ARV Therapy in Pediatrics

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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. September 14, 2011; pp 1-207. Available at *http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf*. Accessed January 27, 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. August 11, 2011; pp 1-268. Available at *http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf*. Accessed January 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 of any age	2 NRTIs + nevirapine (only if no peripartum nevirapine exposure)
> 6 yrs	2 NRTIs + darunavir + low dose RTV 2 NRTIs + fosamprenavir + low dose RTV
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 mo) Tenofovir + (lamivudine or emtricitabine) (> 12 yrs and Tanner Stage IV or V) Zidovudine + (lamivudine or emtricitabine)
Alternative	Didanosine + (lamivudine or emtricitabine) Tenofovir + (lamivudine or emtricitabine) (> 12 yrs and Tanner Stage III) Zidovudine + abacavir Zidovudine + didanosine
Use in Special Circumstances	Stavudine + (lamivudine + emtricitabine) Tenofovir + (lamivudine or emtricitabine) (> 12 yrs and Tanner Stage 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

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.

Not Recommended/Insufficient Data to Recommend for Initial Therapy

Initial Regimens
TDF-containing regimens in children < 12 yrs or children ≥ 12 yrs and Tanner Stage I
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, **or** T-20
Unboosted ATV-containing regimens in children < 13 yrs and/or body wt < 39 kg Unboosted DRV-containing regimens Once-daily dosing of LPV/r, boosted DRV, or boosted or unboosted FPV
Triple-NRTI regimens other than ABC + ZDV + 3TC Regimens with dual-NRTI backbones of ABC + ddI, ABC + TDF, ddI + TDF, and ddI + d4T

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 + 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
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/mm^3 or in boys with CD4 > 400 cells/mm^3	Higher incidence of symptomatic hepatic events; use only if potential benefits outweigh risks

INTEGRASE INHIBITOR

Raltegravir (Isentress®, RAL) H C

Dosage form: 25, 100 mg (scored) chewable tabs, 400 mg film coated tab (contains phenylketonuria)

Pediatric dose:

(< 2 yrs) Safety and effectiveness not established

(≥ 2 to < 12 yrs) 10 kg < 25 kg: Use chewable-weight-based table (max 300 mg) bid

(6 < 12 yrs) ≥ 25 kg: Use chewable-weight-based table (max 300 mg) or 400 mg film coated tab po bid

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 transaminase elevations. 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)	**Dose** (po, bid)	**Chewable Tablets** (po, bid)[4, 5]
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

4. Wt-base dosing for the chewable tab is based on 6 mg/kg/dose po bid
5. 100 mg tabs can be divided into equal halves

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ALSO AVAILABLE FOR ORDER and DOWNLOAD:

ARV Therapy in Adults & Adolescents

Hepatitis C in HIV/AIDS

Opportunistic Infections (OIs) in HIV/AIDS

Oral Manifestations Associated with HIV/AIDS

Post-Exposure Prophylaxis (PEP) & Pre-Exposure Prophylaxis (PrEP)

Post-Exposure Prophylaxis (PEP) in Pediatrics/Adolescents

Treatment of Tuberculosis (TB) in HIV/AIDS

Treatment of STDs in HIV-Infected Patients

To order additional topics or to request an alternate format of this card:

www.FCAETC.org/Treatment

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

Class adverse effects: *Lactic acidosis with hepatic steatosis*

Abacavir (Ziagen®, ABC) ★ H

Dosage form: 300 mg tab, 20 mg/mL soln (240 mL/bottle)
Neonates/Infants: Not approved in children < 3 mo

Pediatric dose
8 mg/kg po bid (max dose 300 mg bid)

Pediatric dose (3 mo-16 yrs)	
Liquid: 8 mg/kg po bid (max dose 300 mg bid)	
Weight	**Tablets**
> 14 kg	Scored 300 mg tabs for body wt
14-21 kg	½ tab bid
> 21 to < 30 kg	½ tab am and 1 tab pm
> 30 kg	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
NOTE: Perform HLA B*5701 test, only use if (-)

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

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) ★ R

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:
(2 wk-3 mo) 50 mg/m²/dose every 12 hrs
(> 3-8 mo) 100 mg/m²/dose every 12 hrs

Pediatric BSA dose (> 8 mo)
120 mg/m² po every 12 hrs; range: 90-150 mg/m²/dose po every 12 hrs (max 200 mg/dose bid)

