cannot be used; see dosing for individual agents
FTC/TDF (Truvada®)[16]	CrCl 30-49: One tab q48h; CrCl < 30: Combo product cannot be used; see dosing for individual agents
FTC/TDF/EFV (Atripla®)[16]	CrCl < 50: Not recommended; see dosing for individual agents
FTC/TDF/RPV (Complera™)[16]	CrCl < 50: Not recommended; see dosing for individual agents
NNRTIs	
Rilpivirine	Severe renal impairment or HD: use with caution and monitor for adverse effects
PIs	
Atazanavir	ARV-naive on HD: ATV 300 mg + RTV 100 mg once daily; ARV-exp on HD: ATV not recommended (unboosted or boosted)
Lopinavir/r	HD: Avoid once daily dosing
CCR5 INHIBITOR	
Maraviroc	CrCl < 30 or HD: Without potent CYP3A inhibitor or inducer, ↓ dose to 150 mg; Not recommended for use with potent CYP3A inhibitor or inducer

14. No renal dose adj for ABC, PIs (except ATV), NNRTIs, RAL, or T-20
15. Dose after hemodialysis (HD) on HD days
16. CAUTION: consider TDF as possible cause for renal dysfunction

CP=Child-Pugh Score (see **Child-Pugh Score Calculation** table to the right)

Ⓗ Hepatic Dose Adjustments[17]

AGENT(S)	DOSE ADJUSTMENT
NRTIs	
Abacavir	CP A: 200 mg bid; CP B or C: contraindicated
NNRTIs	
Delavirdine or Efavirenz	Use with caution-no recommendation
Etravirine	CP A or B: no adjustment; CP C: no recommendation
Nevirapine	CP B or C: contraindicated
Rilpivirine	CP A or B: no adjustment; CP C: no data
PIs	
Atazanavir	CP B: 300 mg once daily (no ritonavir boosting); Class C: not recommended
Darunavir	CP A or B: no adjustment; CP C: not recommended
Fosamprenavir	PI-naïve-CP A or B: 700 mg bid; CP C: 350 mg bid; PI-naïve or exp-CP A: 700 mg bid + RTV 100 mg once daily; CP B: 450 mg bid + RTV 100 mg once daily; CP C: 300 mg bid + RTV 100 mg once daily
Indinavir	CP A or B with cirrhosis: 600 mg q8h; CP C: no data
Lopinavir	Use with caution-no recommendation
Nelfinavir	CP A: no adjustment; CP B or C: not recommended
Ritonavir	Refer to recommendations for the primary PI
Saquinavir	CP A or B: use with caution; CP C: contraindicated
Tipranavir	CP A: use with caution; CP B or C: contraindicated
CCR5 INHIBITOR	
Maraviroc[18]	No adjustment recommendation (concentrations likely ↑); evidence of systemic allergic reaction (pruritic rash, eosinophilia or elevated IgE) may occur prior to hepatotoxicity; monitor closely for toxicity
INTEGRASE INHIBITOR	
Raltegravir	CP A or B: no adjustment; CP C: no recommendation

17. There are no hepatic dose adjustment recommendations for other NRTIs, or for T-20
18. Selzentry® (maraviroc) Product Information. Pfizer Labs, May 2010 www.viivhealthcare.com/products/~/media/Files/G/GlaxoSmithKline-Plc/Attachments/pdfs/products/selzentry_maraviroc_tablets_5May2010.pdf

Child-Pugh (CP) Score Calculation[19]

Score	1	2	3
Encephalopathy[20]	None	Grade 1 - 2	Grade 3 - 4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory to diuretics
Albumin	> 3.5 g/dL	2.8 - 3.5 g/dL	< 2.8 g/dL
Total Bilirubin or	< 2 mg/dL	2 - 3 mg/dL	> 3 mg/dL
Modified Total Bilirubin[21]	< 4 mg/dL	4 - 7 mg/dL	> 7 mg/dL
Prothrombin Time	< 4	4 - 6	> 6
or INR	< 1.7	1.7 - 2.3	> 2.3

