ARV Therapy in Pediatrics

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Unless otherwise noted, tables and information adapted from Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection February 23, 2009. *www.aidsinfo.nih.gov*

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

Non-Nucleoside Reverse Transcriptase Inhibitor-Based Regimens	
Preferred	Children ≥ 3 yrs: 2 NRTIs + efavirenz Children < 3 yrs or who can't swallow caps: 2 NRTIs + nevirapine
Alternative	2 NRTIs + nevirapine (children ≥ 3 yrs)
Protease Inhibitor-Based Regimens	
Preferred	2 NRTIs + lopinavir/ritonavir
Alternative	2 NRTIs + atazanavir + low dose ritonavir (children ≥ 6 yrs) 2 NRTIs + fosamprenavir + low dose ritonavir (children ≥ 6 yrs) 2 NRTIs + nelfinavir (children ≥ 2 yrs)
Use in Special Circumstances	
2 NRTIs + fosamprenavir (children ≥ 2 yrs)	
2NRTIs + atazanavir ≥ 13 years and > 39 kg unable to tolerate nelfinavir (must boost if used with tenofovir)	
Zidovudine + lamivudine + abacavir	
Dual NRTI Combination Recommendations	
Preferred	Abacavir + (lamivudine or emtricitabine) Didanosine + emtricitabine Tenofovir + (lamivudine or emtricitabine) (for Tanner Stage 4 or post-pubertal adolescents only) Zidovudine + (lamivudine or emtricitabine)
Alternative	Abacavir + zidovudine Zidovudine + didanosine
Used in Special Circumstances	Stavudine + (lamivudine or emtricitabine)

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-naive 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

To Request Resistance Testing Consultation

Download a request form at **http://www.FCAETC.org/RTC**
Serving clinicians in Florida, Puerto Rico, and the U.S. Virgin Islands.

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

Class adverse effects: *Lactic acidosis with hepatic steatosis*

Abacavir (Ziagen®, ABC) ☆ 🍽 ⊘ H

Dosage form: 300 mg tab, 300 mg scored tab, 20 mg/mL soln (240 mL/bottle)
Neonates: Not approved in children < 3 mo
Pediatric dose (3 mo-16 yrs): 8 mg/kg po bid (max dose 300 mg bid)
Adolescent dose: Limited data; can use 300 mg po bid
Adult dose (> 16 yrs): 300 mg po bid or 600 mg po once daily
Note: Perform HLA B*5701 test prior, only use if negative
Important Points:
- Do not stop and restart medication without consulting your doctor
- Alcohol ↑ ABC levels 41%; potential for adverse effects
- AEs: nausea, vomiting, headache, diarrhea, rash, fever, increased liver enzymes, possible increased risk of MI (rare)

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 first 6 weeks of therapy and has occurred after a single dose. Stop ABC and do not restart.

Didanosine (Videx EC®, ddI) ☆ ⊘ R

Dosage form: Pediatric powder for soln (2 or 4 g bottle), reconstituted with antacid=10 mg/mL
Generic ddI delayed release cap: 200, 250, 400 mg [delayed-release (DR) cap]
Videx EC® tab 125, 200, 250, 400 mg (DR cap)
Neonates/Infants: 2 wk-8 mo of age: 100 mg/m²/dose po q12h
Pediatric dose (> 8 mo): 120 mg/m²/dose po bid
range: 90-150 mg/m²/dose po q 12 hrs
For tx-naive children age 3-21 yrs,
240 mg/m² BSA po once daily (max dose 400 mg)
(DR cap) (6-18 yrs) 20 to < 25 kg: 200 mg once daily
≥ 25 to < 60 kg: 250 mg once daily
≥ 60 kg: 400 mg once daily
Adolescents/Adults: ≥ 60 kg: 200 mg oral soln po bid or 400 mg DR po once daily
< 60 kg: 125 mg oral soln po bid or 250 mg DR po once daily
Dose with tenofovir: ≥ 60 kg and CrCl ≥ 60 ml/min: 250 mg once daily
< 60 kg and CrCl ≥ 60 ml/min: 200 mg once daily (limited data)
No data in pts < 18 yrs or CrCl < 60 ml/min
Important Points:
- Swallow DR caps whole on empty stomach, 30 min ac or 2 hr pc (except when given with TDF—can be with or without food)
- Risk factors for lactic acidosis: women, obesity, prolonged NRTI exposure
- AEs: diarrhea, abdominal pain, nausea, vomiting, peripheral neuropathy, electrolyte abnormalities, hyperuricemia, hepatic toxicity and failure, retinal depigmentation, peripheral neuropathy (dose related, more common in advanced disease)
- Refrigerate soln, stable for 30 days, shake well

