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ARV Therapy in Pediatrics

May 2013

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Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. July 31, 2012; Available at *http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf*. Accessed August 3, 2012 [pp 138-139, tables 8 & 9]

Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. November 05, 2012. Available at *http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf*. Accessed November 27, 2012

Choice of Antiretroviral Agents for Treatment of Established HIV Infection[1,2,3]

Preferred Regimens	
Children ≥ 42 wks postmenstrual age, > 14 days postnatal age and < 3 yrs	2 NRTIs + lopinavir/ritonavir
≥ 3 yrs	2 NRTIs + efavirenz 2 NRTIs + lopinavir/ritonavir
≥ 6 yrs	2 NRTIs + atazanavir + low dose RTV 2 NRTIs + efavirenz 2 NRTIs + lopinavir/ritonavir
Alternative Regimens	
Children ≥ 6 mos	2 NRTIs + FPV plus low-dose RTV (FPV to be given only for infants >38 wks gestation and >28 days postnatal age)
≥ 3 yrs	2 NRTIs + DRV plus low-dose RTV
Children all ages	2 NRTIs + NVP
Regimens for Use in Special Circumstances	
2 NRTIs + atazanavir unboosted (for tx-naïve adolescents ≥ 13 yrs and ≥ 39 kg) 2 NRTIs + fosamprenavir unboosted (≥ 2 yrs) 2 NRTIs + nelfinavir (≥ 2 yrs) Zidovudine + lamivudine + abacavir	
Dual NRTI Combination Recommendations	
Preferred	Abacavir + (lamivudine or emtricitabine) (≥ 3 mos) Tenofovir + (lamivudine or emtricitabine) (Tanner Stage IV or V)[4] Zidovudine + (lamivudine or emtricitabine)
Alternative	Didanosine + (lamivudine or emtricitabine) Tenofovir + (lamivudine or emtricitabine) (Tanner Stage III)[4] Zidovudine + abacavir Zidovudine + didanosine
Use in Special Circumstances	Tenofovir + (lamivudine or emtricitabine) (prepubertal children aged ≥ 2 yrs and adolescents, Tanner stage I or II)

1. Adolescents in early puberty (Tanner Stage I-II) should be dosed using the pediatric schedules, whereas older children (Tanner Stage IV) should be dosed using adult schedules. Adolescents who are in their growth spurt (Tanner III females and Tanner IV males) should be monitored closely for efficacy. Toxicity and therapeutic drug monitoring should be considered if there are concerns.
2. Resistance testing is recommended for all ARV-naïve children prior to beginning ARV therapy and prior to making a change in the ARV regimen
3. Perform HLA B*5701 testing prior to starting abacavir
4. Pediatric dosages for TDF (2 yrs to < 18 yrs) are now available in package insert

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Not Recommended/Insufficient Data to Recommend for Initial Therapy

Initial Regimens
TDF-containing regimens for children aged < 2 yrs
Dual (full-dose) PI regimens; Triple-class regimens, including NRTI + NNRTI + PI; Full-dose RTV **or** use of RTV as the sole PI
Regimens containing ETV, EFV (< 3 yrs), NFV (< 2 yrs), TPV, SQV, IDV, MVC, RAL, Rilpivirine, T-20, **or** EVG
Unboosted ATV-containing regimens in children < 13 yrs and/or body weight (wt) < 39 kg; Unboosted DRV-containing regimens; Once-daily dosing of boosted DRV in children aged < 12 yrs; Once daily dosing of LPV/r or boosted/unboosted FPV
Triple-NRTI regimens other than ABC + ZDV + 3TC; Regimens with dual-NRTI backbones with ABC + ddI, ABC + TDF and ddI + TDF; 4 drug regimens with 3 NRTIs + NNRTI

Antiretroviral Regimens or Components Not Recommended at Any Time

Regimens	Comments
Monotherapy	Zidovudine may be considered for use to prevent perinatal transmission if VL controlled < 1000 copies/mL; ZDV prophylaxis is the standard regimen (1st 6 wks) for HIV exposed infants
2-agent drug combinations	Resistance develops rapidly. Inferior to ≥ 3 drugs. If virologic goals achieved, some clinicians may choose to continue
Dual-NNRTI	Enhanced toxicity
ABC + TDF + 3TC (or FTC)	High rate of early virologic non-response seen in ARV-naïve pts
TDF + ddI + 3TC (or FTC)	High rate of early virologic non-response seen in ARV-naïve pts
d4T + ZDV	Both thymidine analogs; antagonistic
d4T + ddI	Increased risk of toxicities; lactic acidosis and pancreatitis; may consider when no other options and potential benefits outweigh risks. Fatalities reported when used in pregnancy
FTC + 3TC	Similar resistance profile; no potential benefit
ddI + TDF	Increased ddI concentrations and serious toxicities including pancreatitis and lactic acidosis
ETR + unboosted PI	ETR may induce metabolism of PIs. Reduce drug exposure
ETR + boosted ATV or FPV	May induce metabolism of PIs. Appropriate PI dose not established
ETR + boosted TPV	Boosted TPV greatly reduces ETR concentrations
amprenavir oral soln	Contains large amounts of propylene glycol; contraindicated in pregnancy, children < 4 yrs, renal or hepatic failure, and those taking metronidazole or disulfiram, or ritonavir oral soln
amprenavir oral soln + ritonavir oral soln	Should not be combined due to propylene glycol in amprenavir soln/alcohol in ritonavir soln
amprenavir + fosamprenavir	Amprenavir is active in both drugs; no benefit
atazanavir + indinavir	Potential for additive hyperbilirubinemia
saquinavir hard gel cap (Invirase®) as single PI	Must combine with other PIs such as ritonavir or lopinavir/ritonavir due to poor bioavailability
EFV in 1st trimester of pregnancy or in women with pregnancy potential	Teratogenic in monkeys-consider use only if no other options available and potential benefits outweigh risks
Unboosted saquinavir, darunavir, or tipranavir	Poor oral bioavailability and inferior virologic activity if unboosted
nevirapine initiation in girls with CD4 > 250 cells/mm³ or in boys with CD4 > 400 cells/mm³	Higher incidence of symptomatic hepatic events; use only if potential benefits outweigh risks

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

Class adverse effects: *Lactic acidosis with hepatic steatosis*

Abacavir (Ziagen®, ABC) G ★ H

Dosage form: 300 mg tab (scored), 20 mg/mL soln (240 mL/bottle)
Neonates/Infants: Not approved in children < 3 mos
Pediatric dose:
(≥ 3 mos) 8 mg/kg oral soln po bid (max dose 300 mg bid)

Pediatric Twice Daily Dose (Tablets)	
Weight (kg)	**Tablets**
14-21	½ tab bid
> 21 to < 30	½ tab am and 1 tab pm
≥ 30	1 tab bid
In clinically stable pts, consider once daily dosing; 16 mg/kg/dose (max dose 600 mg daily); possible increased risk of MI in adults, no data in children	

Adolescents/Adults:
(≥ 16 yrs) 300 mg po bid **or** 600 mg po once daily
Important Points:
- Instruct pt to not stop and restart medication
- Does not inhibit and is not metabolized by Cytochrome P450 (CYP450) enzymes
- Alcohol ↑ ABC levels 41%; potential for adverse effects

NOTE: Perform HLA B*5701 test prior to treatment with abacavir. Only use if test is negative.

