

Pediatric/Neonatal Doses of Antiretroviral Drugs

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Abacavir (ZIAGEN®, ABC)

Dose	<p><u>Neonatal/Infant:</u></p> <ul style="list-style-type: none"> Not approved for infants less than 3 months. 1 – 3 months: 8 mg/kg/dose po BID (investigational) <p><u>Pediatric/Adolescent (3 months to 12 years):</u></p> <ul style="list-style-type: none"> 8 mg/kg/dose po BID Maximum: 300 mg po BID <p><u>Adult (>16 years):</u></p> <ul style="list-style-type: none"> 300 mg po BID or 600 mg once daily
How Supplied/Storage	<ul style="list-style-type: none"> 20 mg/mL banana-strawberry liquid (240 mL bottle). Store at room temperature. 300 mg tablet Scored 300mg tablet for pediatric use (> 14 kg) (available in US only) <u>Combination tablet:</u> <ul style="list-style-type: none"> TRIZIVIR® = 300 mg zidovudine; 150 mg lamivudine; 300 mg abacavir KIVEXA® = 600 mg abacavir; 300 mg lamivudine
Food Restrictions	May take with or without food.
Comments	<ul style="list-style-type: none"> Watch for hypersensitivity reaction (~ 5% incidence; usually within first 6 weeks): fever, rash, fatigue, n/v, diarrhea, abdominal pain and respiratory symptoms. Do NOT rechallenge. Patients who experience a hypersensitivity reaction should be reported to the Abacavir HS Registry 1-800-270-0425. KIVEXA®: Film coated immediate release tablet however no studies regarding stability of split or crushed tablets. (Email communication, GlaxoSmithKline, May 2008) TRIZIVIR®: Film coated immediate release tablet however no studies regarding stability of split or crushed tablets.
Didanosine (VIDEX®, VIDEX EC®, ddl)	
Dose	<p><u>Neonatal/Infant (2 weeks to less than 3 months):</u></p> <ul style="list-style-type: none"> 50 mg/m²/dose po BID recommended by ARV Guidelines¹ manufacturer recommends 100 mg/m²/dose po BID <p><u>Pediatric:</u></p> <p><u>3 mos to 8 mos:</u></p> <ul style="list-style-type: none"> 100 mg/m²/dose po BID <p><u>more than 8 months:</u></p> <ul style="list-style-type: none"> 120 mg/m²/dose po BID (range 90 – 150 mg/m²/dose po BID) Treatment naïve (3-21 years): 240 mg/m²/dose po once daily to a maximum of 400mg (PACTG 1021) >20 kg and can swallow capsules: see adult dosing for Videx EC <p><u>Adult/Adolescent:</u></p>

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	<ul style="list-style-type: none"> • <u>Suspension</u> : <ul style="list-style-type: none"> – 60 kg or more: 200 mg po BID or 400 mg po once daily – Less than 60 kg: 125 mg po BID or 250 mg po once daily – Note: twice daily dosing preferred due to better therapeutic response • <u>VIDEX EC</u>: <ul style="list-style-type: none"> – 60 kg or more: 400 mg po once daily – 25 kg to less than 60 kg: 250 mg po once daily – 20 kg to less than 25 kg: 200mg po once daily • <u>VIDEX EC in combination with tenofovir</u>: <ul style="list-style-type: none"> – 60 kg or more: 250 mg po once daily – Less than 60 kg: 200 mg po once daily
How Supplied/ Storage	<ul style="list-style-type: none"> • 4 g pediatric powder for oral solution (final concentration of 10 mg/mL). Refrigerate for up to 30 days (shake well before using). Available through Special Access Program². • VIDEX EC delayed release capsules: 125 mg, 200mg, 250 mg and 400 mg
Food Restrictions	<ul style="list-style-type: none"> • Take on an empty stomach. Do not give with fruit juices or acidic drinks, feeds or milk (one published study suggested children may take with food). • When coadministered, ddl delayed release capsules and tenofovir may be taken under fasted conditions or with a light meal.
Comments	<ul style="list-style-type: none"> • Space from f-APV, ATV, IDV, LPV, NFV & RTV, by 1-2 hours. • 4 g: Add 200 mL purified water to powder, shake, and then add 200 mL antacid (suitable antacid: MAALOX Extra Strength). • Combination of d4T and ddl is not recommended (unless benefits outweigh the risks) due to overlapping toxicities. • Until further information is available, combination of ddl and tenofovir should be avoided wherever possible due to high failure rates (in combination with NNRTIs) and decline in absolute CD4 cells.
Lamivudine (3TC®)	
Dose	<p><u>Neonatal/Infant (infants less than 30 days):</u></p> <ul style="list-style-type: none"> • 2 mg/kg/dose po BID <p><u>Pediatric:</u></p> <ul style="list-style-type: none"> • 4 mg/kg/dose po BID; maximum 150 mg po BID <p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> • 50 kg or more: 150 mg po BID or 300 mg po once daily • Less than 50 kg: 2 mg/kg/dose po BID (maximum 150 mg po BID)
How Supplied/ Storage	<ul style="list-style-type: none"> • 10 mg/mL strawberry-banana oral liquid (240 mL bottle). Store at room temperature. • 150 mg and 300 mg tablets • <u>Combination tablets</u>: <ul style="list-style-type: none"> – COMBIVIR® = 300 mg zidovudine; 150 mg lamivudine – TRIZIVIR® = 300 mg zidovudine; 150 mg lamivudine; 300 mg abacavir – KIVEXA® = 600 mg abacavir, 300 mg lamivudine