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

NRTIs (Continued)

Emtricitabine (Emtriva®, FTC) 🍽 ⊘ R

Dosage form: 200 mg cap, 10 mg/mL oral soln (170 mL/bottle)
Neonates/Infants: Not approved in children < 3 mo
Pediatric dose (3 mo-17 yrs): For weight < 33 kg: 6 mg/kg oral soln once daily (max dose 240 mg)
For weight > 33 kg: 200 mg cap po once daily
Adolescents/Adults: 200 mg cap or 24 mL soln po once daily
Important Points:
- AEs: headache, insomnia, diarrhea, nausea, rash, hyperpigmentation of palms and soles seen in up to 6% of pts (more common in Black and Hispanic pts), neutropenia, lactic acidosis, severe hepatomegaly with steatosis (all rare)
- Refrigerate oral soln, OK at room temp if used within 3 months

Exacerbations of hepatitis B infection have been seen in co-infected pts when FTC is discontinued.

Lamivudine (Epivir®, 3TC) ☆ 🍽 ⊘ R

Dosage form: 10 mg/mL soln (240 mL/bottle), 5 mg/mL (Epivir HBV), 100 mg (Epivir HBV), 150 mg scored tab, 300 mg tab
Neonates (< 30 days): 2 mg/kg/dose po bid
Pediatric dose: 4 mg/kg/dose po bid (max 150 mg po bid)
14-21 kg: 75 mg po bid (1/2 tab [150 mg])
> 21 kg to < 30 kg: 75 mg (1/2 tab) in am and 150 mg (1 tab) in pm (total dose 225 mg)
> 30 kg 150 mg po bid
Adolescents/Adults: ≥ 50 kg: 150 mg po bid or 300 mg po once daily
< 50 kg: 4 mg/kg/dose po bid (max dose 150 mg bid)
Important Points:
- AEs: headache, fatigue, nausea, decreased appetite, diarrhea, skin rash, abdominal pain, pancreatitis (in advanced disease), anemia, decreased neutrophil count

Exacerbations of hepatitis B infection have been seen in co-infected pts when 3TC is discontinued. 3TC is indicated for the treatment of HBV, under the care of a specialist.

Stavudine (Zerit®, d4T) ☆ 🍽 ⊘ R

Dosage form: 15, 20, 30, 40 mg cap, 1 mg/mL soln (200 mL/bottle) (Now available in generic)
Neonates (birth-13 days): 0.5 mg/kg/dose po q12hr
Pediatric dose: < 30 kg: 1 mg/kg/dose po q12hr
Adolescents/Adults: 30-59 kg: 30 mg po bid
≥ 60 kg: 40 mg po bid
Important Points:
- AEs: headache, GI disturbances, skin rash, peripheral neuropathy, pancreatitis, lipodystrophy, hyperlipidemia; Rare: increased liver enzymes, progressive ascending motor weakness
- Refrigerate soln and shake well, discard after 30 days if reconstituted

When combined with didanosine, same Black Box Warnings.

Tenofovir (Viread®, TDF) 🍽 ⊘ R

Dosage form: 300 mg tab - Powder formulation under study
Neonates/Infants: Not approved
Pediatric dose (investigational): 2-8 yrs: 8 mg/kg once daily
> 8 yrs: 210 mg/m² once daily (max 300 mg) (only available preparation 300 mg tab)
Adolescents/Adults: 300 mg po once daily

🍽 = Take with food ⊘ = Take without food 🍽⊘ = Take with or without food
R = Renal Adjustment* H = Hepatic Adjustment* ☆ = Med. available in Pediatric Formula

*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 and Adolescents card or to package inserts for guidelines on dose adjustments.