Approximately 5% of adults and children receiving ABC develop a potentially fatal hypersensitivity reaction. Usually characterized by > 2 of the following groups: 1) fever; 2) rash; 3) gastrointestinal (nausea, vomiting, diarrhea, or abdominal pain); 4) constitutional (malaise, fatigue, or achiness); and 5) respiratory (dyspnea, cough, or pharyngitis). Generally occurs in the 1st 6 wks of therapy and has occurred after a single dose. Stop ABC and do not restart.

Didanosine (Videx® EC, ddI) G ★

Dosage form: Pediatric powder for soln (2 or 4 g bottle), reconstituted with antacid = 10 mg/mL
Videx® EC cap 125, 200, 250, 400 mg
(Available in generic except for 125 mg)
Neonates/Infants: (Body Surface Area [BSA] = m^2)
(2 wks-3 mos) 50 mg/m^2/dose every 12 hrs
(≥ 3 mos to ≤ 8 mos) 100 mg/m^2/dose every 12 hrs

Pediatric BSA Dose (> 8 mos)	
120 mg/m^2 po every 12 hrs; range: 90-150 mg/m^2/dose po every 12 hrs (max 200 mg/dose bid)	
Pediatric Dose (6 yrs-18 yrs and ≥ 20 kg)	
Weight (kg)	**EC or Generic Caps** (once daily)
20 to < 25	200 mg
≥ 25 to < 60	250 mg
≥ 60	400 mg
Tx-naïve children age 3 yrs-21 yrs	
240 mg/m^2 BSA po once daily (oral soln or capsules)	

Adolescents/Adults: < 60 kg: 125 mg oral soln po bid **or** 250 mg EC
≥ 60 kg: 200 mg oral soln po bid **or** 400 mg EC
with Tenofovir: < 60 kg and CrCl ≥ 60 mL/min: 200 mg po once daily EC once daily (limited data)
≥ 60 kg and CrCl ≥ 60 mL/min: 250 mg po once daily EC once daily (limited data)
Important Points:
- Admin ddI on an empty stomach. To improve adherence, some practitioners admin ddI without regard to timing of meals
- Lactic acidosis risk factors: women, obesity, prolonged NRTI exposure
- Oral soln contains antacids

Didanosine (Continued)

- Refrigerate soln, stable for 30 days, shake well
- AEs: diarrhea, abdominal pain, nausea, vomiting, peripheral neuropathy, electrolyte abnormalities, hyperuricemia, hepatic toxicity and failure, retinal depigmentation, optic neuritis, lactic acidosis, severe hepatic steatosis, and insulin resistance/DM. Potential association with noncirrhotic portal hypertension, increased LFTs/ALK phos, and thrombocytopenia

Fatal and nonfatal pancreatitis have occurred with didanosine. Fatal lactic acidosis reported in pregnant women receiving didanosine and stavudine in combination.

Emtricitabine (Emtriva®, FTC) ★ R

Dosage form: 200 mg cap, 10 mg/mL oral soln (170 mL/bottle)
Neonates/Infants:
(< 3 mos) 3 mg/kg oral soln once daily
Pediatric dose: < 33 kg: 6 mg/kg oral soln once daily (max dose 240 mg)
(≥ 3 mos to 17 yrs) > 33 kg: 200 mg po once daily
Adolescents/Adults:
(≥ 18 yrs) 200 mg cap or 240 mg (24 mL soln) po once daily
Important Points:
- Refrigerate oral soln, OK at room temp if used within 3 mos
- AEs: headache, insomnia, diarrhea, nausea, rash, hyperpigmentation of palms and soles in up to 6% of non-white pts, neutropenia, lactic acidosis, and severe hepatomegaly with steatosis (all rare). No CYP450 interactions

Exacerbations of HBV have been seen in co-infected pts who D/C FTC Screen pt for HBV before use. Severe exacerbation of HBV can occur when medication is D/C'd.

Lamivudine (Epivir®, 3TC) ★ R

Dosage form: 10 mg/mL soln (240 mL/bottle), 5 mg/mL (Epivir-HBV®), 100 mg (Epivir-HBV®), 150 (scored), 300 mg tab

Age Groups	Weight (kg)	Dosing	Max dose (mg)
Neonates/Infants: (< 4 wks)	-	2 mg/kg oral soln bid	-
Pediatric dose: (≥ 4 wks)	-	4 mg/kg/dose po bid	150 bid
	14-21	75 mg (1/2 tab) po bid	total 150 per day
	> 21 to < 30	75 mg am + 150 mg po pm	total 225 per day
	≥ 30	150 mg po bid	total 300 per day
Adolescents/Adults:	< 50	4 mg/kg/dose po bid	150 bid
	≥ 50	150 mg po bid **or** 300 mg po once daily	-

Important Points:
- Expert Panel supports consideration for switching from bid to once daily dosing (8-10 mg/kg, max 300 mg) in children ≥ 3 yrs of age, and clinically stable, with undetectable viral load and stable CD4 count.
- AEs: headache, fatigue, nausea, decreased appetite, diarrhea, skin rash, abdominal pain, anemia, and decreased neutrophil count. Less common: Peripheral neuropathy, pancreatitis, lipodystrophy/lipoatrophy.

Exacerbations of HBV have been seen in co-infected pts who D/C 3TC. Screen pt for HBV before use. Severe exacerbation of HBV can occur when medication is D/C'd.