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Food Restrictions	Take with or without food.
Comments	May cut lamivudine tablet in half (not scored) or crush.

Stavudine (ZERIT®, d4T)	
Dose	<u>Neonatal/Infant (birth up to 13 days) :</u> <ul style="list-style-type: none"> • 0.5 mg/kg po q12h <u>Pediatric (14 days up to a weight of 30 kg):</u> <ul style="list-style-type: none"> • 1 mg/kg/dose po q12h <u>Adult/Adolescent:</u> <ul style="list-style-type: none"> • 60 kg or more: 40 mg po BID • Less than 60 kg: 30 mg po BID
How Supplied/Storage	<ul style="list-style-type: none"> • 1 mg/mL fruit flavored suspension (200 mL bottle). Available through Special Access program². Stable for 30 days in fridge. Shake well. • 15, 20, 30, 40 mg capsules
Food Restrictions	Take with or without food.
Comments	<ul style="list-style-type: none"> • May open capsule and give in small portion of food or 5-10 mL cool tap water. • Should not be administered with zidovudine due to poor antiretroviral effect. • Combination of d4T and ddl is not recommended (unless benefits outweigh the risks) due to overlapping toxicities.

Tenofovir (VIREAD®, TDF)	
Dose	<u>Neonatal/Infant:</u> <ul style="list-style-type: none"> • Not approved for use. <u>Pediatric:</u> <ul style="list-style-type: none"> • Not approved for use in children less than 12 years. • Clinical trials are underway with investigational formulations. • Investigational dose: <ul style="list-style-type: none"> – children aged 2 to 8 years: 8 mg/kg/dose PO once daily; – children more than 8 years median dose of 210 mg/m²/dose PO once daily, maximum dose of 300 mg daily. • Study Gilead 926: 175 mg/m²/dose po once daily • Study Gilead 927: Given po once daily <ul style="list-style-type: none"> – 10 to less than 20 kg: 75 mg – 20 to less than 35 kg: 150 mg – 30 to less than 50 kg: 225 mg – More than 50 kg: 300 mg

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	<u>Adult/Adolescent (more than 12 years and more than 35 kg):</u> <ul style="list-style-type: none"> • 300 mg po once daily
How Supplied/Storage	<ul style="list-style-type: none"> • 300 mg tablet • <u>Combination tablets:</u> <ul style="list-style-type: none"> – TRUVADA® = 300 mg tenofovir; 200 mg emtricitabine – ATRIPLA® = 300 mg tenofovir; 200 mg emtricitabine; 600 mg efavirenz
Food Restrictions	Take with food.
Comments	<ul style="list-style-type: none"> • Tenofovir: Crushed tabs dissolve in 100mL of water, grape juice, or grapefruit juice within 20 minutes. Consume immediately. Unpalatable bitter taste. May split tab and insert in empty gelatin capsule to mask bitter taste. Pediatric suspension under development. • Tenofovir may decrease atazanavir (ATV) plasma concentrations. In adults, a boosting dose of 100 mg ritonavir is recommended (ATV 300 mg/RTV 100 mg) if coadministered with tenofovir. • TRUVADA®: May split tablets. May crush and stir into water, grapefruit juice or orange juice. The stability of the mixture is unknown. (Email communication, Gilead, May 2008) • ATRIPLA®: No studies regarding stability of split or crushed tablets. Splitting or crushing is not recommended. Efavirenz not soluble in water. (Email communication, Gilead, May 2008)
Zidovudine (RETROVIR®, AZT, ZDV)	
Dose	<u>Perinatal Exposure:</u> <ul style="list-style-type: none"> • Start ZDV within less than 6-12 hours after birth and administer for 6 weeks. • <i>Less than 30 weeks:</i> <ul style="list-style-type: none"> – PO: 2 mg/kg/dose po q12h for 4 weeks, then q8h for last 2 weeks – IV: 1.5 mg/kg/dose IV q12h for 4 weeks, then q8h for last 2 weeks • <i>30 – 34 weeks:</i> <ul style="list-style-type: none"> – PO: 2 mg/kg/dose po q12h for 2 weeks, then q8h for last 4 weeks – IV: 1.5 mg/kg/dose q12h for 2 weeks, then q8h for last 4 weeks • <i>More than 35 weeks:</i> <ul style="list-style-type: none"> – PO: 2 mg/kg/dose po q6h – IV: 1.5 mg/kg/dose IV q6h <u>Pediatric (6 weeks – 12 years):</u> <ul style="list-style-type: none"> • PO: 160 mg/m²/dose po q8h (range 90-180) or 180 - 240 mg/m²/dose po q12h <u>or</u>: • MG/KG DOSING: <ul style="list-style-type: none"> – 4 kg to < 9kg: 12 mg/kg BID – 9 kg to < 30 kg: 9 mg/kg BID – ≥ 30kg: 300mg BID • IV: 120 mg/ m²/dose q6h or 20 mg/m²/hour <u>Adult/Adolescent (12 years or older):</u> <ul style="list-style-type: none"> • 600 mg/day po in 2-3 divided doses