NRTIs (Continued)

Tenofovir (Viread®, TDF)(Continued)

Important Points:

- Drugs which reduce renal function or compete for active tubular secretion may change the tenofovir concentration and/or other renally eliminated drugs (e.g. cidofovir, acyclovir, valalacyclovir, ganciclovir, valganciclovir)- dosage adjustment information available
- Interacts with Videx EC® (See Videx EC® for dosing) and atazanavir (See atazanavir for dosing)
- Dosage should be adjusted in pts with renal insufficiency and CrCl < 50 ml/min
- AEs: nausea, diarrhea, vomiting, flatulence; less common: decreased bone mineral density, renal tubular dysfunction, Fanconi syndrome

Exacerbations of hepatitis B infection have been seen in co-infected pts who discontinue TDF.

Zidovudine (Retrovir®, AZT, ZDV) ☆ ⊘ ⊗ Ⓡ

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

PROPHYLAXIS

Neonates:

(term infants) 2 mg/kg/dose po q6h
1.5 mg/kg/dose IV q6h (infuse over 30 min)

Premature Infants:

(< 30 wks gestation) 1.5 mg/kg/dose IV q12h or
2 mg/kg/dose po q12h for 4 weeks, then q8h

(≥ 30 wks gestation) 1.5 mg/kg/dose IV q12h or
2 mg/kg/dose po q12h for 2 weeks, then q8h

TREATMENT

Pediatric dose: 240 mg/m² q12h or 160 mg/m² q8h
(6 wks-18 yrs) Or mg/kg dosing:
4 to < 9 kg: 12 mg/kg q12h
9 to < 30 kg: 9 mg/kg q12h
≥ 30 kg: 300 mg q12h

Adolescents/Adults: 300 mg po bid, 200 mg po tid
(≥ 18 yrs)

Important Points:

- AEs: headache, nausea, vomiting, fatigue, myositis, liver toxicity, lactic acidosis, and severe hepatomegaly with steatosis and increased risk of hypospadias after 1st trimester exposure observed in one cohort study

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

Combination Products: These can be used in adolescents at appropriate Tanner Stage (Tanner Stage III or higher) and weight (> 40 kg).

Atripla® ⊘ ⊗ Ⓡ* H

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

Combivir® ⊘ ⊗ Ⓡ*

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

Epzicom® ⊘ ⊗ Ⓡ* H

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

Trizivir® ⊘ ⊗ Ⓡ* H

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

Truvada® ⊘ ⊗ Ⓡ*

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

*These fixed dose combination medications should not be used in pts with creatinine clearance measurements < 50 mL/minute and < 30 mL/minute for Truvada®.

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

***Class adverse effects: WARNING:** Rash - mild to severe, usually within first 6 weeks. Discontinue the drug if severe rash (with blistering, desquamation, muscle involvement or fever).*

Delavirdine (Rescriptor®, DLV) ⊘ ⊗ H

Rarely, if ever, used in children

Efavirenz (Sustiva®, EFV) ☆ ⊘ ⊗ H

Dosage form: 50, 200 mg cap, 600 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved in children < 3 yrs
Approved for age > 3 yrs and >10 kg weight
10 to < 15 kg: 200 mg po qhs
15 to < 20 kg: 250 mg po qhs
20 to < 25 kg: 300 mg po qhs
25 to < 32.5 kg: 350 mg po qhs
32.5 to < 40 kg: 400 mg po qhs
≥ 40 kg: 600 mg po qhs
Adolescents/Adults: 600 mg po once daily at bedtime

Important Points:

- Avoid high fat meal (tab ideally taken on an empty stomach)
- CYP450 inducer/inhibitor - multiple drug interactions
- Pregnancy Category D - avoid, especially in first trimester
- Take at bedtime to lessen CNS side effects
- Caps may be opened and added to grape jelly to disguise taste
- Interacts with estrogen containing OCs, recommend another form of birth control
- AEs: CNS - dizziness, insomnia, abnormal dreaming, agitation, hallucinations. Begins 1st or 2nd day and generally resolves in 2-4 weeks. Caution - drowsiness, ↑ transaminases, false positive cannabinoid test

Etravirine (Intelence™, ETR) ⊘ H

Dosage form: 100 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved
Adults: ARV-experienced 200 mg po bid

Important Points:

- ETR is an inducer of CYP3A4 and inhibitor of CYP2C9 and CYP2C19, with multiple drug interactions
- Do not use with ATV/r, FPV/r, TPV/r, unboosted PIs, or any other NNRTI
- Tab can be dispersed in a glass of water, then stirred and consumed. Glass should be rinsed several times, and each rinse completely swallowed.
- AEs: nausea, rash. Rash occurs in 2nd week, usually resolves after 1-2 weeks and is mild. Rarely the rash can be more severe including Erythema multiforme (EM), hypersensitivity, or Stevens-Johnson Syndrome (SJS.) Discontinue drug if a severe rash occurs. Pts with a previous history of NNRTI-related rash do not appear to be at increased risk of developing a rash with ETR.
- Store tabs in original container with dessicant

Nevirapine (Viramune®, NVP) ☆ ⊘ ⊗ H

Dosage form: 200 mg tab, 10 mg/mL suspension
Neonates/Infants: 2 mg/kg as single dose between birth and age 3 days
(age ≤ 14 days) to prevent mother-to-child transmission. Treatment dose not defined.
Pediatric dose: 150 mg/m² (maximum dose, 200 mg) daily for 14 days, then increase to 150 mg/m² bid if tolerated. Younger children (eg, ≤ 8 yrs) may require up to 200 mg/m² bid. Total daily dose should not exceed 400 mg.
(≥ 15 days)
Adolescents/Adults: 200 mg po once daily for 14 days, then 200 mg po bid
Or dose can be expressed in volume of Viramune suspension (dose 150 mg/m²): SEE TABLE A

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NNRTIs (Continued)

Nevirapine (Viramune®, NVP)(Continued)

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. Auto-induction of metabolism occurs at 2-4 weeks with 1.5-2 fold increase in clearance.
- Interacts with oral contraceptives (OCs); use alternate/additional contraception (other then estrogen containing OCs)
- If NVP dosing interrupted for more than 7 days, restart once daily dosing before escalating to full twice daily dosing
- AEs: Hepatotoxicity; most common in first 12 weeks of therapy and often rash-associated, but can occur later in up to 30% of pts; greater risk if elevated baseline LFTs, history of hepatitis infection, female gender, CD4 > 250 in women and > 400 in men. D/C drug permanently if severe hepatic, skin or hypersensitivity reactions occur. Follow 14-day lead-in period (lower dose) strictly.
- Store suspension at room temperature, shake well

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) ⊘ Ⓡ H

Dosage form: 100, 150, 200, 300 mg cap
Neonates/Infants: Not approved, risk of hyperbilirubinemia
Pediatric Dose: 15 to < 25 kg: ATV 150 mg + RTV 80 mg once daily with food
(6-18 yrs) 25 to < 32 kg: ATV 200 mg + RTV 100 mg once daily with food
32 to < 39 kg: ATV 250 mg + RTV 100 mg once daily with food
≥ 39 kg: ATV 300 mg + RTV 100 mg once daily with food
Tx-naïve ATV 400 mg (unboosted) with food
(≥ 13 yrs and > 39 kg and intolerant of RTV)
Adolescents/Adults: 400 mg po once daily in ARV-naïve pts;
(> 16 yrs) Use boosted dose in ARV-experienced pts or in combination with TDF or EFV
Boosted ATV 300 mg + RTV 100 mg po once daily
Therapy-naïve ATV 400 mg + RTV 100 mg + EFV 600 mg all once daily but at separate times; RTV with food, EFV on empty stomach.
Tx-experienced Should not get EFV and ATV (with or without RTV)
ATV + TDF 300 mg ATV + 100 mg RTV + 300 mg TDF, all once daily with food

Important Points:

- ATV interacts with antacids (give ATV 2 hrs before or one hr after). H2-receptor antagonists (unboosted ATV in treatment-naïve pts) ATV 400 mg should be administered at least 2 hours before or at least 10 hours after a dose of the H2-receptor antagonist. Please refer to guidelines and package insert for details about dose adjustments with ATV and H2-blockers, PPIs and/or TDF.
- ATV is a substrate and inhibitor of CYP3A4 enzyme system. ATV competitively inhibits CYP1A2 and CYP2C9 ATV inhibits glucuronidation enzyme uridine diphosphate glucoronosyltransferase (UGT1A1)
- There are significant drug interactions. ATV and NVP should not be used together.
- ATV is a weak inhibitor of CYP2C8
- Must be boosted when used with TDF, EFV or MVC
- 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