Stavudine (Zerit®, d4T) G ★ R

Dosage form: 15, 20, 30, 40 mg cap, 1 mg/mL soln (200 mL/bottle)
Neonates:
(birth-13 days) 0.5 mg/kg/dose po bid
Pediatric dose:
(14 days and < 30 kg) 1 mg/kg/dose po bid
Adolescents/Adults:
(≥ 30 kg) 30 mg po bid
Important Points:
- Refrigerate soln and shake well, discard after 30 days if reconstituted
- Fatal lactic acidosis has been reported in pregnant women who received the combination of stavudine and didanosine.
- Fatal and nonfatal pancreatitis have occurred when ZERIT® was part of a combination regimen that included didanosine.
- AEs: mitochondrial toxicity, headache, GI disturbances, skin rash, peripheral neuropathy, pancreatitis, lactic acidosis/severe hepatomegaly with hepatic steatosis, lipoatrophy/lipodystrophy, hyperlipidemia, insulin resistance/DM; Rare: increased liver enzymes, progressive ascending motor weakness

When combined with didanosine, same Black Box Warnings.

Tenofovir (Viread®, TDF) B R

Dosage form: 150, 200, 250, 300 mg tabs,
40 mg per 1 g/1 scoop powder formulation
Neonates/Infants: Safety and efficacy not established in children < 2 yrs of age
Pediatric dose: (use with caution)
(≥ 2 yrs to < 12 yrs) 8 mg/kg (max 300 mg) po once daily

Weight (kg)	Scoops of Powder[8] (once daily)	Tablets (once daily)
10 to < 12	2	-
12 to < 14	2.5	-
14 to < 17	3	-
17 to < 19	3.5	150 mg
19 to < 22	4	150 mg
22 to < 24	4.5	200 mg
24 to < 27	5	200 mg
27 to < 29	5.5	See table below
29 to < 32	6	250 mg
32 to < 34	6.5	250 mg
34 to < 35	7	250 mg
≥ 35	7.5	300 mg

Dosing Recommendations for Pediatric Patients ≥ 2 yrs and ≥ 17 kg Using Tenofovir Tablets	
Weight (kg)	**Tablets** (once daily)
17 to < 22	150 mg
22 to < 28	200 mg
28 to < 35	250 mg
≥ 35	300 mg

8. Powder formulations (use supplied scoop) should be mixed with soft food (e.g., applesauce, yogurt). Ingest immediately to avoid bitter taste. Do not add liquid since powder will float to top.

Adolescents/Adults:
(≥ 12 yrs and ≥ 35 kg) 300 mg po once daily
Important Points:
- Some experts recommend monitoring for proteinuria and glycosuria every 6-12 mos.
- Drugs which reduce renal function or compete for active tubular secretion may change the tenofovir concentration and/or other renally eliminated drugs- dosage adjustment is needed
- Interacts with ddI (See ddI for dosing) and ATV (See ATV for dosing)
- Adjust dosage in pts with renal insufficiency and CrCl < 50 mL/min
- AEs: nausea, diarrhea, vomiting, flatulence, headache, asthenia, renal insufficiency, proximal renal tubular dysfunction that may include Fanconi syndrome. Concerns about decreased bone mineral density (BMD), pre-pubertal pts (Tanner stages I and II) are at higher risk

Exacerbations of HBV have been seen in co-infected pts who D/C TDF. Screen pt for HBV before use. Severe exacerbation of HBV can occur when medication is D/C'd.

Zidovudine (Retrovir®, AZT, ZDV) G ★ R

Dosage form: 300 mg tab, 100 mg cap;
10 mg/mL syrup (240 mL/bottle); 10 mg/mL injectable

Infant ARV Prophylaxis or Treatment			
Age Groups	**Gestational Age**	**Dosing** (start as soon after birth as possible, preferably within 6-12 hrs of birth, 6 wks total)	
Neonates/ Term Infants	≥ 35 wks	4 mg/kg/dose body wt po bid	3 mg/kg/dose IV every 12 hrs (change to oral dosing when possible)
Premature Infants	< 35 to ≥ 30 wks	2 mg/kg/dose po every 12 hrs for 2 wks, then advanced to 3 mg/kg/dose po every 12 hrs at ≥ 15 days of age	1.5 mg/kg/dose IV every 12 hrs for 2 wks, then advanced to 2.3 mg/kg/dose IV every 12 hrs at ≥ 15 days of age
	< 30 wks	2 mg/kg/dose po every 12 hrs for 4 wks, then advanced to 3 mg/kg/dose po every 12 hrs after age 4 wks	1.5 mg/kg/dose IV every 12 hrs for 4 wks, then advanced to 2.3 mg/kg/dose IV every 12 hrs after age 4 wks

Zidovudine (Continued)

Pediatric dose: 180-240 mg/m^2 po every 12 hrs
or 160 mg/m^2 every 8 hrs

Pediatric Dose (6 wks to < 18 yrs)	
Weight (kg)	**Dosing** (twice-daily)
4 to < 9	12 mg/kg
9 to < 30	9 mg/kg
≥ 30	300 mg

Adolescents/Adults:
(≥ 18 yrs) 300 mg po bid
Important Points:
- AEs: headache, nausea, vomiting, insomnia, asthenia, bone marrow suppression, macrocytic anemia, neutropenia, fatigue, myositis, liver toxicity, lactic acidosis/severe hepatomegaly with steatosis, nail pigmentation, insulin resistance/DM, lipoatrophy, hyperlipidemia. Increased risk of hypospadias after 1st trimester exposure observed in 1 cohort study

May be associated with hematologic toxicities, including granulocytopenia, and severe anemia. Prolonged use may be associated with myopathy.

Combination Products:

Atripla® R* H
Each tab contains: FTC 200 mg + TDF 300 mg + EFV 600 mg
Adolescent dose:
(≥ 12 yrs and ≥ to 40 kg) 1 tablet once daily
Adult dose: 1 tab po once daily at bedtime

Combivir® R*
Each tab contains: ZDV 300 mg + 3TC 150 mg
Adolescent dose:
(≥ 30 kg) 1 tablet twice daily
Adult dose: 1 tab po bid

Complera® R*
Each tab contains: RPV 25 mg + FTC 200 mg + TDF 300 mg
Adult dose: 1 tab po once daily

Epzicom® R* H
Each tab contains: 3TC 300 mg + ABC 600 mg
Adolescent dose:
(≥ 16 yrs and > 50 kg) 1 tab po once daily
Adult dose: 1 tab po once daily

Stribild™ R*B TB
Each tab contains: FTC 200 mg + TDF 300 mg + Elvitegravir 150 mg + Cobicistat 150 mg
ARV naïve adults: 1 tab po once daily

Trizivir® R* H
Each tab contains: ZDV 300 mg + 3TC 150 mg + ABC 300 mg
Adolescent dose:
(≥ 40 kg) 1 tab po bid
Adult dose: 1 tab po bid

Truvada® R*
Each tab contains: FTC 200 mg + TDF 300 mg
Adolescent dose:
(≥ 12 yrs and ≥ 35 kg) 1 tablet once daily
Adult dose: 1 tab po once daily

* All these fixed dose combination products should not be used if creatinine clearance is < 50 ml/minute except for Truvada (do not use if CrCl is < 30 ml/min).