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How Supplied/ Storage	<ul style="list-style-type: none"> • 10 mg/mL strawberry syrup (240 mL bottle). Store at room temperature. • 100 mg capsules • 200 mg/20 mL vial (intravenous) • <u>Combination tablets:</u> <ul style="list-style-type: none"> - COMBIVIR® = 300 mg zidovudine; 150 mg lamivudine - TRIZIVIR® = 300 mg zidovudine; 150 mg lamivudine; 300 mg abacavir
Food Restrictions	<p>Take with or without food.</p>
Comments	<ul style="list-style-type: none"> • If zidovudine upsets stomach, take with food. • Should not be administered with d4T due to poor antiretroviral effect. • May open capsule and give in small portion of food or 5 – 10 mL cool tap water. • COMBIVIR®: Film coated immediate release tablet; however. no studies regarding stability of split or crushed tablets. (Email communication, GlaxoSmithKline, May 2008) • TRIZIVIR®: Film coated immediate release tablet; however. no studies regarding stability of split or crushed tablets.

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Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Efavirenz (SUSTIVA®, EFV)

Dose	<p><u>Neonatal/Infant:</u></p> <ul style="list-style-type: none"> Not approved for use. <p><u>Pediatric (more than 3 years and ≥ 10 kg):</u></p> <ul style="list-style-type: none"> Give once daily (PO) 10 to less than 15 kg: 200 mg 15 to less than 20 kg: 250 mg 20 to less than 25 kg: 300 mg 25 to less than 32.5 kg: 350 mg 32.5 to less than 40 kg: 400 mg More than 40 kg: 600 mg No data on appropriate dosage for children less than 3 years. <p><u>Adult/Adolescent (weight 40 kg or more):</u></p> <ul style="list-style-type: none"> 600 mg po once daily <i>Efavirenz in combination with maraviroc:</i> 600mg EFV daily plus MVC 600 mg BID
How Supplied/Storage	<ul style="list-style-type: none"> Pediatric suspension 30 mg/mL (180 mL bottle) strawberry mint. Available through expanded access program³ (1-877-372-7097). 50, 100, 200 mg capsules 600 mg tablet <u>Combination tablet:</u> <ul style="list-style-type: none"> – ATRIPLA® = 300 mg tenofovir; 200 mg emtricitabine; 600 mg efavirenz
Food Restrictions	May take with or without food but do not take with high fat meal (significantly increases AUC and side effects).
Comments	<ul style="list-style-type: none"> Bedtime dosing recommended first 2-4 weeks to decrease CNS side effects. Capsules may be opened and added to liquids or foods but peppery taste. Grape jelly may mask taste. Efavirenz: For NG administration, may open capsules and mix with 15 mL Ora-Sweet (grind powder to enhance dissolution). Powder insoluble in water. Do not mix with polyethylene glycol - will decrease bioavailability. Insoluble in water. Mixed inducer/inhibitor of CYP450 3A4. CHECK FOR DRUG INTERACTIONS. ATRIPLA®: No studies regarding stability of split or crushed tablets. Splitting or crushing is not recommended. Efavirenz not soluble in water. (Email communication, Gilead, May 2008)
Etravirine (ETR, Intelence®, TMC 125)	
Dose	<p><u>Neonatal/ Infant/ Pediatric:</u></p> <ul style="list-style-type: none"> Not approved for use. <p><u>Adult:</u></p> <ul style="list-style-type: none"> 200 mg po BID
How Supplied/	<ul style="list-style-type: none"> 100mg tablets

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Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Storage	<ul style="list-style-type: none"> Tablets sensitive to moisture. Store in original container with desiccant at room temperature.
Food Restrictions	<ul style="list-style-type: none"> Take with food.
Comments	<ul style="list-style-type: none"> Inducer of CYP3A4; Inhibitor of CYP2C9/2C19. CHECK FOR DRUG INTERACTIONS. May disperse tablets in a small amount of water, stir, and consume immediately. Rinse glass with water several times and swallow rinses to ensure entire dose consumed.