PIs (Continued)

Darunavir (Prezista®, DRV)

Dosage form: 75 mg, 400 mg, 600 mg tab
Neonates/Infants: Not approved in children < 3 yrs
Pediatric dose:
(3-6 yrs) Safety and efficacy not established
(6 to < 18 yrs) ≥ 20 to < 30 kg: DRV 375 mg (five 75 mg tabs) + RTV 50 mg (0.6ml of 80mg/ml)
≥ 30 to < 40 kg: DRV 450 mg (six 75 mg tabs) + RTV 60 mg (0.8 ml of 80 mg/ml)
≥ 40 kg: DRV 600 mg (one 600 mg tab) + RTV 100 mg (one 100 mg gelcap)
Adolescents/Adults:
Tx-naïve DRV 800 mg (two 400 mg tabs) + RTV 100 mg once daily
Tx-experienced DRV 600 mg (one 600 mg tab) + RTV 100 mg both twice daily
DRV + MVC DRV 600 mg + RTV 100 mg both twice daily, 150mg MVC twice daily

Important Points:
- Should not be used without RTV
- DRV should be reserved for adults/adolescents who exhibit multiple PI viral mutations, are treatment-experienced, and continue to show evidence of ongoing viral replication despite continued treatment
- Sulfa derivative; use with caution in pt with sulfa allergy
- DRV is metabolized by P450 3A4, while RTV inhibits CYP3A4 increasing the level of DRV
- Multiple drug interactions are possible
- AEs: diarrhea, nausea, vomiting, abdominal pain, headache and fatigue. Less common reactions include skin rash (including erythema multiforme and Stevens-Johnson syndrome), fever, and drug-induced hepatotoxicity.
- Store at room temperature

Fosamprenavir (Lexiva®, FPV)

Prodrug of amprenavir
Dosage form: 700 mg tab, 50 mg/mL suspension (225 mL/bottle)
Neonates/Infants: Not approved
Pediatric dose:
(2-18 yrs) Once daily dosing not recommended
ARV-naïve
(2-5 yrs) 30 mg/kg po bid (max dose 1400 mg)
(> 6 yrs) 30 mg/kg po bid (without RTV – maximum dose 1400 mg) or 18 mg/kg po bid (max dose 700 mg) plus RTV 3 mg/kg (max dose 100 mg) po bid
ARV-experienced
(> 6 yrs) 18 mg/kg (max dose 700 mg) po bid plus RTV 3 mg/kg (max dose 100 mg) po bid (if FPV is used with EFV and MVC, boost FPV)
Adolescents/Adults:
ARV-naïve 1400 mg po bid for pts > 47 kg
FPV 1400 mg + RTV 200 mg po once daily
FPV 1400 mg + RTV 100 mg po once daily
FPV 700 mg + RTV 100 mg po bid
PI-experienced FPV 700 mg + RTV 100 mg po bid
Boosted FPV bid when combining with EFV
Boosted FPV + EFV once daily only in PI-naïve pts

Important Points:
- Oral contraceptives (OCs) ↓ FPV levels; do not co-administer
- Take APV one hour before or after antacids or buffered ddI
- AEs: Skin rash (19%), nausea, vomiting, diarrhea, caution with sulfa allergy, perioral paresthesias, and headache

Indinavir (Crixivan®, IDV)

Dosage form: 100, 200, 333, 400 mg cap
Neonates/Infants: Not approved, risk of hyperbilirubinemia
Pediatric dose: Not approved
Investigational dose 500mg/m²/dose po q8h
Adolescents/Adults: 800 mg po q8h
Boosted PI dosing: IDV 800 mg + RTV 100-200 mg po q12h
Dosing w/ NNRTIs: IDV 1000 mg po q8h + 600 mg EFV once daily

Important Points:
- Take on empty stomach; 1 hr ac or 2 hr pc. Can be taken with low fat/ protein snack. No food restrictions when boosted.
- Drink 48 ounces of fluid each day (water preferred)
- Separate by ≥ 1 hr from doses of ddI (Videx® only, OK with Videx EC®)
- AEs: nephrolithiasis is more common in children perhaps due to poor hydration, hyperbilirubinemia, nausea, abdominal pain, headache, metallic taste, dizziness, asymptomatic hyperbilirubinemia, pruritis and rash
- Store in original container with desiccant