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INTEGRASE INHIBITOR

Raltegravir (Isentress®, RAL) H C ★ TB

Dosage form: 25 mg, 100 mg (scored) chewable tabs
400 mg film-coated tab (contains phenylalanine)
Film-coated tabs and chewable tabs are not interchangeable
Pediatric dose:
(< 2 yrs) Safety and efficacy not established
(≥ 2 yrs to < 12 yrs) < 25 kg: chewable tab po bid as per weight based table (max 300 mg bid)
≥ 25 kg: 400 mg film-coated tab bid or chewable tabs as per the table
Adolescents/Adults:
(>12 yrs) 400 mg film-coated tab bid
Important Points:
- Caution should be used when coadministering RAL with strong inducers of uridine diphosphate glucuronosyltransferase (UGT) 1A1 (e.g., rifampin, TPV). ATV is an inhibitor of UGT1A1 which can ↑ RAL concentrations
- AEs: limited data in children; psychomotor hyperactivity, abnormal behavior and insomnia, allergic rash and ↑ LFTs. In adults, diarrhea, nausea, headache and pyrexia, elevation of ALT, AST and CPK, myopathy, rash, Stevens-Johnson syndrome (SJS), thrombocytopenia, and rhabdomyolysis have been reported

Weight (kg)	Dosing	# of Chewable Tablets (bid)[5,6,7]
10 to < 14	75 mg	3 x 25 mg
14 to < 20	100 mg	1 x 100 mg
20 to < 28	150 mg	1.5 x 100 mg
28 to < 40	200 mg	2 x 100 mg
≥ 40	300 mg	3 x 100 mg

5. ISENTRESS® [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2012
6. Wt-based dosing for the chewable tab is based on 6 mg/kg/dose po bid
7. 100 mg tabs can be divided into equal halves

Elvitegravir (EVG)

Dosage form: Only available in fixed dose combination tablets (Stribild)
Elvitegravir (EVG) + cobicistat (COBI) + emtricitabine (FTC) + tenofovir disoproxil fumarate (TDF)
EVG 150 mg + COBI 150 mg + FTC 200 mg + TDF 300 mg
Pediatric dose:
(< 18 yrs) Not FDA-approved or recommended for use in children < 18 yrs
Adolescents/Adults:
(> 18 yrs) 1 tablet po once daily in antiretroviral naïve adults
Important Points:
- Take with food
- Do not initiate in patients with a baseline CrCL < 70 mL/min
- Discontinue if CrCL < 50 mL/min
- Abrupt withdrawal can cause chronic active hep B flares
- Monitor estimated creatinine clearance, urine glucose and urine protein
- Many drug interactions via CYP3A, CYP2D6, and p-glycoprotein pathways (see package insert)
- Separate from antacids (e.g., aluminum or magnesium hydroxide, calcium carbonate) by at least 2 hrs, no adjustments needed with H2 blockers or PPIs
- Do not administer with other antiretrovirals; avoid concomitant use of nephrotoxic agents
- AEs: Nausea, diarrhea, modest ↑ SCr expected (mean: 0.14 ± 0.13 mg/dL), acute renal failure, and proximal tubular dysfunction, nausea, flatulence, renal insufficiency, decreased bone mineral density

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 with individual tx decisions for their pt.

Visit *www.FCAETC.org/treatment* for the most up-to-date version of this resource.

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

Class adverse effects: *Rash-mild to severe, usually within 1st 6 wks (rarely SJS). Evaluate, may need to D/C the drug if severe rash, ↑ LFTs, many drug interactions.*

Efavirenz (Sustiva®, EFV)

Dosage form: 50, 200 mg cap, 600 mg tab
Neonates: Not approved
Infants/Pediatric dose:
Approved for ≥ 3 mos weighing at least 3.5 kg

Pediatric Dose (≥ 3 mos once daily, preferably at bedtime) [9,10]	
Weight (kg)	**Dosing** (po bedtime)
3.5 to < 5	100 mg
5 to < 7.5	150 mg
7.5 to < 15	200 mg
15 to < 20	250 mg
20 to < 25	300 mg
25 to < 32.5	350 mg
32.5 to < 40	400 mg
≥ 40	600 mg

9. No data on dosage for children < 3 yrs
10. Approved for age > 3 yrs and ≥ 10 kg wt

Adolescents/Adults: 600 mg po once daily, preferably at bedtime
*Some experts recommend 367 mg/m² (max 600 mg)

Important Points:
- Avoid high fat meals (tab ideally taken on an empty stomach)
- Metabolized by CYP450, CYP3A4 inducer/inhibitor-multiple drug interactions
- Pregnancy Category D-avoid, especially in 1st trimester
- Take at bedtime to lessen CNS side effects
- Caps may be added to liquid or small amounts of food; grape jelly can disguise taste
- Interacts with estrogen containing oral contraceptives (OCs), advise another form of birth control
- AEs: CNS symptoms: dizziness, insomnia, abnormal dreams, agitation, hallucinations, impaired concentration, rash
  Caution: drowsiness, seizures, ↑ LFTs, lipohypertrophy; false positive cannabinoid and benzodiazepine test

Etravirine (Intelence®, ETR)

Dosage form: 25, 100, 200 mg tab
Pediatric dose: Not approved for use in children < 6 yrs old

Pediatric Dose (≥ 6 yrs-18 yrs)	
Weight (kg)	**Dosing**
≥ 16 to < 20	100 mg bid
≥ 20 to < 25	125 mg bid
≥ 25 to < 30	150 mg bid
≥ 30	200 mg bid

Adults: 200 mg po bid after meal in ARV-experienced pts
Important Points:
- ETR is an inducer of CYP3A4 and inhibitor of CYP2C9, CYP2C19, and P-glycoprotein with multiple drug interactions
- Do not use with "F.A.T" (FPV/r, ATV/r, TPV/r), unboosted PIs, or any other NNRTI
- Always take after a meal. Tab can be dispersed in small amount of water only, stirred, and consumed. Glass should be rinsed several times with water, orange juice or milk and fully consumed.
- Store tabs in original container with the 3 desiccant pouches.
- Pts who have a hx of severe rash with prior NNRTIs should not receive etravirine
- AEs: nausea, rash, including SJS, hypersensitivity reactions have been reported.