19. Class A: Score 5-6; Class B: Score 7-9; Class C: Score > 9
20. Grade 1: mild confusion, anxiety, restlessness, fine tremor, slowed coordination; Grade 2: drowsiness, disorientation, asterixis; Grade 3: somnolent but rousable, marked confusion, incomprehensible speech, incontinent, hyperventilation; Grade 4: coma, decerebrate posturing, flaccidity
21. Modified Total Bilirubin used to score pts with Gilbert's Syndrome or taking IDV or ATV

ARV Components Not Recommended as Part of Initial Therapy

AGENT(S)	COMMENTS
ABC/AZT/3TC ± TDF (BI)	↓ virologic efficacy
ABC + (ddI or TDF) (BIII)	Insufficient data in ARV-naïve
d4T + 3TC (BI)	Lipoatrophy, peripheral neuropathy, symptomatic lactic acidosis, hepatic steatosis, and pancreatitis
ddI + (3TC or FTC) (BIII)	↓ virologic efficacy
DLV (BII)	↓ virologic efficacy; inconvenient dosing
ETR (BIII)	Insufficient data in ARV-naïve
FPV (unboosted) (BIII)	Less potent than RTV-boosted: may select for mutations that impact DRV
IDV (± RTV) (BIII)	Nephrolithiasis, meal/fluid requirements
NFV (BI)	↓ virologic efficacy; ↑ diarrhea
RTV as sole PI (BIII)	Pill burden; GI intolerance
TPV/r (BI)	↓ virologic efficacy
ENF (BIII)	Insufficient data in ARV-naïve

Please visit our website at:
www.FCAETC.org

Antiretroviral Regimens or Components Not Recommended at Any Time

REGIMENS/ COMPONENTS	COMMENTS
Monotherapy (AII)	Rapid development of resistance; inferior to ≥ 3 drugs
Dual-NNRTI (AI)	Adverse events and drug-drug interactions prevent benefit
Dual-NRTI (AI)	Rapid development of resistance; inferior to ≥ 3 drugs. May be considered for PEP
Triple NRTI (AI) exceptions: ABC/AZT/3TC (BI) and possibly TDF/ AZT/3TC (BII)	Consider exceptions when preferred/ alternative not feasible; ↑ early virologic non-response with ABC/TDF/3TC or TDF/ddI/3TC
d4T + AZT (AII)	Both thymidine analogs; antagonistic
d4T + ddI (AII)	Toxicities: pancreatitis, neuropathy, ↑ lactate. Fatalities (lactic acidosis w/ hepatic steatosis w/ or w/o pancreatitis) in pregnancy
ddI + TDF	↑ ddI levels and toxicity, ↑ virologic failure/ resistance, potential for immunologic nonresponse/CD4 ↓; consider altering regimen even if clinically stable on ddI/TDF containing regimen
FTC + 3TC (AIII)	Similar resistance profile; no benefit
EFV in 1st trimester or if pregnancy potential (AIII)	Teratogenic - use only if no other options and potential benefits > risks (BIII)
ETR + all unboosted PIs, ATV/r, FPV/r, or TPV/r (AIII)	Do not combine; standard dosing with DRV/r, LPV/r, or SQV/r
NVP in ARV-naïve ♀ w/ CD4 > 250 or ♂ w/ CD4 > 400 (BI)	↑ symptomatic hepatic events; use only if potential benefits > risks
ATV + IDV (AIII)	Potential for additive hyperbilirubinemia
TPV + PIs (± RTV)	Do not combine
Unboosted DRV, SQV, TPV (AII)	Should only be used with low-dose RTV

SPECIAL THANKS TO:

Colorado AIDS Education and Training Center
for medication images
(images are not actual size and colors may vary)

and

www.AIDSmeds.com
for phonetic pronunciations

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

***Class adverse effects:** Lactic acidosis with hepatic steatosis.*

Abacavir (Ziagen®, ABC)
(uh-BACK-ah-veer) H C

Dosage form: 300 mg tab, 20 mg/mL soln (240 mL/bottle)
Adult dose: 300 mg po bid or 600 mg po once daily
Note: Peform HLA-B*5701 test prior; only use if negative