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

Dosage form: 400/100 mg per 5 mL soln (160 mL/bottle), 200/50 mg tab, 100/25 (pediatric tab)
Neonates/Infants: (14 days-6 mo) 300/75 mg/m² or 16/4 mg/kg bid
Pediatric dose: (6 mo-18 yrs)
< 15 kg: 12/3 mg/kg po bid
15-40 kg: 10/2.5 mg/kg po bid
> 40 kg: 400/100 mg po bid, or 230/57.5 mg/m² po bid (max dose 400/100 mg/dose)
With NVP, EFV, or FPV
7 < 15 kg: 13/3.25 mg/kg po bid or 300/75 mg/m²
15-45 kg: 11/2.75 mg/kg po bid or 300/75 mg/m²
> 45 kg: 533/133 mg po bid with food or liquid 600/150 mg (three 200/50 mg tabs) po bid
BSA dose: 300/75 mg/m2 bid
SEE TABLE B
Adolescents/Adults: 400/100 (5 mL or two tabs) bid (ARV-exp or naïve)
800/200 (10 mL or four tabs) qd (ARV-naïve)
600/150 (7.5 mL or three tabs) bid with NVP or EFV
qd dosing should not be used with NVP, EFV, FPV, NFV
LPV/RTV + SQV: 1000 mg SQV + 400m LPV /100mg RTV both twice daily
LPV/RTV + MVC: 50 mg MVC twice daily + 400 mg LPV/100 mg RTV twice daily

Important Points:
- Must swallow tabs whole; cannot be chewed, broken, or crushed
- Tabs can be taken without food, soln should be taken with food
- Oral soln contains 42% alcohol
- AEs: GI intolerance (nausea, vomiting, diarrhea), asthenia, headache, rash in association with other ARVs
- 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 weeks is not recommended

Nelfinavir (Viracept®, NFV)

Dosage form: 250, 625 mg tab,
50 mg/g oral powder=1 level scoop (144 g/bottle)
Neonates/Infants: (< 2 yrs) Dose under investigation
Pediatric dose: (2-13 yrs) 45-55 mg/kg po bid
25-35 mg/kg po tid
Large inter-patient variability in NFV levels
Adolescents/Adults: 750 mg po tid or 1250 mg po bid

Important Points:
- Do not mix powder with acidic food or juice due to resulting bad taste
- Powder best mixed with water, pudding, ice cream or formula; must be used within 6 hours of mixing
- Tabs can be dissolved in water; consume immediately
- Loperamide or calcium carbonate may be used for drug related diarrhea
- AEs: diarrhea, abdominal pain, weakness, rash, exacerbation of chronic liver disease

Ritonavir (Norvir®, RTV)

Dosage form: 80 mg/mL soln (240 mL/bottle) (Oral soln contains 43% alcohol by vol.), 100 mg cap
Neonates/Infants: Not approved in children < 1 mo age
Pediatric dose: (> 1 mo) Start at 250 mg/m²/dose po bid, ↑ to the usual dose 350-400 mg/m²/dose po bid over 5 days (max dose 600 mg)
Adolescent/Adults: Used to boost other PIs only

Important Points:
- OK with Videx EC®
- Liquid tastes bad; techniques to increase tolerance: Take med prior to or after ingesting any of the following: milk, chocolate milk or syrup, vanilla or chocolate pudding or ice cream; dull taste buds before administration by chewing ice, sucking on popsicles; coat mouth with peanut butter before dose; give strong tasting foods (maple syrup, cheese, chewing gum) 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 par esthesias, allergic reactions, anorexia, exacerbation of chronic liver disease, prolongation of the PR interval and 2nd or 3rd degree AV block (rare)
- Store liquid at room temperature, not refrigerated. Shelf life of 6 months.
- Caps should be refrigerated but may be stored at room temperature for up to 30 days - avoid excessive heat

Saquinavir (Invirase®-HGC or tab, SQV)

Dosage form: 200 mg hard gel cap or 500 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved, clinical trials ongoing
Adolescents/Adults: Unboosted SQV not recommended;
SQV 1000 mg + RTV 100 mg po bid