Nevirapine (Viramune®, Viramune® XR™ NVP)

Dosage form: 100 (XR), 200, 400 mg tab (XR), 10 mg/mL suspension

Infant ARV Prophylaxis NVP Dose	
Birth Weight (kg)	**Dosing** (given orally)
1.5-2	8 mg total for each dose
> 2	12 mg total for each dose

3 NVP doses in the 1st wk of life (given in addition to ZDV):
- 1st dose within 48 hrs of birth (birth-48 hrs); 2nd dose 48 hrs after 1st; 3rd dose 96 hrs after 2nd

Pediatric dose:
(> 15 days to < 8 yrs)
200 mg/m² (max dose, 200 mg) daily for 14 days, if no rash or untoward effects, ↑ to bid.
(≥ 8 yrs) 120-150 mg/m² (max dose, 200 mg) daily for 14 days, if no rash or untoward effects, ↑ to bid.
(6 to < 18 yrs) Dosing based on BSA in table below:

BSA range (m²)	Viramune® XR™ tabs dose (mg)
0.58-0.83	200 mg po once daily (2 x 100 mg)
0.84-1.16	300 mg po once daily (3 x 100 mg)
≥ 1.17	400 mg po once daily (1 x 400 mg)

(Viramune® XR™ tabs must be swallowed whole. Do not crush, chew or divide.)

Adolescents/Adults: 400 mg extended release once daily. Initiate tx with 200 mg daily for 14 days, if no rash or untoward effects, ↑ to 400 mg extended release once daily. If pt already receiving full dose NVP, may switch to extended release tabs without a lead period

Important Points:
- NVP should not be used with ATV boosted or unboosted
- Drug interactions: CYP450 inducer-CYP3A and CYP2B6 which can lead to drug interactions.
- Interacts with oral contraceptives (OCs); use alternate/additional contraception (other than estrogen containing OCs)
- There is a 3-fold increased risk of rash and hepatotoxicity in children if NVP initiated with a CD4 percentage >15%
- If NVP therapy is interrupted for 14 days or less, restart NVP at full dose
- Store suspension at room temp, shake well
- AEs: hepatitis and hepatotoxicity, most common in the 1st 12 wks of therapy, is often rash-associated and can lead to hepatic failure. D/C drug permanently if severe hepatic, skin, or hypersensitivity reactions occur

Rilpivirine (Edurant®, RPV)

Dosage form: 25 mg film-coated tabs
Infants/Pediatric dose:
Safety and efficacy have not been established
Adolescents/Adults:
(≥ 18 yrs) 25 mg once daily, take with a meal
Important Points:
- Take with a meal of at least 500 calories (protein drink is not sufficient)
- Increased Virologic Failure rate and cross-resistance to NRTIs/NNRTIs has been reported.
- Interacts with acid-reducing agents
  - PPIs (e.g., omeprazole, lansoprazole) contraindicated
  - 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 interval
- AEs: hepatotoxicity, rash, depressive disorders, mood changes, insomnia, and headache

= Take with food	= Take without food
= Take with or without food	= Renal Adjustment*
= Hepatic Adjustment*	= Available in Pediatric Formula
B, C, D = Pregnancy Category	= Generic Available
TB = See Treatment of Tuberculosis (TB) in HIV/AIDS Pocketcard for drug interactions. Located at www.FCAETC.org/Treatment	

* There is little or no data on dosage adjustment for hepatic impairment and renal insufficiency in children. Refer to the AETC ARV Therapy in Adults & Adolescents card or to package inserts for guidelines on dose adjustments.

PROTEASE INHIBITORS (PIs)

Class adverse effects: *Hyperglycemia, hyperlipidemia (except atazanavir), lipodystrophy, increased transaminases, increased bleeding disorders in hemophiliacs, fat redistribution, and lipid abnormalities. Can induce metabolism of ethinyl estradiol; use alternate contraception (other than estrogen containing OCs). All undergo hepatic metabolism mostly by CYP3A4 - Many drug interactions!*

Atazanavir (Reyataz®, ATV)

Dosage form: 100, 150, 200, 300 mg cap
Neonates/Infants: Not approved, risk of hyperbilirubinemia
Pediatric dose: Not recommended for children aged < 6 yrs

Pediatric Dose (≥ 6 yrs-18 yrs) [11]	
Tx-naïve	
Weight (kg)	**Once daily dose (with food)**
15 to < 20	ATV 150 mg + RTV 100 mg
Tx-naïve or Tx-experienced	
Weight (kg)	**Once daily dose (with food)**
20 to < 32	ATV 200 mg + RTV 100 mg
32 to < 40	ATV 250 mg + RTV 100 mg
≥ 40	ATV 300 mg + RTV 100 mg
Adolescents/Adults (≥ 18 yrs) [11]	
400 mg po once daily (ARV-naïve only) Use boosted dose in ARV-experienced pts or in combination with TDF or EFV	
Boosted tx-naïve	
300 mg + RTV 100 mg po once daily (naïve, experienced or with TDF) **or** ATV 400 mg + RTV 100 mg + EFV 600 mg all po once daily but at separate times, RTV with food and EFV on empty stomach Higher than adult doses may be needed in adolescents if ATV not boosted with RTV.	
Tx-experienced ATV + TDF	
Should not get EFV and ATV with or without RTV. ATV 300 mg + RTV 100 mg + TDF 300 mg, all once daily with food. Only RTV-boosted ATV should be used in combination with TDF	