Nevirapine (VIRAMUNE®, NVP)

Dose	<p><u>Newborn perinatal prophylaxis:</u></p> <ul style="list-style-type: none"> <u>Single Dose:</u> Mother received nevirapine more than 1 hour prior to delivery: 2 mg/kg/dose po x 1 dose given at 48-72 hours of age <u>2-Dose:</u> Mother received nevirapine less than 1 hour prior to delivery: 2 mg/kg/dose po X 2 doses – the 1st dose given immediately after birth, the 2nd dose at 48-72 hours of age. <p><u>Pediatric:</u></p> <p><u>less than 8 years:</u></p> <ul style="list-style-type: none"> 200 mg/m²/dose po once daily x 14 days, then 200 mg/m²/dose po BID (if no rash or ADRs; maximum 200 mg per dose) <p><u>more than 8 years:</u></p> <ul style="list-style-type: none"> 120-150mg/m²/dose po once daily X 14 days, then 120-150mg/m²/dose po BID (if no rash or ADRs; maximum 200mg per dose) <p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> 200 mg po BID (Note: Initiate dose at 200 mg once daily x 14 days then increase dose to 200 mg po BID) 400 mg po once daily also being investigated <i>Nevirapine in combination with maraviroc:</i> 200 mg NVP BID plus MVC 300 mg BID
How Supplied/ Storage	<ul style="list-style-type: none"> 10 mg/mL sweet flavored syrup (240 mL bottle). Available through Special Access program¹. Store at room temperature. 200 mg tablet
Food Restrictions	May take with or without food.
Comments	<ul style="list-style-type: none"> Do not increase dose if rash occurs within 1st 14 days. May crush tablets, mix in water and give orally or by G-tube. Induces CYP450 3A4 – may need to increase dose of other drugs metabolized by P450 enzymes in the liver. CHECK FOR DRUG INTERACTIONS. If nevirapine dosing is interrupted for > 7 days, should be restarted with once daily dosing for 14 days followed by dose escalation. When switching from efavirenz to nevirapine, the 14-day escalation of nevirapine is not required. Full doses of nevirapine can be used as of the first day.

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Protease Inhibitors (PIs)

Atazanavir (Reyataz®, ATV)

Dose	<p><u>Neonatal/infant:</u></p> <ul style="list-style-type: none"> • Not approved for use. • Should not be administered to infants less than 3 months due to risk associated with hyperbilirubinemia. <p><u>Pediatric (6-18 years):</u></p> <ul style="list-style-type: none"> – 15 to < 25 kg: Atazanavir 150 mg/ritonavir 80 mg po once daily – 25 to < 32 kg: Atazanavir 200 mg/ritonavir 100 mg po once daily – 32 to < 39 kg: Atazanavir 250 mg/ritonavir 100 mg po once daily – > 39 kg: Atazanavir 300 mg/ritonavir 100mg po once daily – > 13 years and > 39 kg (treatment naïve): May use atazanavir 400 mg once daily (if cannot tolerate ritonavir) <p><u>Adult/Adolescent (16 years or older):</u></p> <ul style="list-style-type: none"> • <i>Antiretroviral naïve:</i> 400 mg po once daily • <i>Antiretroviral experienced:</i> 300 mg atazanavir/100 mg ritonavir both po once daily • <i>Atazanavir in combination with efavirenz:</i> 400 mg atazanavir/100 mg ritonavir both po once daily (<i>naïve only</i>) • <i>Atazanavir in combination with tenofovir:</i> 300 mg atazanavir/100 mg ritonavir both po once daily • <i>Atazanavir in combination with maraviroc:</i> 300 mg atazanavir/100 mg ritonavir both po once daily plus MVC 150 mg BID
How Supplied/Storage	<ul style="list-style-type: none"> • 100, 150, 200, and 300 mg capsules • 50 mg/1.5 g dispersible oral powder (180 g/bottle) – investigational use only in Europe
Food Restrictions	Take with food.
Comments	<ul style="list-style-type: none"> • Antacids and buffered medications (including ddl buffered tablets) decrease ATV concentrations if taken at the same time – space by 1 – 2 hours. • H₂ receptor antagonists decrease ATV levels. If given concurrently, separate by 12 hours or use boosted atazanavir. • Coadministration of atazanavir and proton pump inhibitors is NOT recommended. • Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.