Important Points:
- Grapefruit juice ↑ SQV level, garlic supplements ↓ SQV level
- Use sunscreen/protective clothing to limit photosensitivity reactions
- AEs: GI intolerance (nausea, diarrhea, abdominal pain, dyspepsia), paresthesias skin rash, exacerbation of chronic liver disease
- Invirase® store at room temperature

Tipranavir (Aptivus®, TPV)

Dosage form: 100 mg/ml solution (95 mL/bottle), 250 mg cap
Neonates/Infants: Not approved
Pediatric dose: (2-18 yrs) TPV 375 mg/m² + RTV 150 mg/m² bid (maxium dose TPV 500 + RTV 200 mg bid)
Alternatively TPV 14 mg/kg + RTV 6 mg/kg bid (maximum dose TPV 500 + RTV 200 mg bid) (for intolerance, doses may be lowered—see guidelines)
Adolescents/Adults: Unboosted TPV not recommended;
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
- AEs: diarrhea, nausea, vomiting, abdominal pain, fatigue, headache, elevated amylase, elevated liver enzymes or cholesterol
- Use soln or caps within 2 months, otherwise refrigerate

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

Warmline: ***National HIV Telephone Consultation Service*** **800-933-3413**

PEPline: ***National Clinicians' Post-Exposure Prophylaxis Hotline*** **888-448-4911**

Perinatal HIV Hotline **888-448-8765**

Medication Patient Assistance Programs Information **www.NeedyMeds.org**

ENTRY INHIBITORS

Fusion Inhibitor

Enfuvirtide (Fuzeon®, T-20, ENF)

Dosage form: Powder for SC inj; mix with 1.1 mL sterile water for final conc 90 mg/mL
Neonates/Infants: Not approved
Pediatric dose: Not approved in children < 6 yrs
(6-16 yrs) 2 mg/kg/dose (max dose: 90 mg) SC bid
Adolescents/Adults: 90 mg SC bid
Important Points:

- Must instruct pt on reconstitution and administration techniques
- Ice, heat and/or massage may minimize the local reactions
- 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: almost all pts (87-98%) experience local injection 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 (3-8%), increased rate of bacterial pneumonia. Rare: hypersensitivity reactions (< 1%) - symptoms can include rash, fever, nausea, vomiting, chills, rigors, hypotension or elevated transaminases. There can also be immune-mediated reactions. Rechallenging is not recommended.
- Reconstituted vial can stand at room temperature up to 45 minutes until powder is completely in soln, do not shake vial
- Reconstituted soln should be refrigerated and used within 24 hours

CCR5 Inhibitor

Maraviroc (Selzentry®, MVC) ⊘ ⊗ Ⓡ Ⓗ

Dosage form: 150 mg, 300 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved
Adolescents/Adults:
(≥ 16 yrs) SEE TABLE C
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
- Monitor adverse effects in pts with moderate liver impairment receiving Cyp3A4 inhibitors with maraviroc
- AEs: Serious adverse effects have occurred in adults (in less than 2% of MVC treated adults) including angina, heart failure, myocardial infarction, 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 increased LFTs combined with rash or other symptoms. Most common: were cough, pyrexia, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, dizziness and orthostatic hypotension.

INTEGRASE INHIBITOR

Raltegravir (Isentress®, RAL) ⊘ ⊗ Ⓗ

Dosage form: 400 mg tab
Neonates/Infants: Not approved
Pediatric dose: Not approved
Adolescents/Adults: 400 mg po bid
(≥ 16 yrs)
Important Points:

- Caution should be used when coadministering RAL with strong inducers of uridine diphosphate glucuronosyltransferase (UGT) 1A1 (eg, rifampin, TPV). ATV is an inhibitor of UGT1A1 which can increase RAL concentrations.
- AEs: dizziness, vomiting, itching, abdominal pain and worsening of liver enzymes in pts with chronic hepatitis B and/or C. Nausea, headache, diarrhea and pyrexia. Creatine kinase elevations have occurred. Myopathy and rhabdomyolysis reported and possibly related.