11. ATV boosted with RTV is preferred for children and adolescents

Important Points:
- ATV interacts with antacids (give ATV 2 hrs before or 1 hr after an antacid or buffered didanosine). H2-receptor antagonists (unboosted ATV in tx-naïve pts) ATV 400 mg should be administered at least 2 hrs before, or at least 10 hrs after a dose of the H2-receptor antagonist.
- ATV is a substrate and inhibitor of CYP3A4 enzyme system. ATV competitively inhibits CYP1A2 and CYP2C9 and inhibits glucuronidation enzyme uridine diphosphate glucoronosyltransferase (UGT1A1)
- There are serious drug interactions. Do not use ATV and NVP together
- ATV is a weak inhibitor of CYP2C8
- Must be boosted when used with TDF or EFV; adequate viral load suppression should be documented
- Consider increasing dose during 3rd trimester of pregnancy. See Perinatal Guidelines, *http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf*
- PPI dosing for children please refer to guidelines and package insert for details about dose adjustments.
- PPIs are not recommended with ATV/r in tx-experienced pts and not in tx-naïve patients if they are receiving ATV (unboosted).
- A PPI (≤ 20 mg of omeprazole) can be used in tx-naïve pts, take 12 hrs before boosted ATV
- Higher than adult doses may be needed in adolescents if ATV not boosted with RTV
- ATV/r with EFV should not be used in treatment experienced patients because EFV decreases exposure to ATV
- ATV inhibits UGT1A1, may increase plasma concentration of raltegravir
- H2 Receptor with ATV/r with Tenofovir in tx experienced pts: increase dose of ATV to 400 mg +100 mg RTV+ TDF 300 mg
- AEs: Increases unconjugated bilirubin levels (common), jaundice or scleral icterus (less common), does not adversely affect lipid profile (even with low-dose ritonavir), prolonged PR interval, headache, fever, arthralgia, nausea, vomiting, diarrhea, paresthesias, rash, DM, nephrolithiasis, ↑ LFTs, hepatotoxicity (rare), AV block, hypersensitivity rxn, cholelithiasis and interstitial nephritis

Darunavir (Prezista®, DRV)

Dosage form: 75, 150, 400, 600, 800 mg tab, 100 mg/mL oral solution
Neonates/Infants: Not approved for use
Pediatric dose: Do not use in children age < 3 yrs
(≥ 3 yrs to <18 yrs) ARV Tx-naive or ARV treatment experienced with no DRV mutations
(> 10 kg to < 15 kg) DRV 35 mg/kg + RTV 7 mg/kg once daily may be used (see table below)
(≥ 15 kg) Refer to once daily dosage in the table below

Pediatric Dose (3 yrs to < 18 yrs and wt ≥ 10 kg)		
Weight (kg)	**Dosing** (Take with food, bid)	Dose (once daily with food)
10 to < 11	DRV 200 mg (2 mL) + RTV 32 mg (0.4 mL)	DRV 3.6 mL‡ (350 mg) with ritonavir 0.8 mL (64 mg)
11 to < 12	DRV 220 mg (2.2 mL) + RTV 32 mg (0.4 mL)	DRV 4 mL‡ (385 mg) with ritonavir 0.8 mL (64 mg)
12 to < 13	DRV 240 mg (2.4 mL) + RTV 40 mg (0.5 mL)	DRV 4.2 mL (420 mg) with ritonavir 1 mL (80 mg)
13 to < 14	DRV 260 mg (2.6 mL) + RTV 40 mg (0.5 mL)	DRV 4.6 mL‡ (455 mg) with ritonavir 1 mL (80 mg)
14 to < 15	DRV 280 mg (2.8 mL) + RTV 48 mg (0.6 mL)	DRV 5 mL‡ (490 mg) with ritonavir 1.2 mL (96 mg)
15 to < 30	DRV 375 mg (tablets or 3.75 mL suspension) + RTV 50 mg (0.6 mL)	DRV (6 mL) 600 mg with ritonavir (1.25 mL) 100 mg
30 to < 40	DRV 450 mg + RTV 60 mg (0.8 mL)	DRV (6.8 mL) 675 mg with ritonavir (1.25 mL) 100 mg
≥ 40	DRV 600 mg + RTV 100 mg	DRV (8 mL) 800 mg with ritonavir (1.25 mL) 100 mg

Adolescents/Adults (Tx-naïve or tx-experienced):
No DRV mutations: DRV 800 mg + RTV 100 mg po once daily with food
At least 1 DRV mutation: DRV 600 mg + RTV 100 mg po bid with food
Important Points:
- Should not be used without RTV
- Sulfa derivative; use with caution in pt with sulfa allergy
- DRV is metabolized by CYP3A4, while RTV inhibits CYP3A4 increasing the level of DRV
- Multiple drug interactions are possible
- Admin with food. Store at room temp
- DRV not approved for once daily use in children < 12 yrs old, or for children ages 12-18 if treatment experienced or has 1 or more DRV associated resistance mutations
- V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, L89V
- AEs: rash, diarrhea, nausea, vomiting, abdominal pain, headache, and fatigue. Less common reactions: serious skin reactions (toxic epidermal necrolysis, SJS), fever, and drug-induced hepatotoxicity, erythema multiforme, hyperlipidemia, hyperglycemia

Fosamprenavir (Lexiva®, FPV)

Prodrug of amprenavir
Dosage form: 700 mg tab, 50 mg/mL suspension (225 mL/bottle)

Pediatric Dose [12,13,14]	
PI-naive infants/children ≥ 4 wks and PI-experienced infants/children ≥ 6 mos	
Weight (kg)	**Dosing**
< 11	FPV 45 mg/kg + ritonavir 7 mg/kg po bid
11 to < 15	FPV 30 mg/kg + ritonavir 3 mg/kg po bid
15 to < 20	FPV 23 mg/kg + ritonavir 3 mg/kg po bid
≥ 20	FPV 18 mg/kg + ritonavir 3 mg/kg po bid

12. Max dose should not exceed FPV 700 mg and RTV 100 mg bid
13. PI naive children ≥ 2 yrs: May use unboosted Fosamprenavir 30 mg/kg po bid (without RTV). Max dose should not exceed 1400 mg bid

Fosamprenavir (Continued)

14. FPV should be administered to infants born at 38 wks gestation or greater who have attained postnatal age of 28 days

Adolescents/Adults > 18 yrs
ARV-naïve
FPV unboosted 1400 mg po bid; FPV 1400 mg + RTV 100-200 mg po once daily FPV 700 mg + RTV 100 mg po bid **(with efavirenz):** FPV 1400 mg + RTV 300 mg + EFV 600 mg po all once daily
PI-experienced
FPV 700 mg + RTV 100 mg po bid **(with efavirenz):** FPV 700 mg + RTV 100 mg bid + EFV 600 mg po once daily

Important Points:
- Fosamprenavir has the potential for multiple drug interactions
- PK and clinical data does not support once daily FPV or FPV/r for < 18 yrs
- PK and clinical data does not support FPV/r in PI-experienced children < 6 mos
- PK and clinical data does not support unboosted FPV in children < 2 yrs
- OCs ↓ FPV levels; do not co-admin
- Take APV 1 hr before or after antacids or buffered ddI
- AEs: Skin rash (19%), nausea, vomiting, diarrhea, caution with sulfa allergy, perioral paresthesias, headache, lipid abnormality (more common); neutropenia, and ↑ CPK (less common); DM, ↑ LFTs, hemolytic anemia, angioedema, and nephrolithiasis (rare)