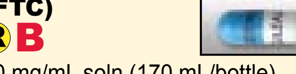
Important Points:
- Alcohol ↑ ABC levels 41%; potential for adverse effects
- Possible ↑ risk of CVD in pts with multiple CV risk factors
- AEs: HSR (2-9%), characterized by sign/symptom from ≥ 2 groups: G1: fever; G2: rash; G3: N/V/D, or abd pain; G4: malaise, fatigue, or achiness; G5: dyspnea, cough, or pharyngitis (onset 4-6 weeks) Discontinue drug promptly and **DO NOT RECHALLENGE!**

Didanosine (Videx EC®, ddI)
(dye-DAH-no-seen) R B

Dosage form: 125, 200, 250, ♦400 mg cap (Videx EC®, generic available)
Ped powder for soln 10 mg/mL (2 or 4 g bottle)
Adult dose[22]: ≥ 60 kg: 400 mg po once daily; < 60 kg: 250 mg po once daily; BID dosing preferred with oral soln (total daily dose divided into 2 doses)

22. ddI + (3TC or FTC) + ATV: ↓ virologic response; DHHS recommends ddI + (3TC or FTC) as an acceptable but inferior NRTI backbone to be used only with EFV

Important Points:
- Empty stomach, 30 min ac or 2 hr pc
- Swallow Videx EC® capsules whole; do not crush, chew or break open
- AEs: Peripheral neuropathy, pancreatitis, diarrhea, nausea, possible association with noncirrhotic portal hypertension

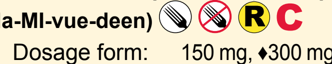


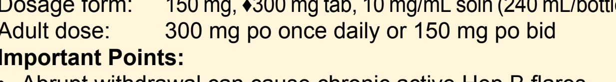
Emtricitabine (Emtriva®, FTC)
(em-trih-SIGH-ta-been) R B

Dosage form: 200 mg cap, 10 mg/mL soln (170 mL/bottle)
Adult dose: 200 mg cap or 240 mg (24 mL) soln po once daily

Important Points:
- Abrupt withdrawal can cause chronic active Hep B flares
- AEs: Generally well-tolerated, ↑ pigmentation of palms/soles (> in black and Hispanic pts)
- Refrigerate soln or room temp if used w/in 3 mos

Lamivudine (Epivir®, 3TC)
(la-MI-vue-deen) R C

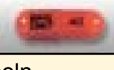




Dosage form: 150 mg, ♦300 mg tab, 10 mg/mL soln (240 mL/bottle)
Adult dose: 300 mg po once daily or 150 mg po bid

Important Points:
- Abrupt withdrawal can cause chronic active Hep B flares
- AEs: Generally well-tolerated

Stavudine (Zerit®, d4T)
(STA-vue-deen) R C

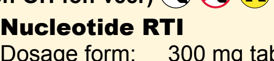


Dosage form: 15, 20, 30, ♦40 mg cap, 1 mg/mL soln (200 mL/bottle); generic available
Adult dose[23]: ≥ 60 kg: 40 mg po bid; < 60 kg: 30 mg po bid

23. WHO recommends 30 mg bid regardless of body weight

Important Points:
- AEs: Peripheral neuropathy, pancreatitis (esp w/ ddI), lipoatrophy, ↑ lipids, rapidly progressing ascending neuromuscular weakness, osteopenia (rare, multifactorial)
- Refrigerate soln and shake well

Tenofovir (Viread®, TDF)
(ten-OH-foh-veer) R B



Nucleotide RTI
Dosage form: 300 mg tab
Adult dose: 300 mg po once daily

Important Points:
- Interacts with ATV (see ATV for dosing)
- Abrupt withdrawal can cause chronic active Hep B flares
- AEs: Flatulence, headache, renal insufficiency, Fanconi Syndrome (rare), ↓ PO_4, osteopenia (rare, multifactorial)