Darunavir (TMC 114, Prezista®, DRV)

Dose	<p><u>Neonatal/ Infant:</u></p> <ul style="list-style-type: none"> • Not approved for use. <p><u>Pediatric (6 years and older):</u></p> <ul style="list-style-type: none"> • ≥ 20 kg-< 30 kg: 375mg DRV/50mg RTV po BID • ≥ 30 kg-< 40 kg: 450mg DRV/60mg RTV po BID • ≥ 40kg: 600mg DRV/100mg RTV po BID <p><u>Adult/Adolescent (18 years or older):</u></p> <ul style="list-style-type: none"> • 600 mg darunavir/100 mg ritonavir po BID • 800 mg darunavir/100mg ritonavir po daily (ARV-naïve patients only)
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Pediatric/Neonatal Doses of Antiretroviral Drugs

Protease Inhibitors (PIs)	
	<ul style="list-style-type: none"> <i>Darunavir in combination with maraviroc</i>: 600 mg DRV/100 mg RTV BID plus MVC 150 mg BID
How Supplied/Storage	<ul style="list-style-type: none"> 400 mg, 600 mg tablets 75 mg pediatric tablet
Food Restrictions	Take with food.
Comments	<ul style="list-style-type: none"> Darunavir contains a sulfa moiety. The potential cross-sensitivity with other sulfa drugs is unknown – caution in patients with sulfonamide allergy. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS. No data available on chewing or crushing. No problems anticipated if tablets chewed or crushed for administration through a nasogastric (NG) tube (Data on file, Tibotec, May 2008)
Fosamprenavir (TELZIR®, f-APV)	
Dose	<p><u>Neonatal/Infant:</u></p> <ul style="list-style-type: none"> Not approved for use. <p><u>Pediatric (2-18 years):</u></p> <ul style="list-style-type: none"> <i>Antiretroviral naïve:</i> <ul style="list-style-type: none"> 2-5 years: 30mg/kg f-APV (max 1400mg) BID >6 years: 30mg/kg f-APV (max 1400mg) BID or 18mg/kg f-APV (max 700mg)/3mg/kg RTV (max 100mg) BID <i>Antiretroviral experienced (> 6 years):</i> 18mg/kg f-APV (max 700mg)/3mg/kg RTV (max 100mg) BID <p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> <i>Antiretroviral naïve:</i> <ul style="list-style-type: none"> 1400 mg po BID (no ritonavir) 1400 mg f-APV /100-200 mg RTV, both po once daily 700 mg f-APV /100 mg RTV, both po BID <i>Protease-inhibitor experienced:</i> 700 mg f-APV/100 mg RTV, both po BID <i>Fosamprenavir in combination with maraviroc:</i> 700mg f-APV/100 mg RTV BID plus MVC 150mg BID
How Supplied/Storage	<ul style="list-style-type: none"> 700 mg tablet (prodrug, equivalent to 600 mg amprenavir) 50 mg/mL oral suspension (225 mL bottle) [calcium prodrug, equivalent to 43 mg/mL amprenavir]. Contains 0.6% propylene glycol. Store suspension between 2-30°C. Discard 28 days after opening. Shake well.
Food Restrictions	<ul style="list-style-type: none"> Tablets may take with or without food. Oral suspension should be taken on an empty stomach (1 hr before or 2 hours after food) in adults. Oral suspension should be given with food in pediatric patients.
Comments	<ul style="list-style-type: none"> Fosamprenavir calcium tablets and suspension are equivalent on a mg per mg basis. APV is a sulfonamide. In pivotal studies there was no evidence of increased rash in patients with a history of sulfonamide allergy. Caution in patients with sulfonamide allergy. The suspension contains propyl and methyl hydroxybenzoate which may cause allergic reactions (delayed in some cases). Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.

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Protease Inhibitors (PIs)

- No data available regarding stability of crushed or dissolved tablet.

Indinavir (CRIXIVAN®, IDV)

Dose	<p><u>Neonatal/Infant:</u></p> <ul style="list-style-type: none"> Not approved for use. Do NOT give due to risk of hyperbilirubinemia <p><u>Pediatric:</u></p> <ul style="list-style-type: none"> Not approved for use. Investigation dose under study (children 4-15 years): 500 mg/m²/dose po q 8 hrs <p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> 800 mg po q8h (or 800 mg IDV/100-200 mg RTV po BID)
How Supplied/Storage	<ul style="list-style-type: none"> 200 and 400 mg capsules. Capsules sensitive to moisture. Store in original container with desiccant at room temperature. 10 mg/ml glass bottle, refrigerate, 14 days (complex compounding formulation³)
Food Restrictions	<ul style="list-style-type: none"> Give on an empty stomach or may give with milk, juice or light snack. When given with RTV, can be taken with or without food.
Comments	<ul style="list-style-type: none"> Can open capsule and mix with water. Very unpalatable, tastes bitter. Drink plenty of liquids (recommended for adults 1.5 L/day). Separate from ddl by at least 1 hour. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.

