Table 1. Dosing guidance in children

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| --- | --- | --- | --- | --- | --- | --- |
| Nucleoside reverse transcriptase inhibitor NRTI | Licensing restrictions | Guideline status | Available formulation | Dose from PENTA Guideline1 | Dose from DHHS guideline2 | Dose from WHO dosing annex 20183 |
|  | EMA / FDA |  |  |  |  |  |
| Abacavir (ABC) | ≥3 months/ ≥3 months | WHO:  First line ≥2 weeks  PENTA: First line ≥3 months  if viral load (VL) >100.000 and child >12 years old, ABC is not preferred. | Liquid: 20 mg/ml  Tablets: 300 mg *scored* | Liquid:  <25 kg ≥3 months old: 8 mg/kg BD or 16 mg/kg QD (max dose 600 mg/day)  Tablets:  14-21 kg: 150mg, ½ tablet BD or 1 tablet QD >21-30 kg: ½ tablet AM + 1 tablet PM or 1½ tablet QD  >30 kg: 1 tablet BD or 2 tablets QD (max dose 600 mg/day) | Liquid:  <25 kg ≥3 months old: 8 mg/kg BD or 16 mg/kg QD (max dose 600 mg/day)  Tablets (300 mg):  14 to <20 kg: ½ tablet BD or 1 tablet QD  20 to <14 kg: ½ tablet AM + 1 tablet PM  >25 kg: 1 tablet BD or 2 tablets QD (max dose 600 mg/day) | ABC/3TC 60/30 mg tablets (dispersible)  3-5.9 kg: 2 tablets QD or 1 tablet BD  6-9.9 kg: 3 tablet QD or 1.5 tablets BD  10-13.9 kg: 4 tablets QD or 2 tablets BD  14-19.9 kg: 5 tablets QD or 2.5 tablets BD  20-24.9 kg: 6 tablets QD or 3 tablets BD  ABC/3TC 120/60 mg (dispersible)  3-5.9 kg: 1 tablet QD  6-9.9 kg: 1.5 tablet QD  10-13.9 kg: 2 tablets QD  14-19.9 kg: 2.5 tablets QD  20-24.9 kg: 3 tablets QD  ABC/3TC 600/300 mg tablets  25-34.9 kg: 1 tablet QD  ABC liquid 20 mg/mL  3-5.9 kg: 3 mL BD  6-9.9 kg: 4 mL BD  10-13.9 kg: 6 mL BD |
| Zidovudine (AZT) | Birth /Birth | WHO: First line 0 to <3 years  Alternative in children ≥3 years  PENTA: Alternative <12 years in combination with 3TC.  DHHS:  First line - birth to <6 years  Alternative - ≥6 years | Liquid: 10 mg/ml  Capsules: 100 mg  Dispersible tablets: 60 mg  IV infusion: 10 mg/ml | Child dosing liquid (from birth):  4-9 kg: 12 mg/kg BD  9-30 kg: 9 mg/kg BD  ≥30 kg: 300 mg BD  Child dosing for capsules:  8-13 kg: 100 mg BD  14-21 kg: 100 mg AM + 200 mg PM  22-30 kg: 200 mg BD; (≥30 kg): 300 mg BD | Liquid:  4 to <9 kg: 12 mg/kg BD (max dose: 300 mg/day)  9 to <30 kg: 9 mg/kg BD (max dose: 300 mg/day)  ≥30 kg: 300 mg BD  IV: 120 mg/m2 every 6 hours (QDS)  Dosing for premature newborns  Gestational age <30 weeks:  Oral dose:  Weeks 0 to <4: 2 mg/kg BD  Weeks 4 to <8: 3 mg/kg BD  Weeks 8 to <10: 12 mg/kg BD  For ≥30 to <35 Weeks Gestation at Birth:  Oral dose:  Week 0 to <2: 2 mg/kg BD  Week 2 to <6: 3 mg/kg BD  Week 6 to <8: 12 mg/kg BD  IV dose:  1.5 mg/kg every 6 hours (QDS) | AZT 60 mg tablets (dispersible)  3-5.9 kg: 1 tablet BD  6-9.9 kg: 1.5 tablets BD  10-13.9 kg: 2 tablets BD  14-19.9 kg: 2.5 tablets BD  20-24.9 kg: 3 tablets BD  AZT 300 mg tablets  25-34.9 kg: 1 tablet BD  For children <4 weeks of age:  AZT liquid 10 mg/mL  2-3 kg: 1 mL BD  3-4 kg: 1.5 mL BD  4-5 kg: 2 mL BD |