Pediatric dose (6-18 yrs)	
Weight	**EC or Generic Caps** (once daily)
20 to < 25 kg	200 mg
≥ 25 to < 60 kg	250 mg
≥ 60 kg	400 mg
Tx-naïve children age 3-21 yrs	
240 mg/m² 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 once daily (limited data)
≥ 60 kg and CrCl ≥ 60 mL/min: 250 mg once daily (limited data)

Didanosine (Videx EC®, ddI) ★ R (Continued)

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
- 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, pancreatitis, 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:
(0-3 mo) 3 mg/kg oral soln once daily
Pediatric dose: < 33 kg: 6 mg/kg oral soln once daily
(3 mo-17 yrs) (max dose 240 mg); > 33 kg: 200 mg 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 in up to 6% of non-white pts, neutropenia, lactic acidosis, and severe hepatomegaly with steatosis (all rare). No CYP450 interactions
- Refrigerate oral soln, OK at room temp if used within 3 mo

Exacerbations of hep-B 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.

Lamivudine (Epivir®, 3TC) ★ R

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

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

Important Points:
- AEs: headache, fatigue, nausea, decreased appetite, diarrhea, skin rash, abdominal pain, pancreatitis (in advanced disease), anemia, and decreased neutrophil count

Exacerbations of hep-B 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.

= Take with food	= Take without food
= Take with or without food	R = Renal Adjustment*
H = Hepatic Adjustment*	★ Available in Pediatric Formula
B, C, D = Pregnancy Category	

* 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.

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 bid
Pediatric dose:
(14 days and < 30 kg) 1 mg/kg/dose po bid
Adolescents/Adults:
30-59 kg: 30 mg po bid, ≥ 60 kg: 40 mg po bid, WHO recommends max d4t dose of 30 mg bid

Important Points:
- AEs: 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
- 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: 150, 200, 250, 300 mg tabs, 40 mg per 1 g/1 scoop powder formulation
Neonates/Infants: Not approved
Pediatric dose: Not approved for age < 12 yrs
(2 to < 18 years) 8 mg/kg (max 300 mg) po once daily

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

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

Adolescents/Adults:
(≥ 12 yrs and > 35 kg) 300 mg po once daily

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, valacyclovir, ganciclovir, valganciclovir)-dosage adjustment info available
- Interacts with Videx EC® (See Videx EC® for dosing) and atazanavir (See atazanavir 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 hep-B 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)

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

Infant ARV Prophylaxis			
Age Groups	**Gestational Age**	**Dosing**	
Neonates/ Term Infants	≥ 35 wks	4 mg/kg/dose body wt po bid (start as soon after birth as possible, preferably within 6-12 hrs of birth, through 6 wks of age)	1.5 mg/kg/dose IV every 6 hrs (start within 6-12 hrs of birth, continue through 6 wks of age or change to oral dosing when possible)
Premature Infants	< 35 to ≥ 30 wks	2 mg/kg/dose po every 12 hrs for 2 wks, then every 8 hrs for last 4 wks (6 wks total)	1.5 mg/kg/dose IV every 12 hrs for 2 wks then every 8 hrs for the last 4 wks (6 wks total)
	< 30 wks	2 mg/kg/dose po every 12 hrs for 4 wks, every 8 hrs for the last 2 wks (6 wks total)	1.5 mg/kg/dose IV every 12 hrs for 4 wks, every 8 hrs for the last 2 wks (6 wks total)

Pediatric dose: 180-240 mg/m² every 12 hrs or 160 mg/m² every 8 hrs
(6 wks to < 18 yrs) wt based dosing:
4 to < 9 kg: 12 mg/kg every 12 hrs
9 to < 30 kg: 9 mg/kg every 12 hrs
≥ 30 kg: 300 mg every 12 hrs

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

Important Points:
- AEs: headache, nausea, vomiting, insomnia, asthenia, bone marrow suppression, macrocytic anemia, neutropenia, fatigue, myositis, myopathy, 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®

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

Combivir®

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

Complera®

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

Epzicom®

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

Trizivir®

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

Truvada®

Each tab contains: FTC 200 mg + TDF 300 mg
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: *Rash-mild to severe, usually within 1st 6 wks. D/C the drug if severe rash (with blistering, desquamation, muscle involvement, or fever).*

Efavirenz (Sustiva®, EFV)

Dosage form: 50, 200 mg cap, 600 mg tab
Neonates/Infants: Not approved

Pediatric dose[6,7]	
Weight	**Dose** (po bedtime)
10 to < 15 kg	200 mg
15 to < 20 kg	250 mg
20 to < 25 kg	300 mg
25 to < 32.5 kg	350 mg
32.5 to < 40 kg	400 mg
≥ 40 kg	600 mg