Lopinavir/ Ritonavir (KALETRA®, LPV/RTV)

Dose	<p><u>Neonatal/Infant <6 months:</u></p> <ul style="list-style-type: none"> <i>Without NVP or EFV:</i> 16 mg/kg LPV BID or 300 mg LPV/m²/dose po BID (Plasma levels among patients 14 days to 6 months were lower than those observed in adults or in older children) Kaletra is not recommended in combination with nevirapine, efavirenz, fosamprenavir, or nelfinavir in patients <6 months of age. <p><u>Pediatrics (6 months – 18 years):</u></p> <ul style="list-style-type: none"> <i>Without NVP or EFV:</i> <ul style="list-style-type: none"> less than 15 kg: 12 mg/kg LPV/3 mg/kg RTV po BID (approx. 230mg/m² LPV /57.5mg/m² RTV/dose) 15 to 40 kg: 10 mg/kg LPV/2.5 mg/kg RTV po BID (approx. 230mg/m² LPV /57.5mg/m² RTV/dose) More than 40 kg: 400 mg LPV/100 mg RTV po BID <i>With NVP or EFV:</i> <ul style="list-style-type: none"> less than 15 kg: 13 mg/kg LPV/3.25 mg/kg RTV po BID (approx. 300mg/m² LPV/75mg/m² RTV/dose) 15-45 kg: 11 mg/kg LPV/2.75 mg/kg RTV po BID More than 45 kg: 600 mg LPV/150 mg RTV po BID tablets or 533mg bid LPV solution
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	<p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> • <i>Without NVP or EFV:</i> <ul style="list-style-type: none"> – > 12 years: 400 mg LPV /100 mg RTV po BID (2 tablets po BID) – > 18 years: 800 mg LPV/200 mg RTV po once daily (4 tablets po daily) for naïve patients • <i>With NVP or EFV (>12 years):</i> <ul style="list-style-type: none"> – 600 mg LPV/150 mg RTV po BID (3 tablets po BID) in experienced patients – 400 mg LPV/100 mg RTV po BID (2 tablets po BID) in naïve patients <p><i>Kaletra in combination with maraviroc:</i> 400 mg LPV/100 mg RTV BID plus MVC 150 mg BID</p>
How Supplied/Storage	<ul style="list-style-type: none"> • Cotton candy flavored oral solution: 80 mg LPV/20 mg RTV per mL (160 mL bottle). Contains alcohol 42.4% v/v and propylene glycol 153 mg/mL. Solution should be refrigerated until dispensed and then stored up to 42 days at room temperature. • 100 mg lopinavir/25 mg ritonavir pediatric tablet. Tablet should be stored at room temperature. Tablets must be swallowed whole; they cannot be broken, chewed, or crushed. • 200 mg lopinavir / 50 mg ritonavir tablet. Tablet should be stored at room temperature. Tablets must be swallowed whole; they cannot be broken, chewed, or crushed.
Food Restrictions	<ul style="list-style-type: none"> • Solution: Take with food to enhance absorption. • Tablets: Take with or without food.
Comments	<ul style="list-style-type: none"> • Give ddl one hour before or two hours after capsules/solution. • Liquid formulation contains alcohol therefore avoid co-medication with metronidazole. • Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.
Nelfinavir (Viracept®, NFV)	
Dose	<p><u>Neonatal/Infant (less than 6 weeks)</u> <u>ant (less than 6 weeks)</u></p> <ul style="list-style-type: none"> • Alberta Health Services Pediatric Infectious Diseases recommend 50mg/kg/dose PO q 12h for use in the perinatal HIV protocol. • PACTG 353 <ul style="list-style-type: none"> – Not approved for use. – High inter-patient variability seen with 40 mg/kg/dose po BID. – Higher doses under investigation. PACTG 356: 55-75 mg/kg/dose PO q12h. • <u>NICHD/HPTN 040/PACTG 1043:</u> <ul style="list-style-type: none"> – More than 3 kg: 200 mg po BID – 2-3 kg: 150 mg po BID – 1.5-2 kg: 100 mg po BID – Less than 1.5 kg: not studied <p><u>Pediatric (2 – 13 years):</u></p>

Pediatric/Neonatal Doses of Antiretroviral Drugs

	<ul style="list-style-type: none"> 50 mg/kg/dose po BID (range 45 – 55 mg/kg/dose) or 25 – 35 mg/kg/dose po TID <u>Adult/Adolescent:</u> <ul style="list-style-type: none"> 1250 mg po BID or 750 mg po TID
How Supplied/ Storage	250 mg and 625 mg tablets
Food Restrictions	Give with food or shortly after food for optimal absorption.
Comments	<ul style="list-style-type: none"> Tabs: Dissolve a 250 mg tablet in 5 ml of sterile water (50 mg/ml). Measure out dose with a syringe that has 1 ml increments. Round dose of tablets to closest 50 mg. Do not mix with formula. For older children, tablets readily dissolve in water and produce dispersion that can be mixed with milk/chocolate milk. Tablets can be crushed and given with pudding. Tablet may be mixed with food or liquid up to 6 hours (refrigerated) before dose is taken. Do not mix with acidic food/juice (orange or apple juice) due to bitter taste. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.
Ritonavir (NORVIR®, RTV)	
Dose	<u>Neonatal/Infant (less than 1 month):</u> <ul style="list-style-type: none"> Not approved. Investigational dose: 450 mg/m²/dose po bid (associated with lower RTV conc. than observed in adults receiving standard dose.) <u>Pediatric (more than 1 month) dose:</u> <ul style="list-style-type: none"> 350-450 mg/m²/dose po BID (maximum 600 mg po BID). To minimize nausea/vomiting, start 250mg/m²/dose bid and increase at 2-3 day intervals by 50 mg/m²/dose bid until at the full dose. <u>Adult/Adolescent:</u> <ul style="list-style-type: none"> 600 mg BID (should be initiated at 300 mg BID and then titrated to full dose over 5-7 days as tolerated). Used at lower doses as pharmacokinetic enhancer of other PIs (ritonavir boosting).
How Supplied/ Storage	<ul style="list-style-type: none"> 80 mg/mL peppermint/caramel liquid (240 mL bottle). Recommended to be stored at room temperature and to use by product expiration date (limited shelf-life). (43% v/v ethanol) 100 mg soft elastic capsule. Refrigerate until dispensed then stable at room temperature x 30 days. (12% v/v ethanol)
Food Restrictions	Take with food.