Indinavir (Crixivan®, IDV)

Rarely, if ever, used
Dosage form: 100 mg, 200 mg, and 400 mg capsules
Neonates/Infants: Not approved, risk of hyperbilirubinemia
Pediatric dose: Not approved, investigational dose has been studied[15,16]
Adolescents/Adults: 800 mg IDV + 100 or 200 mg RTV every 12 hrs
See *www.merck.com/product/usa/pi_circulars/c/crixivan/crixivan_pi.pdf* for more information about this drug

15. Do not exceed adult dose
16. Pediatric IDV 234-500 mg/m²/dose boosted with low dose RTV has been studied.

Lopinavir/Ritonavir (Kaletra®, KAL, LPV/r)

Dosage form: 80 mg/20 mg LPV/r per mL (contains 42.4% alcohol), Film-coated tablets: 200 mg/50 mg LPV/r, 100 mg/25 mg LPV/r
Neonates/Infants:
(< 14 days) No data on appropriate dose or safety. Do not admin to neonates before post-menstrual age of 42 wks and postnatal age of at least 14 days
(14 days-12 mos) 300 mg/75 mg/m² of body surface area twice daily
Pediatric dose:
(>12 mos-18 yrs) Tx experienced patients or patients receiving concomitant NVP, EFV, FPV or NFV should receive 300 mg/m²/dose bid (see table below for tablets)
Tx naïve patients or patients not receiving NVP, EFV, FPV or NFV should receive 230 mg/m² dose bid (see table below for tablets)

Pediatric Dose (> 12 mos-18 yrs)		
Weight based dosing for tablets for Children/Adolescents		
	Tx Experienced pts or pts receiving concomitant NVP, EFV, FPV or NFV 300 mg/m²/dose bid	**Tx naïve pts or pts not receiving NVP, EFV, FPV or NFV 230 mg/m²/dose bid**
Weight (kg)	Number of 100/25 mg LPV/r tablets po bid	Number of 100/25 mg LPV/r tablets po bid
15 to 20	2	2
> 20 to 25	3	2
> 25 to 30	3	3
> 30 to 35	4[17]	3
> 35 to 45	4	4
> 45	4 or 5[18]	4

17. Note that 4 of the 100 mg/25 mg LPV/r tablets can be substituted by 2 tablets each containing 200 mg/50 mg LPV/r, but the 200 mg/50 mg LPV/r tablets are bigger and may be difficult to swallow
18. In patients receiving concomitant NVP, EFV, FPV, or NFV, for body weight > 45 kg, the FDA-approved adult dose is 500 mg/125 mg LPV/r twice daily, given as a combination of two tablets of 200/50 mg LPV/r and one tablet of 100 mg/25 mg LPV/r. Some Panel members would use 600 mg/150 mg LPV/r for ease of dosing.

Adolescents/Adults (> 18 yrs):
Pts with < 3 LPV associated mutations:
800 mg/200 mg LPV/r po once daily
or 400 mg/100 mg LPV/r po bid
Pts with > 3 LPV associated mutations:
400 mg/100 mg LPV/r po bid
Pts receiving concomitant NVP, EFV, FPV, or NFV:
500 mg/125 mg LPV/r po bid
or 600 mg/150 mg LPV/r po bid
Pts receiving concomitant SQV or MVC:
400 mg/100 mg LPV/r + 1000 mg SQV po bid
400 mg/100 mg LPV/r + 150 mg MVC po bid

Important Points:
- Must swallow tabs whole; cannot be chewed, broken, or crushed
- Tabs can be taken without food, soln should be taken with food (admin with or after meals may enhance GI tolerability)
- Not recommended to immediately reduce dose at 12 mos for infants receiving LPV/r
- Tablets are often better tolerated than the caps
- Poor palatability, do not crush or split tablets
- Refrigerate soln or store at room temp (up to 77°) for up to 60 days
- Tabs do not require refrigeration; store in original container; exposure to high humidity for > 2 wks is not recommended
- Consider increasing dose during 3rd trimester of pregnancy
- Do not use LPV/r once daily if 3 or more of these mutations are present: L10 F/I/R/V, K20 M/N/R, L24I, L33F, M36I, I47V, G48V, I54 L/T/V, V82 A/C/F/S/T, and I84V
- For patients already receiving LPV/r, immediate dose reduction at age 12 mos is not recommended.
- AEs: GI intolerance (nausea, vomiting, diarrhea), asthenia, headache, rash in association with other ARVs, dyslipidemia (common); DM, pancreatitis, hepatitis, PR and QT interval prolongation, and torsade de pointes (rare), toxic epidermal necrolysis, and SJS

Nelfinavir (Viracept®, NFV)

Dosage form: 250, 625 mg tab
Neonates/Infants:
(< 2 yrs) NFV should not be used
Pediatric dose: 45-55 mg/kg po bid
Adolescents/Adults: 1250 mg po bid
Important Points:
- Tabs can be crushed and administered with pudding or non-acidic foods or dissolved in water, consume immediately
- Can use loperamide or calcium carbonate for drug-related diarrhea
- CYP2C19 and 3A4 substrate
- CYP3A inhibitor
- AEs: diarrhea, abdominal pain, weakness, rash, hyperlipidemia, hyperglycemia, ↑ LFTs

Ritonavir (Norvir®, RTV)

Dosage form: 80 mg/mL soln (240 mL/bottle) (Oral soln contains 43% alcohol by vol), 100 mg cap, 100 mg tab
Neonates/Infants: Not approved in children < 1 mo
Pediatric/Adolescent/Adult dose:
RTV is a PK enhancer of other protease inhibitors. Dosage varies and is specific to the drug combination selected. See dosing info for specific PIs

Important Points:
- OK with Videx® EC
- Liquid has poor palatability. Techniques to ↑ tolerance may include dulling the taste buds before administration and eat strong-tasting foods immediately after dose
- RTV is extensively metabolized by and is an inhibitor of CYP3A, potential for multiple drug interactions
- AEs: nausea, vomiting, diarrhea, abdominal pain, pancreatitis, perioral paresthesias, allergic reactions, anorexia, exacerbation of chronic liver disease, prolongation of the PR interval, Toxic Epidermal Necrolysis (TEN), SJS, and 2nd or 3rd degree AV block (rare)
- Store liquid at room temp, not refrigerated. Shelf life of 6 mos
- Caps should be refrigerated, but may be stored at room temp for up to 30 days, avoid excess heat. Tabs do not need refrigeration