Zidovudine (Retrovir®, AZT, ZDV)
(zye-DOE-vue-deen) R C

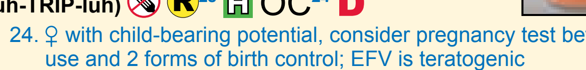
Dosage form: ♦300 mg tab, 100 mg cap, 10 mg/mL IV soln, 10 mg/mL syrup (240 mL/bottle)
Adult dose: 300 mg po bid or 200 mg po tid
Intrapartum: 2 mg/kg IV over 1 hr then 1 mg/kg/hr until cord clamping

Important Points:
- AEs: Headache, nausea, ↑ pigmentation skin/nails, ↓ H/H, ↓ WBC, myopathy

Combination Products:
(see individual drug components for important points)

Atripla®
(uh-TRIP-luh) R[25] H OC[24] D

24. ♀ with child-bearing potential, consider pregnancy test before use and 2 forms of birth control; EFV is teratogenic



Each tablet contains: 600 mg EFV + 200 mg FTC + 300 mg TDF
Adult dose: 1 tab po once daily at bedtime

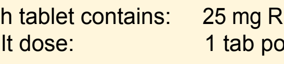
Combivir®
(COM-bih-veer) R[25] C

Each tablet contains: 300 mg AZT + 150 mg 3TC
Adult dose: 1 tab po bid

Complera™
(com-PLAIR-uh) R[25] H B

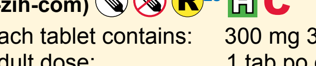
Each tablet contains: 25 mg RPV + 200 mg FTC + 300 mg TDF
Adult dose: 1 tab po once daily

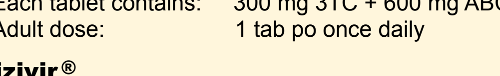
Epzicom®
(EP-zih-com) R[25] H C



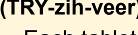
Each tablet contains: 300 mg 3TC + 600 mg ABC
Adult dose: 1 tab po once daily

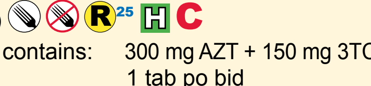
Trizivir®
(TRY-zih-veer) R[25] H C



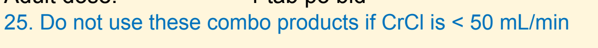


Each tablet contains: 300 mg AZT + 150 mg 3TC + 300 mg ABC
Adult dose: 1 tab po bid

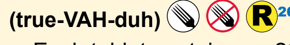




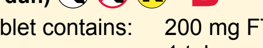
25. Do not use these combo products if CrCl is < 50 mL/min



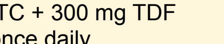
Truvada®
(true-VAH-duh) R[26] B



Each tablet contains: 200 mg FTC + 300 mg TDF
Adult dose: 1 tab po once daily



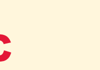
26. Do not use this combo product if CrCl is < 30 mL/min



NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

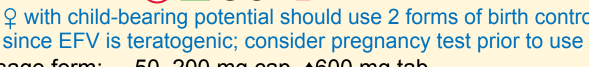
***Class adverse effects:** rash (rarely Stevens-Johnson Syndrome), ↑ LFTs, many drug interactions.*

Delavirdine (Rescriptor®, DLV)
(deh-LAH-ver-deen) H ↑OC C



Rarely, if ever, used

Efavirenz (Sustiva®, EFV)
(eh-FAH-vih-rehnz) H OC[27] D

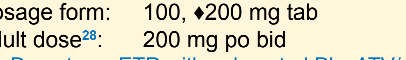


27. ♀ with child-bearing potential should use 2 forms of birth control since EFV is teratogenic; consider pregnancy test prior to use

Dosage form: 50, 200 mg cap, ♦600 mg tab
Adult dose: 600 mg po once daily at bedtime

Important Points:
- Take at bedtime w/o food to ↓ CNS side effects
- False + cannabinoid or benzodiazepine test (usually on screening, confirmatory test should be negative)
- Use with caution in pts with unstable psych disorder
- AEs: Drowsinesss, dizziness, insomnia, abnormal dreaming, agitation (generally resolves in 2-4 weeks), hallucinations (rare), ↑ lipids