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Comments	<ul style="list-style-type: none"> Liquid is unpalatable, bad aftertaste. Tips: <ul style="list-style-type: none"> Mix oral solution with milk/chocolate milk, or pudding. Give after popsicle/frozen juice to dull taste buds. Give after grape jelly, maple syrup, or peanut butter which coats mouth. Give strong flavor after dose: syrup, cheese, chewing gum During encapsulation process, exposure to soya protein lecithin and fractionated coconut oil occurs. As peanut and soy are from the same plant family, some patients allergic to peanuts may also be allergic to soy. Consult an allergist prior to taking capsules. Liquid formulation contains alcohol therefore avoid co-medication with metronidazole. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.
Saquinavir (INVIRASE®, SQV)	
Dose	<p><u>Neonatal/infant:</u></p> <ul style="list-style-type: none"> Not approved for use. <p><u>Pediatric (more than 2 years):</u></p> <ul style="list-style-type: none"> 5 to less than 15 kg: SQV 50 mg/kg/dose + RTV 3 mg /kg/dose po BID 15 to less than 40 kg: SQV 50 mg/kg/dose + RTV 2.5 mg/kg/dose po BID more than 40 kg: SQV 50 mg/kg/dose + RTV 100 mg/dose po BID <p><u>Adult/Adolescent (more than 16 years):</u></p> <ul style="list-style-type: none"> <i>Unboosted (not recommended)</i> <i>Boosted (recommended):</i> 1000 mg SQV/100 mg RTV, both given po BID <i>Saquinavir in combination with maraviroc:</i> 1000 mg SQV/100 mg RTV BID plus MVC 150mg BID
How Supplied/Storage	<ul style="list-style-type: none"> 500 mg tablet (INVIRASE®). Store at room temperature.
Food Restrictions	Take with food to increase absorption (within 2 hours after a full meal).
Comments	<ul style="list-style-type: none"> INVIRASE® should only be used when combined with ritonavir. Hard gel capsule contains powder, so can be opened and sprinkled on food or water, but unpalatable taste. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS.

Pediatric/Neonatal Doses of Antiretroviral Drugs

Protease Inhibitors (PIs)	
Tipranavir (APTIVUS®, TPV)	
Dose	<p><u>Neonatal/Infant:</u></p> <ul style="list-style-type: none"> Not approved. <p><u>Pediatric (2-18 years):</u></p> <ul style="list-style-type: none"> 14 mg/kg TPV/6 mg/kg RTV po BID (375 mg/m² TPV/150 mg/m² RTV) (max. 500 mg TPV + 200 mg RTV BID) For patients with intolerance or toxicity physicians may consider decrease in dose to 12 mg/kg TPV/5 mg/kg RTV po BID (290 mg/m² TPV/115 mg/m² RTV BID) if the virus is not resistant to multiple PIs. <p><u>Adult/Adolescent:</u></p> <ul style="list-style-type: none"> 500 mg TPV/200 mg RTV po BID Tipranavir in combination with maraviroc: 500 mg TPV/200 mg RTV BID plus MVC 300 mg BID
How Supplied/ Storage	<ul style="list-style-type: none"> 250 mg capsule Refrigerate the capsules until dispensed then stable at room temperature x 60 days 100 mg/mL oral solution available in the US only. Note: solution contains 116 IU/mL vitamin E. Store oral solution at room temperature (25°C). Use solution within 60 days of opening the bottle.
Food Restrictions	Take with food.
Comments	<ul style="list-style-type: none"> Indicated for adults who are highly treatment experienced or have resistance to multiple PIs. TPV is a sulfonamide. The potential cross-sensitivity with other sulfa drugs is unknown – caution in patients with sulfonamide allergy. Protease inhibitors are extensively metabolized by as well as inhibit CYP450 3A4. CHECK FOR DRUG INTERACTIONS. Cannot be split or crushed (Verbal communication, Boehringer Ingelheim, May 2008).