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

Adolescents/Adults:
600 mg po once daily 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 interactions
- Pregnancy Category D-avoid, especially in 1st trimester
- Take at bedtime to lessen CNS side effects
- Caps may be added to liquid or 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 (if occurs, begins 1st or 2nd day and usually resolves in 2-4 wks). Caution: drowsiness, seizures, ↑ transaminases, lipohypertrophy; false positive cannabinoid and benzodiazepine test

Etravirine (Intelence™, ETR)

Dosage form: 100, 200 mg tab
Pediatric dose:
(6-11 yrs) (Investigational) 5.2 mg/kg (max 200 mg) po bid
Adolescent:
(12-17 yrs) Not approved. (200 mg bid was used in 2 European studies and demonstrated good tolerability and virologic responses)
Adults: 200 mg po bid after meal in ARV-experienced pts

Important Points:
- ETR is an inducer of CYP3A4 and inhibitor of CYP2C9 and CYP2C19, 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 a glass of water, stirred, and consumed. Glass should be rinsed several times, each rinse fully swallowed
- AEs: nausea rash (approximately 10%). Rash occurs in 2nd wk, usually resolves after 1-2 wks and is mild. Rarely rash can be more severe including erythema multiforme (EM), hypersensitivity (< 0.1%, more common in females), or Stevens-Johnson Syndrome (SJS). D/C drug if a severe rash occurs. Pts with a previous hx of NNRTI-related rash do not appear to be at increased risk of developing a rash with ETR
- 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

Nevirapine (Viramune®, NVP)

Dosage form: 200 mg tab;
10 mg/mL suspension;
extended release 400 mg tab

Infant ARV prophylaxis NVP dose	
Birth Weight	**Dose** (given orally)
1.5-2 kg	8 mg per dose
> 2 kg	12 mg per 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. [No need to lower dose in child turning 8 yrs if tolerating med]

Adolescents/Adults:
400 mg extended release once daily.
Initiate therapy 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. Auto-induction of metabolism occurs at 2-4 wks with 1.5-2 fold ↑ in clearance
- Interacts with oral contraceptives (OCs); use alternate/additional contraception (other than 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 1st 12 wks of therapy and often rash-associated, but can occur later in up to 30% of pts; greater risk if elevated baseline LFTs, hx 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. In pts with renal failure an additional dose of NVP should be given following dialysis. NVP extended release tabs must not be chewed, crushed, or divided
- Store suspension at room temp, shake well

Rilpivirine (Edurant™, RPV)

Dosage form: 25 mg film coated tabs
Infants/Pediatrics:
Safety and efficacy have not been established

Adolescents/Adults:
(≥ 18 yrs) 25 mg once daily

Important Points:
- Take with a meal
- Metabolized by CYP450 enzymes. Multiple drug interactions. Use with caution with drugs that ↑ gastric *pH*, in pts with severe hepatic and renal impairment, and in pts with HIV RNA > 100,000 copies/mL due to ↑ risk of virologic failure. Do not take with other NNRTIs
- Side effects include rash, depressive disorders, mood changes, insomnia, and headache

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	
Tx-naïve[8]	
Weight	**Tablets**
15 to < 25 kg	ATV 150 mg + RTV 80 mg once daily with food (6-18 yrs)
Tx-naïve or -experienced	
Weight	**Tablets once daily with food**
25 to < 32 kg	ATV 200 mg + RTV 100 mg
32 to < 39 kg	ATV 250 mg + RTV 100 mg
≥ 39 kg	ATV 300 mg + RTV 100 mg
Adolescents/Adults (≥ 18 yrs)	
400 mg po once daily in ARV-naïve pts Use boosted dose in ARV-experienced pts or in combination with TDF or EFV	
Boosted therapy-naïve	
ATV 300 mg + RTV 100 mg po once daily **or** 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 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	

8. ATV boosted with RTV is preferred for pts intolerant of RTV

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. Please refer to guidelines and package insert for details about dose adjustments with ATV and H2-blockers, PPIs and/or TDF. PPIs not recommended in tx-experienced pts
- 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
- Please refer to Adult/Adolescent card and package insert for details about dose adjustments with ATV and H2-blockers. PPIs, and/or TDF
- Consider increasing dose during 3rd trimester of pregnancy. See Perinatal Guidelines, *http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf*
- 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, increased transaminases, hepatotoxicity (rare)