| Emtricitabine (FTC) | ≥4 months/ Birth | WHO: Second line <10 years, First line >10 years  PENTA: Second line <12 years  First line ≥12 years  DHHS: First line ≥6 years with estimated CrCl ≥30 mL/min | Liquid: 10 mg/ml  Capsules: 200 mg | Liquid  ≥4 months: 6 mg/kg QD (max dose: 240 mg/day)  Capsules  ≥33 kg: 200 mg QD (liquid and capsules not bioequivalent) | Liquid: 0 to <3 months: 3 mg/kg QD (max dose: 240 mg/day)  ≥4 months: 6 mg/kg QD (max dose: 240 mg/day)  ≥33 kg: 240 mg QD  Capsules: ≥33 kg: 200 mg QD (liquid and capsules not bioequivalent) | No dose in annex |
| Lamivudine (3TC) | ≥3 months/ Birth | WHO: First line in all children  PENTA: First line in all children  DHHS:  First line in all children | Liquid: 10mg/ml  Tablets: 150mg s*cored*  300mg, 100mg | Liquid:  Child dosing (≥3 months): 4 mg/kg BD, or 8 mg/kg QD (max 300 mg/day)  Tablets (≥3 years):  14-21 kg: ½ tablet BD or 1 tablet QD  >21-30 kg: ½ tablet AM and 1 tablet PM or 1½ QD  >30 kg: 1 tablet BD or 2 tablets QD | Neonates (≥32 weeks gestation at birth)  Liquid:  0 to <4 weeks: 2 mg/kg BD  4 weeks to <3 months: 4 mg/kg BD  Child dosing (≥3 months):  ≥3 months to 3 years: 5 mg/kg BD (max 150 mg BD)  ≥3 years: 5 mg/kg BD (max 150 mg BD) or 10 mg/kg QD (max 300 mg)  Tablet 150 mg (≥ 3 years):  14 to <21 kg: ½ tablet BD or 1 tablet QD;  21 to <30 kg: ½ tablet AM + 1 tablet PM or 1½ tablet QD  ≥30 kg: 1 tablet BD or 2 tablets QD  Tablet 300 mg (≥12 years):  150 mg BD or 300 mg QD | ABC/3TC 60/30 mg tablets (dispersible)  3-5.9 kg: 2 tablets QD or 1 tablet BD  6-9.9 kg: 3 tablet QD or 1.5 tablets BD  10-13.9 kg: 4 tablets QD or 2 tablets BD  14-19.9 kg: 5 tablets QD or 2.5 tablets BD  20-24.9 kg: 6 tablets QD or 3 tablets BD  ABC/3TC 120/60 mg (dispersible)  3-5.9 kg: 1 tablet QD  6-9.9 kg: 1.5 tablet QD  10-13.9 kg: 2 tablets QD  14-19.9 kg: 2.5 tablets QD  20-24.9 kg: 3 tablets QD  ABC/3TC 600/300 mg tablets  25-34.9 kg: 1 tablet QD  3TC liquid 10 mg/mL  3-5.9 kg: 3 mL BD  6-9.9 kg: 4 mL BD  10-13.9 kg: 6 mL BD  For children <4 weeks of age:  AZT liquid 10 mg/mL  2-3 kg: 0.5 mL BD  3-4 kg: 0.8 mL BD  4-5 kg: 1 mL BD |