TABLE A: Nevirapine (Viramune®, NVP)

BSA range (m2)	Volume (ml)
0.06 - 0.12	1.25
0.12 - 0.25	2.5
0.25 - 0.42	5
0.42 - 0.58	7.5
0.58 - 0.75	10
0.75 - 0.92	12.5
0.92 - 1.08	15
1.08 - 1.25	17.5
> 1.25	20

TABLE B: Lopinavir/Ritonavir (Kaletra®, KAL, LPV/r)

WITH Concomitant Nevirapine, Efavirenz or Fosamprenavir

Weight (kg)	Volume of Oral Soln[1] Twice Daily	Number of 100/25 mg or 200/50 mg Tabs Twice Daily
7 - 10 kg	1.5 mL	Tabs are not recommended
> 10 < 15 kg	2 mL	Tabs are not recommended
15 - 20 kg	2.5 mL	2 x 100/25 mg
> 20 - 25 kg	3.25 mL	3 x 100/25 mg
> 25 - 30 kg	4 mL	3 x 100/25 mg
> 30 - 35 kg	4.5 mL	2 x 200/50 mg
> 35 - 40 kg	5 mL	2 x 200/50 mg
> 40 - 45 kg	5.75 mL	2 x 200/50 mg
> 45 kg	6.5 mL	3 x 200/50 mg

WITHOUT Concomitant Nevirapine, Efavirenz or Fosamprenavir

Weight (kg)	Volume of Oral Soln[1] Twice Daily	Number of 100/25 mg or 200/50 mg Tabs[2] Twice Daily
7 - 10 kg	1.25 mL	Tabs not recommended
> 10 < 15 kg	1.75 mL	Tabs not recommended
15 - 20 kg	2.25 mL	2 x 100/25 mg
> 20 - 25 kg	2.75 mL	2 x 100/25 mg
> 25 - 30 kg	3.5 mL	3 x 100/25 mg
> 30 - 35 kg	4 mL	3 x 100/25 mg
> 35 - 40 kg	4.75 mL	2 x 200/50 mg
> 40 kg	5 mL	2 x 200/50 mg

1. 80 mg LPV/20 mg RTV per mL
2. 100 mg LPV/25 mg RTV tab or 200 mg LPV/50 mg RTV tab

TABLE C: Maraviroc (Selzentry®, MVC)

Concomitant Medications	Adult Dose
CYP3A inhibitors (w/ or w/o a CYP3A inducer): • protease inhibitors (except tipranavir/ritonavir) • delavirdine • ketoconazole, itraconazole, clarithromycin • other strong CYP3A inhibitors (e.g., nefazadone, telithromycin)	150 mg po bid
CYP3A inducers (without a strong CYP3A inhibitor) including: • efavirenz, etravirine • rifampin • carbamazepine, phenobarbital, and phenytoin	600 mg po bid
Other concomitant medications, including: • tipranavir/r • nevirapine • all NRTIs • enfuvirtide	300 mg po bid

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 (first 6 weeks) for HIV exposed infants
Two-agent drug combinations	Resistance develops rapidly. Inferior to ≥ 3 drugs. If virologic goals achieved, some clinicians may choose to continue
ABC + TDF + 3TC (or FTC)	High rate of early virologic non-response seen in ARV-naïve patients
TDF + ddI + 3TC (or FTC)	High rate of early virologic non-response seen in ARV-naïve patients
d4T + AZT	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
amprenavir oral soln	Contains large amounts of propylene glycol; contraindicated in pregnancy, children < 4 y/o, 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 component of both drugs; no benefit in combination
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
efavirenz in 1st trimester of pregnancy or in women with pregnancy potential	Teratogenic in monkeys - consider use only when no other options available and potential benefits outweigh risks
nevirapine initiation in women with CD4 > 250 or in men with CD4 > 400	Higher incidence of symptomatic hepatic events; use only if potential benefits outweigh risks

Insufficient Data to Recommend

Initial Regimens
Tenofovir-containing regimens in children in Tanner Stages I-III
Dual (full dose) PI regimens
NRTI + NNRTI + PI
Regimens containing enfuvirtide, darunavir, tipranavir, maraviroc, raltegravir or etravirine (except for use in salvage therapy, based on genotype or phenotype analysis)
Low dose ritonavir-boosted PI regimens, with exceptions of lopinavir/ritonavir, fosamprenavir/ritonavir in children ≥ 6 yrs, and low dose ritonavir in combination with atazanavir, indinavir, or saquinavir in post-pubertal adolescents who can receive adult dose
Unboosted atazanavir-containing regimens in children < 13 yrs and/or < 39 kg

Please visit our website at
www.FCAETC.org