Etravirine (Intelence®, ETR)
(eh-truh-VIGH-reen) H ↑OC B

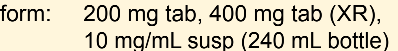


Dosage form: 100, ♦200 mg tab
Adult dose[28]: 200 mg po bid

28. Do not use ETR with unboosted PIs, ATV/r, FPV/r, TPV/r. Standard dosing with DRV/r, LPV/r, SQV/r.

Important Points:
- Take following a meal
- May disperse tabs in water, stir well, drink immediately and rinse glass several times and drink rinse
- AEs: Nausea, hypersensitivity reactions with rash, constitutional findings, hepatic failure have been reported

Nevirapine (Viramune®, Viramune XR®, NVP)
(nah-VAIR-ah-peen) H ↓OC B



Dosage form: 200 mg tab, 400 mg tab (XR), 10 mg/mL susp (240 mL bottle)
Adult dose[29]: 200 mg po once daily x 14d, then [200 mg po bid or 400 mg (XR) po once daily]

29. If NVP discontinued ≥ 7d, restart at lower dose x 14d; pts taking NVP immediate release (200 mg bid or 400 mg once daily) can switch to XR 400 mg once daily without 200 mg daily lead-in dosing; If mild rash occurs and hepatotoxicity ruled out, can continue 200 mg daily lead-in dose for up to 28d. See Viramune XR® Package Insert (March 2011)

Important Points:
- 400 mg XR tabs are extended-release and should not be crushed, chewed, or broken
- AEs: Rash - mild to severe, usually within 1st 6 wks, D/C if severe; ↑ LFTs (Monitor LFTs - baseline, 2 wks, then q4wks x 1st 3 mos, then q3mos); Hepatotoxicity often rash-associated, check LFTs in any pt with rash; ♀ and ♂ w/ pre-ART CD4 > 250 and > 400, respectively and pts with chronic active hep B or C co-infection are at ↑ risk for ↑ LFTs

Rilpivirine (Edurant™, RPV)
(ril-pih-VIGH-reen) R H B

Dosage form: 25 mg tab
Adult dose[30]: 25 mg once daily with food

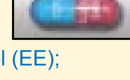
30. Approved for use in ARV-naïve pts only (Use in pts with VL > 100,000 copies/mL associated with more failures and resistance)

Important Points:
- Take with food
- Interacts with acid-reducing agents
  - Proton pump inhibitors (e.g. omeprazole, lansoprazole): Contraindicated, do not combine
  - H2-receptor blockers (e.g. famotidine, ranitidine) should be taken at least 12 hrs before or 4 hrs after RPV
  - Antacids (e.g. aluminum or magnesium hydroxide, calcium carbonate) should be taken at least 2 hrs before or 4 hrs after RPV
- Caution with drugs that prolong the QT_c interval
- AEs: Depression, insomnia, headache, rash

PROTEASE INHIBITORS (PIs)

Class adverse effects:** ↑ glucose, ↑ lipids (less with ATV), lipodystrophy, ↑ LFTs, ↑ bleeding in hemophiliacs. All undergo hepatic metabolism mostly CYP3A4 - **Many drug interactions!

Atazanavir (Reyataz®, ATV)
(ah-ta-ZA-na-veer) R H OC[31] B



31. ATV/r: OC dose minimum 35 mcg ethinyl estradiol (EE); ATV: OC dose maximum 30 mcg EE; OCs with < 25 mcg EE, progestins other than norethindrone or norgestimate; other hormonal contraceptives (e.g. patch, ring, injectable) not studied, alternative contraception recommended

Dosage form: 100, 150, 200, ♦300 mg cap
Adult dose: 400 mg po once daily (ARV-naïve only)
300 mg + RTV 100 mg po once daily (naïve, exp, or w/TDF)
Combining with NNRTIs: Do not use ATV (± RTV) with ETR, NVP, or EFV (in ARV-exp pts); can use ATV/r with ↑ dose with EFV but not a DHHS recommended regimen in ARV-naïve pts