Pediatric/Neonatal Doses of Antiretroviral Drugs

Entry and Fusion Inhibitors

Enfuvirtide (Fuzeon®, T-20)

Dose	<p><u>Neonatal/ Infant/ Pediatrics (less than 6 years):</u></p> <ul style="list-style-type: none"> Not approved for use in children less than 6 years. <p><u>Pediatric/Adolescent (6-16 years):</u></p> <ul style="list-style-type: none"> For children 6 years or more: 2 mg/kg/dose twice daily, maximum dose 90 mg (1 mL) twice daily injected subcutaneously into upper arm, anterior thigh, or abdomen. <p><u>Adult/Adolescent (more than 16 years):</u></p> <ul style="list-style-type: none"> 90 mg (1 mL) twice daily injected subcutaneously into the upper arm, anterior thigh, or abdomen.
How Supplied/ Storage	<ul style="list-style-type: none"> Injection: lyophilized powder for injection 108 mg of enfuvirtide, when reconstituted with 1.1 mL sterile water to deliver 90 mg/mL. Convenience kit: 60 single use vials of enfuvirtide (90 mg strength), 60 vials of sterile water for injection, 60 reconstitution syringes (3 mL), 60 administration syringes (1 mL), alcohol wipes Reconstituted vial should be allowed to stand until the powder goes completely into solution (may take up to 45 min). Do not shake. Once reconstituted, enfuvirtide should be injected immediately or stored in the fridge in the original vial until use. Must be used within 24 hrs after reconstitution
Comments	Injection sites should be rotated. Enfuvirtide should not be injected into moles, scar tissue, bruises, or the navel.

Maraviroc (Celsentri®, MVC)

Dose	<p><u>Neonatal/ Infant/ Pediatric/ Adolescent (< 16 years):</u></p> <ul style="list-style-type: none"> Not approved for use in children less than 16 years. <p><u>Adult/Adolescent (≥16 years):</u></p> <ul style="list-style-type: none"> With CYP inhibitor (i.e. protease inhibitors (except TPV), DLV, ketoconazole, itraconazole, clarithromycin): 150 mg MVC po BID Not CYP inducer/inhibitor (i.e. TPV, NVP, T-20, NRTIs): 300 mg MVC po BID With CYP inducer (i.e. EFV, rifampin, carbamazepine, phenobarbital, phenytoin): 600 mg MVC po BID
How Supplied/ Storage	150 mg and 300 mg film-coated tablets. Store between 15-30°C in a USP tight container.
Food Restrictions	Take with or without food.
Comments	<ul style="list-style-type: none"> CYP450 3A and PGP substrate. CHECK FOR DRUG INTERACTIONS. Must have HIV tropism checked to exclude CXCR4/mixed tropic strain. Film coated immediate release tablet however no studies regarding stability of split or crushed tablets. (Verbal communication, Pfizer, May 2008).

Pediatric/Neonatal Doses of Antiretroviral Drugs

Integrase Inhibitors	
Raltegravir (Isentress®, RAL, RGV)	
Dose	<u>Neonatal/ Infant/ Pediatric/Adolescent (<16 years):</u> <ul style="list-style-type: none"> Not approved for use in children less than 16 years. Investigational dose: <ul style="list-style-type: none"> - more than 6 years and more than 25 kg: 400 mg po BID <u>Adult/Adolescent (≥16 years):</u> <ul style="list-style-type: none"> 400 mg RAL po BID
How Supplied/ Storage	400 mg tablet. Store at room temperature (15-30°C) .
Food Restrictions	Take with or without food
Comments	<ul style="list-style-type: none"> Clearance through UGT1A1. CHECK FOR DRUG INTERACTIONS. Crushing tablets not recommended. Granules (sub-units of the tablet) dissolve faster than intact tablets and may result in faster release of drug which could affect in-vivo performance. (Data on file, Merck Frosst, May 2008) Drug has a bitter taste which is masked by the film coating.

Footnotes

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. December 1, 2009; 1-161. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed (Oct 4, 2010).
2. Contact one of the outpatient pharmacies (UAH or RAH) to initiate the ordering process. For nevirapine and stavudine liquids, additional paperwork is required in addition to the special access request forms which are available on the Health Canada website (http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-droques/sapf1_pasf1-eng.php). Special Access Program ph: 613-941-2108.
3. To obtain the Sustiva liquid, call 1-877-372-7097. The Pediatric Research Nurses should be consulted first since appropriate physician/institution documentation must be in place prior to use of the liquid formulation.
4. AJHP 2000;57:1332-9.

References:

- Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. August 16, 2010. (Updated guidelines available at <http://www.aidsinfo.nih.gov/guidelines/>).
- Tseng A, Foisy M. Handbook of HIV Drug Therapy, 2010.

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Re-posted on Regional Pharmacy Services website January 2011.