Darunavir (Prezista®, DRV)

Dosage form: 75, 150, 400, 600, 800 (in development) mg tab, 100 mg/mL suspension
Neonates/Infants: Not approved in children < 3 yrs

Pediatric dose[9] (3 to < 6 yrs)[10]	
Weight	**Take with food bid**
10 to < 15 kg	DRV/r 25/3 mg/kg
15 to < 20 kg	DRV/r 375/50 mg
Pediatric dose[9] (6 to < 18 yrs)	
Weight	**Take with food bid**
≥ 20 to < 30 kg	DRV 375 mg (5 x 75 mg tabs) + RTV 50 mg **or** (liquid DRV/r 3.8 mL/0.6 mL)
≥ 30 to < 40 kg	DRV 450 mg (6 x 75 mg tabs) **or** (3 x 150 mg tabs) + RTV 60 mg **or** (liquid DRV/r 4.6 mL/0.75 mL)
≥ 40 kg	DRV 600 mg (tab) + RTV 100 mg (cap or tab) **or** (liquid DRV/r 6 mL/1.25 mL)
Tx-naïve (12-18 yrs)	
Weight	**Tablets po once daily with food**
> 40 kg	DRV 800 mg + RTV 100 mg

9. Safety and efficacy have not been established
10. Recent trial 48 wks data (Ariel trial) used DRV/r in 3 to < 6 yrs along with an OBR

Adolescents/Adults (Tx-naïve or -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
- AEs: rash, diarrhea, nausea, vomiting, abdominal pain, headache, and fatigue. Less common reactions: serious skin reactions (toxic epidermal necrolysis, Stevens-Johnson syndrome), fever, and drug-induced hepatotoxicity
- Admin with food. Store at room temp

Fosamprenavir (Lexiva®, FPV)

Prodrug of amprenavir
Dosage form: 700 mg tab, 50 mg/mL suspension (225 mL/bottle)
Neonates/Infants: Not approved

Pediatric dose
ARV-naïve (2 to ≥ 6 yrs)
30 mg/kg po bid (without RTV-max dose 1400 mg) **or** 18 mg/kg po bid (max dose 700 mg) + RTV 3 mg/kg (max dose 100 mg) po bid
ARV-experienced (> 6-18 yrs)
Boosting preferred 18 mg/kg po bid (max dose 700 mg) + RTV 3 mg/kg (max dose 100 mg) po bid
1400 mg po bid for pts ≥ 47 kg (this is the only time unboosted FPV can be used)
Adolescents/Adults
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 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 once daily

Fosamprenavir (Continued)

Important Points:

- Fosamprenavir has the potential for multiple drug interactions
- 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, ↑ transaminases, hemolytic anemia, angioedema, and nephrolithiasis (rare)

Indinavir (Crixivan®, IDV)

Dosage form: 100, 200, 400 mg cap
Neonates/Infants: Not approved, risk of hyperbilirubinemia
Pediatric dose: Not approved; investigational dose has been studied
Adolescents/Adults:
800 mg po every 8 hrs
Boosted PI: IDV 800 mg + RTV 100-200 mg po every 12 hrs
with NNRTIs: IDV 1000 mg po every 8 hrs + EFV 600 mg 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 oz of fluid each day (water preferred)
- Separate by ≥ 1 hr from doses of ddI (Videx® only, OK with Videx EC®)
- CYP3A4 inhibitor and substrate
- AEs: nephrolithiasis is more common in children perhaps due to poor hydration, hyperbilirubinemia, nausea, abdominal pain, headache, metallic taste, dizziness, asymptomatic hyperbilirubinemia, pruritus, hepatitis, renal dysfunction, 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 mg tab (pediatric tab)
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 mo) 300 mg/75 mg/m^2 **or** 16 mg/4 mg/kg LPV/r bid