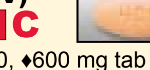
ACID-REDUCING AGENTS	TREATMENT-NAÏVE	TREATMENT-EXPERIENCED
Antacids or buffered medications	• ATV or ATV/r: Give **≥ 2 hrs before or 1 hr after** antacid	• ATV/r: Give **≥ 2 hrs before or 1 hr after** antacid
H2 Receptor Antagonists (H2RAs)	• ATV: Give **≥ 2 hrs before or 10 hrs after** H2RA. Max dose of famotidine 20 mg bid (not to exceed 20 mg in single dose) [or equivalent] • ATV/r: Give simultaneously **with or ≥ 10 hrs after** H2RA. Max dose of famotidine 40 mg bid [or equivalent]	• ATV/r: Give simultaneously **with or ≥ 10 hrs after** H2RA. Max dose of famotidine 20 mg bid [or equivalent] • ATV/r (400/100 mg) with TDF: Give simultaneously **with or ≥ 10 hrs after** H2RA. Max dose of famotidine 20 mg bid [or equivalent]
PPIs	• ATV: **not recommended** • ATV/r: Max dose of omeprazole 20 mg once daily [or equivalent] **taken ≥ 12 hrs prior to** ATV/r	• ATV/r: **not recommended**

(PIs)(Continued)

Atazanavir (Reyataz®, ATV) (Continued)

Important Points:
- AEs: ↑ unconjugated bili (common), jaundice or scleral icterus (less common); less adverse effects on lipid profile; prolonged PR interval, asymptomatic 1st degree AV block (rare); nephrolithiasis (rare)

Darunavir (Prezista®, DRV)
(da-ROO-nuh-veer) H ↓OC C



Dosage form: 75, 150, ♦400, ♦600 mg tab
Adult dose: 800 mg + RTV 100 mg po once daily [ARV-naïve or exp if no DRV mutations (V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, L89V)][32]
600 mg + RTV 100 mg po bid (ARV-naïve or exp)
Combining with NNRTIs: DRV/r standard dosing with ETR and NVP; with EFV, standard DRV/r dose but monitor closely (DRV C_{min} ↓ 31% and EFV AUC ↑ 21%)

32. www.prezista.com/sites/default/files/pdf/us_package_insert.pdf

Important Points:
- Take with food
- AEs: Rash 10%, abd pain, headache, hepatotoxicity, caution with sulfa allergy (not contraindicated)

Fosamprenavir (Lexiva®, FPV)
(foss-am-PREH-nah-veer) [33] H OC C

33. Suspension: adults without food; peds with food

Prodrug of amprenavir

Dosage form: 700 mg tab, 50 mg/mL susp (225 mL/bottle)
Adult dose: 1400 mg po bid or
1400 mg + RTV 100-200 mg po once daily (ARV-naïve only)
700 mg + RTV 100 mg po bid (PI-exp or naïve)
Combining with NNRTIs: With EFV (standard dose), use FPV 1400 mg + RTV 300 mg once daily or FPV 700 mg + RTV 100 mg bid; With ETR do not use FPV (± RTV) ; With NVP (standard dose), use FPV 700 mg + RTV 100 mg bid

Important Points:
- OCs ↓ FPV levels; do not coadminister
- Acid-reducing Agents: PPI coadministration allowed; H2RA use with caution due to ↓ APV levels; separate administration
- AEs: Skin rash (19%), N/V/D, caution with sulfa allergy (not contraindicated)
- Refrigeration of susp not required but may improve taste, shake well before each use

Indinavir (Crixivan®, IDV)
(in-DIH-nuh-veer) [34] H C

34. If given without RTV (rarely if ever done), take 1 hr ac or 2 hr pc or with low fat/protein snack.

Dosage form: 100, 200, 333, ♦400 mg cap
Adult dose: 800 mg + RTV 100-200 mg po bid
Combining with NNRTIs: With EFV (standard dose), use IDV 1000 mg q8h or IDV 800 mg + RTV 100-200 mg bid, do not use IDV with ETR (no data with IDV/RTV)

Important Points:
- Drink 6 eight oz glasses fluid each day (water preferred)
- AEs: Nephrolithiasis, ↑ unconjugated bili
- Store in original container with desiccant