Saquinavir (Invirase®-HGC or tab, SQV)

Dosage form: 200 mg hard-gel caps, 500 mg film-coated tab
Neonates/Infants: Not approved

Pediatric Dose (≥ 2 yrs) [19]	
Weight (kg)	**Dose SQV+RTV** (bid)
5 to < 15	SQV 50 mg/kg + RTV 3 mg/kg
15-40	SQV 50 mg/kg + RTV 2.5 mg/kg
≥ 40	SQV 50 mg/kg + RTV 100 mg
In combination with LPV/r	
Pediatric Dose (≥ 7 yrs) [19]	
SQV 750 mg/m² (max 1600 mg) + LPV/r 400/100 mg/m² bid **or** SQV 50 mg/kg + LPV/r 230 mg/m² both bid	

19. Conditional dosing based on limited data

Adolescents/Adults:
(≥ 16 yrs) 1000 mg SQV + 100 mg RTV po bid
Never give unboosted, give with RTV **or** LPV/r
Important Points:
- Grapefruit juice ↑ SQV level, garlic supplements ↓ SQV level
- Admin within 2 hrs after a meal
- Use sunscreen/protective clothing to limit photosensitivity reactions
- AEs: GI intolerance (nausea, diarrhea, abdominal pain, dyspepsia), paresthesias, skin rash, ↑ LFTs, hyperglycemia, hyperlipidemia, PR and QT interval prolongation, torsades de pointes
- Pretherapy ECG recommended
- Store at room temp

Tipranavir (Aptivus®, TPV)

Dosage form: 100 mg/mL soln 116 IU VitE/mL (95 mL/bottle), 250 mg cap
Neonates/Infants: Not approved
Pediatric dose:
(2 yrs to 18 yrs)[20] TPV 375 mg/m² + RTV 150 mg/m² po bid (max dose TPV 500 + RTV 200 mg bid) **or** TPV 14 mg/kg + RTV 6 mg/kg po bid (max dose TPV 500 + RTV 200 mg bid) (for intolerance, doses may be lowered-see guidelines)

20. TPV must be used with RTV boosting. TPV/RTV is not recommended for treatment naïve patients

Adolescents/Adults: 500 mg po bid with ritonavir 200 mg po bid
Important Points:
- Use with caution if sulfa allergy, unknown cross-sensitivity
- TPV should be used with caution in pts who may be at increased risk of bleeding from trauma, surgery, or other medical conditions including the use of other medications such as; anti-platelet agents or anticoagulants, or in pts taking high doses of Vitamin E
- CYP3A4 substrate, potential for many drug interactions
- Use soln or caps within 2 mos, refrigerate caps if longer storage required
- AEs: diarrhea, nausea, vomiting, abdominal pain, fatigue, headache, elevated amylase, elevated liver enzymes, elevated cholesterol, skin rash, hepatotoxicity, epistaxis, and rare cases of intracranial hemorrhage (ICH), TPV contraindicated in patient with moderate or severe hepatic impairment

Severe hepatotoxicity possible, especially in pts with coinfection with hepatitis B or C. Rare but possibly associated with ↑ intracranial hemorrhage.

ENTRY INHIBITORS

Fusion Inhibitor

Enfuvirtide (Fuzeon®, T-20, ENF)

Dosage form: 108 mg vial of ENF powder for SQ inj, mix with 1.1 mL sterile water for final conc 90 mg/mL
Convenience Kit: 60 single use vials of ENF (90 mg), 60 vials of sterile water, reconstitution syringes, administration syringes, and alcohol wipes
Neonates/Infants: Not approved
Pediatric dose: Not approved in children < 6 yrs
(6 yrs-16 yrs) 2 mg/kg/dose (max dose: 90 mg) SQ bid
Adolescents/Adults: 90 mg SQ bid
Important Points:
- Must instruct pt on reconstitution and administration techniques
- Ice, heat, and/or massage may minimize the local reactions
- Admin subcutaneous in upper arm, anterior thigh, or abdomen (do not inject into naval area, scar tissue, bruise, mole, or area with inj site reaction)
- Rotate inj sites
- AEs: almost all pts (87-98%) experience local inj site reactions-pain, discomfort, induration, erythema, nodules, cysts, itching, ecchymosis (These are usually mild to moderate and last 3-7 days). Less common: local site cellulitis, increased rate of bacterial pneumonia, hypersensitivity reactions, and ↑ LFTs. There can also be immune-mediated reactions. Rechallenge is not recommended
- Reconstituted vial can stand at room temp up to 45 mins until powder is completely in soln, do not shake vial
- Reconstituted soln should be refrigerated and used within 24 hrs

CCR5 Inhibitor

Maraviroc (Selzentry®, MVC)

Dosage form: 150, 300 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved

Adolescents/Adults (≥ 16 yrs)	
Concomitant Medications	**Adult Dose** (po bid)
CYP3A inhibitors (with or without a CYP3A inducer): • protease inhibitors (except tipranavir/ritonavir) • delavirdine • ketoconazole, itraconazole, clarithromycin • other strong CYP3A inhibitors (e.g., nefazodone, telithromycin)	150 mg
CYP3A inducers (without a strong CYP3A inhibitor) including: • efavirenz, etravirine • rifampin • carbamazepine, phenobarbital, and phenytoin	600 mg
Other concomitant medications, including: • NRTIs, enfuvirtide, tipranavir/ritonavir, raltegravir, nevirapine, and drugs that are not potent CYP3A inhibitors or inducers	300 mg

Important Points:
- An HIV tropism assay is required prior to use to exclude the presence of CXCR4-using or mixed/dual tropic HIV
- CYP3A substrate, interactions possible with inhibitors or inducers Only combine MVC with CYP3A inhibitors in pts with CrCL < 50 mL/min if benefits outweigh the risk
- Monitor adverse effects in pts with moderate liver impairment receiving CYP3A4 inhibitors with MVC
- AEs: Serious adverse effects have occurred in adults including angina, heart failure, MI, cirrhosis, liver failure, cholestatic jaundice, viral pneumonia, myositis, osteonecrosis, and rhabdomyolysis. Hepatoxicity with allergic features has been reported. D/C with S/S of hepatitis or ↑ LFTs. Most common: cough, pyrexia, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, dizziness, and orthostatic hypotension