Pediatric dose (> 12 mo-18 yrs)		
Pts receiving concomitant Nevirapine, Efavirenz, Fosamprenavir, or Nelfinavir[11, 12]		
Weight	**Volume of Oral Solution** (po bid)	**Number of 100/25 mg or 200/50 mg Tablets** (po bid)
7-10 kg	1.5 mL	Tabs are not recommended
> 10 to < 15 kg	2.0 mL	Tabs are not recommended
15-20 kg (BSA > 0.6 to < 0.8 m^2)	2.5 mL	2 x 100/25 mg
> 20-30 kg (BSA > 0.8 to < 1.2 m^2)	3.25-4.0 mL	3 x 100/25 mg
> 30-45 kg (BSA > 1.2 to < 1.7 m^2)	4.5-5.75 mL	4 x 100/25 mg **or** 2 x 200/50 mg
> 45 kg (BSA > 1.7 m^2)	6.5 mL	4 or 6 x 100/25 mg **or** 2 x 200/50 mg
Pts not receiving concomitant Nevirapine, Efavirenz, Fosamprenavir, or Nelfinavir[13]		
Weight	**Volume of Oral Solution** (po bid)	**Number of 100/25 mg or 200/50 mg Tablets** (po bid)
7-10 kg	1.25 mL	Tabs are not recommended
> 10 to < 15 kg	1.75 mL	Tabs are not recommended
15-25 kg (BSA > 0.6 to < 0.9 m^2)	2.25-2.75 mL	2 x 100/25 mg
> 25-35 kg (BSA > 0.9 to < 1.4 m^2)	3.5-4 mL	3 x 100/25 mg
> 35 kg (BSA > 1.4 m^2)	4.75-5 mL	4 x 100/25 mg **or** 2 x 200/50 mg

Lopinavir/Ritonavir (Continued)

11. Higher dose can be considered in tx-experienced pts when ↓ sensitivity to LPV is suspected
12. Once daily dosing not recommended for neonates/infants, pediatric/adolescent pts and any pt receiving concomitant therapy with NVP, EFV, FPV, or NFV
13. ARV-naïve: 230/57.5 mg LPV/r/m² po bid, ARV-experienced: 300 mg/75 mg LPV/r/m² po bid

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 mo for infants receiving LPV/r
- Oral soln contains 42% alcohol, poor palatability
- 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
- AEs: GI intolerance (nausea, vomiting, diarrhea), asthenia, headache, rash in association with other ARVs, hyperlipidemia, hypertriglyceridemia (common); DM, pancreatitis, hepatitis, PR and QT interval prolongation, and torsade de pointes (rare)

Nelfinavir (Viracept®, NFV)★ H

Dosage form: 250, 625 mg tab

Neonates/Infants:
(< 2 yrs) NFV should not be used

Pediatric dose:
(2-13 yrs) 25-35 mg/kg po tid, inter-pt variance 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; refrigerated mixture must be used within 6 hrs of mixing
- 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, and irritation of chronic liver disease

Ritonavir (Norvir®, RTV) ★ H

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: take before or after ingesting milk, chocolate milk, vanilla or chocolate pudding, or ice cream; dull taste buds before administration by chewing ice or sucking on popsicles; coat mouth with peanut butter; eat strong tasting foods (maple syrup, cheese, chewing gum) immediately after dose

Ritonavir (Continued)

- 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, and 2nd or 3rd degree AV block (rare)
- Store liquid at room temp, not refrigerated. Shelf life of 6 mo
- 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) H

Dosage form: 200 mg hard gel cap or 500 mg tab

Neonates/Infants: Not approved

Pediatric dose[14] (≥ 2 yrs)	
Weight	**Tablets** (bid)
5 to < 15 kg	SQV 50 mg/kg + RTV 3 mg/kg
15-40 kg	SQV 50 mg/kg + RTV 2.5 mg/kg
≥ 40 kg	SQV 50 mg/kg + RTV 100 mg
In combination with LPV/r	
Pediatric dose[14] (≥ 7 yrs)	
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	

14. 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, ↑ transaminases, hyperglycemia, hyperlipidemia, PR and QT interval prolongation, torsades de pointes
- Pretherapy ECG recommended
- Store at room temp

Tipranavir (Aptivus®, TPV) H

Dosage form: 100 mg/mL soln 116 IU VitE/mL (95 mL/bottle), 250 mg cap

Neonates/Infants: Not approved

Pediatric dose (2 yrs-18 yrs)
TPV 375 mg/m² + RTV 150 mg/m² 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)

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, elevated cholesterol, skin rash, hepatotoxicity, epistaxis, and rare cases of intracranial hemorrhage (ICH)
- Use soln or caps within 2 mo, refrigerate caps if longer storage required

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 SC 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:
(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
- Admin SC in upper arm, anterior thigh, or stomach (do not inj into naval area, scar tissue, bruise, mole, or area with inj site reaction)
- Rotate injection 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 (3-8%), increased rate of bacterial pneumonia, hypersensitivity reactions (rare, < 1%) (symptoms can include: rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated transaminases). 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) R H

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 CTP3A 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 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: cough, pyrexia, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, dizziness, and orthostatic hypotension