Lopinavir/Ritonavir (Kaletra®, KAL, LPV/r)
(lo-PIN-uh-veer/rih-TAH-nuh-veer) H ↓OC C

Dosage form: ♦200/50 mg, 100/25 mg tab
400/100 mg per 5 mL soln (160 mL/bottle)
Adult dose[35]: 2 tabs po bid (PI-naïve or exp) or 4 tabs po once daily (PI-naïve or exp with ≤ 3 significant mutations[36])

35. Once daily dosing should not be used in pregnant women
36. Dose LPV/r bid in pts with ≥ 3 of the following PI mutations: L10F/I/R/V, K20M/N/R, L24I, L33F, M36I, I47V, G48V, I54L/T/V, V82A/C/F/S/T, and I84

Combining with NNRTIs: With EFV or NVP (standard dosing), ↑ LPV to 500/125 mg (two 200/50 mg and one 100/25 mg) tabs bid or 533/133 mg soln bid; with ETR, use standard dosing of each

Important Points:
- Swallow tablets whole; cannot be chewed, broken, or crushed
- May take tablets without food, soln should be taken with food
- Oral soln contains 42% alcohol
- AEs: GI intolerance (N/V/D), asthenia, prolonged PR, rare cases of 2nd/3rd degree AV block; prolonged QT interval, rare cases of torsade de pointes (causality not established)
- Do not take tabs out of container for > 2 wks especially in areas of ↑ humidity
- Refrigerate soln (stable until label date) or store at room temp (max 25°C/77°F) for up to 60 days

Nelfinavir (Viracept®, NFV)
(nell-FIH-nuh-veer) H ↓OC B

Dosage form: 250 mg, ♦625 mg tab, 50 mg/g oral powder (144 g/bottle)
Adult dose: 1250 mg po bid, 750 mg po tid
Combining with NNRTIs: With EFV or NVP (standard dosing) using NFV standard dose; with ETR, do not use NFV

Important Points:
- Take with meal or snack
- Do not use PPIs with NFV (based on data indicating omeprazole → ↓ NFV levels)
- AEs: Diarrhea (can use OTC loperamide to treat diarrhea; calcium carbonate 1-2 tabs with each dose may lessen diarrhea)

Ritonavir (Norvir®, RTV)
(rih-TAH-nuh-veer)

Dosage form: ♦100 mg tab, ♦100 mg cap, 80 mg/mL soln (240 mL/bottle)
Used only at low doses with other PIs (see primary PI for dosing and adverse effects)

Important Points:
- Store tabs at room temp; refrigerate caps (stable until label date), can store caps at room temp (max 25°C/77°F) for up to 30 days; do not refrigerate soln

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(PIs)(Continued)

Saquinavir (Invirase®-HGC or tab, SQV)
(sa-KWIH-nuh-veer) H ↓OC B

Dosage form: 200 mg hard gel cap or ♦500 mg tab
Adult dose: 1000 mg + RTV 100 mg po bid
Combining with NNRTIs: With EFV, ETR, or NVP (standard dosing), use SQV standard dosing (1000 mg + RTV 100 mg po bid)

Important Points:
- Take within 2 hrs of a meal
- Grapefruit juice ↑ SQV level, garlic supplements ↓ SQV level (potential interaction with all PIs/NNRTIs)
- Precaution: ↑ QT interval in healthy volunteers; do not use in pts with QT prolongation, preexisting conduction system disease, ischemic heart disease, cardiomyopathy, or underlying structural heart disease; do not use in pts taking Class IA (e.g. quinidine) or Class III (e.g. amiodarone) antiarrhythmics.
- AEs: GI intolerance (nausea, diarrhea, abdominal pain, dyspepsia)

Tipranavir (Aptivus®, TPV)
(ti-PRAN-a-veer) H ↓OC C

Dosage form: 250 mg cap
100 mg/mL soln (95 mL/bottle)
Adult dose: 500 mg + RTV 200 mg po bid
Combining with NNRTIs: With EFV or NVP (standard dosing) use TPV/RTV standard dose; with ETR, do not use TPV/RTV

Important Points:
- Antacids ↓ TPV; take TPV 2 hrs before or 1 hr after antacids
- AEs: Hepatotoxicity-monitor LFTs closely; Rash 8% ♂, 10% ♀, > in women taking estrogen; N/V/D; caution in pts. at risk for ↑ bleeding (intracranial hemorrhage reported rarely); caution with sulfa allergy (not contraindicated)
- Keep caps in refrigerator (stable until label date) or store at room temp (max 25°C/77°F) for up to 60 days; Oral soln should be kept at room temp for up to 60 days-do not refrigerate or freeze soln

ENTRY INHIBITORS

Fusion Inhibitor

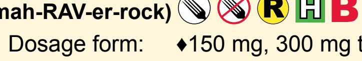
Enfuvirtide (Fuzeon®, T-20, ENF)
(en-FEW-ver-tide) B

Dosage form: Powder for SC inj, mix with 1.1 mL sterile water for final conc 90 mg/mL
Adult dose: 90 mg SC bid

Important Points:
- Must instruct pt on reconstitution and administration techniques
- Administer SC in upper arm, upper leg, or stomach (do not inject into naval area, scar tissue, bruise, mole, or area with injection site reaction)
- Rotate injection sites
- AEs: Injection site reactions (mild/moderate, can be severe), itching, swelling, redness, pain/tenderness, induration, nodules, cysts; ↑ bacterial pneumonia; HSR (< 1%) - sxs. include rash, fever, N/V, chills, rigors, ↓ BP, or ↑ LFTs **DO NOT RECHALLENGE!**
- Store unopened vials at room temp (max 25°C/77°F). Reconstituted soln should be refrigerated and used within 24 hrs

CCR5 Inhibitor

Maraviroc (Selzentry®, MVC)
(mah-RAV-er-rock) R H B



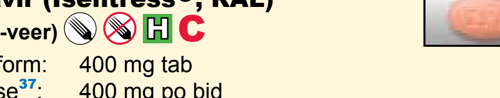
Dosage form: ♦150 mg, 300 mg tab
Note: Do not use in pts with dual/mixed tropic or CXCR4-tropic virus. Perform tropism assay prior to use.

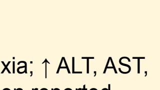
CONCOMITANT MEDICATIONS	ADULT DOSE
CYP3A inhibitors (w/ or w/o a CYP3A inducer): • protease inhibitors (except TPV/r), DLV • ketoconazole, itraconazole, clarithromycin • other strong CYP3A inhibitors (e.g., nefazadone, telithromycin)	150 mg po bid
CYP3A inducers (w/o a strong CYP3A inhibitor) including: • EFV, ETR • rifampin • carbamazepine, phenobarbital,and phenytoin	600 mg po bid
Other concomitant medications, including: TPV/r, NVP, all NRTIs, T-20, RAL	300 mg po bid

Important Points:
- AEs: Hepatotoxicity: may be preceded by a systemic allergic reaction (↑ LFTs, pruritic rash, ↑ eos, other systemic symptoms), dizziness/postural hypotension, cough, pyrexia, URI, rash, musculoskeletal symptoms, abd pain, ↑ CV events (MI, ischemic events)

INTEGRASE INHIBITOR

Raltegravir (Isentress®, RAL)
(ral-TEG-ra-veer) H C





Dosage form: 400 mg tab
Adult dose[37]: 400 mg po bid

Important Points:
- AEs: Diarrhea, nausea, headache, and pyrexia; ↑ ALT, AST, CPK; myopathy and rhabdomyolysis have been reported

37. 800 mg po bid if used with rifampin

♦ = dosage in photo, when multiple dosage forms are available
= Take with food = Take without food
= Take with or without food
H = Hepatic Adjustment (See table)
R = Renal Adjustment (See table)
B, C, D = Pregnancy Category
↑OC = ↑ Combination Oral Contraceptive Level
↓OC = ↓ Combination Oral Contraceptive Level; Use alternate/additional form of birth control
OC = Do not coadminister with Combination Oral Contraceptive

NOTE: Medication images are NOT actual size, and colors may vary.