| Tenofovir Disoproxil fumarate (TDF) | ≥2 years / ≥2 years | WHO: alternative >3 years  First line ≥10 years  PENTA:  Alternative <12 years old.  First line ≥12 years old  DHHS:  Alternative <12 years old  First line ≥12 years in combination with FTC | Oral powder:  40mg TDF/g  Tablets: 150mg, 200mg, 250mg, 300mg | Child dosing granule (1 scoop (scp) = 40mg)  (≥2 years – 12 years):  10-12 kg: 8 mg/kg QD  10-12 kg: 2 scp QD  12-14 kg: 2.5 scp QD  14-17 kg): 3 scp QD  17-19 kg: 3.5 scp QD  19-22 kg: 4 scp QD  22-24 kg: 4.5 scp QD  24-27 kg: 5 scp QD  27-29 kg: 5.5 scp QD  29-32 kg: 6 scp QD  32-34 kg: 6.5 scp QD  34-35 kg: 7 scp QD  ≥35 kg: 7.5 scp QD  Child dosing tablet (≥2 yrs):  17-22 kg: 150 mg QD  22-28 kg: 200 mg QD  28-35 kg: 250 mg QD  ≥35 kg: 300 mg QD | Child dosing granule (1 scoop (scp) = 40mg)  (≥2 years – 12 years):  10-12 kg: 8 mg/kg QD  10-12 kg: 2 scp QD  12-14 kg: 2.5 scp QD  14-17 kg): 3 scp QD  17-19 kg: 3.5 scp QD  19-22 kg: 4 scp QD  22-24 kg: 4.5 scp QD  24-27 kg: 5 scp QD  27-29 kg: 5.5 scp QD  29-32 kg: 6 scp QD  32-34 kg: 6.5 scp QD  34-35 kg: 7 scp QD  ≥35 kg: 7.5 scp QD  Child dosing tablet (≥2 yrs):  17-22 kg: 150 mg QD  22-28 kg: 200 mg QD  28-35 kg: 250 mg QD  ≥35 kg: 300 mg QD | No dose in annex |
| Tenofovir Alafenamide (TAF) | ≥6 years / ≥6 years in children >35 kg  Or in children >25 kg without a PI | WHO: Not included  PENTA: Not preferred  DHHS: First line for children ≥6 years with estimated CrCl ≥30 mL/min | For HIV only available in combination tablets | Not recommended in children | For HIV only available in fixed dose combination (FDCs) tablets  In combination tablet:  ≥25 kg: 1 tablet QD not to be used with PIs  ≥35 kg: 1 tablet QD | No dose in annex |
| Non-nucleoside reverse transcriptase inhibitor (NNRTI) | Licensing restrictions | Guideline status | Available formulation | Dose from PENTA Guideline1 | Dose from DHHS guideline2 | Dose from WHO dosing annex 20183 |
|  | EMA / FDA |  |  |  |  |  |
| Efavirenz (EFV) | ≥ 3 months/≥ 3 months (weighing at least 3.5 kg) | WHO: First line in children ≥3 years old  PENTA: First line in children ≥3 years old  DHHS: Alternative in children ≥3 years old | Capsule: 50 mg, 200 mg (scored)  Tablet: 600 mg | Child dosing liquid  ≥3-5 years  13-15 kg: 360 mg QD  15-20 kg: 390 mg QD  20-25 kg: 450 mg QD  25-32.5 kg: 510 mg QD  ≥ 5 years  13-15 kg: 270 mg QD  15-20 kg: 300 mg QD  20-25 kg: 360 mg QD  25-32.5 kg: 450 mg QD  32.5-40 kg: 510 mg QD  ≥40 kg: 720 mg (max dose)  Child dosing capsules (≥3 years):  13-15 kg: 200 mg QD  15-20 kg: 250 mg QD  20-25 kg: 300mg QD  25-32.5 kg: 350 mg QD  32.5-40 kg: 400 mg QD  ≥40 kg: 600 mg QD | EFV not recommended for children <3 years old.  Capsules:  (≥3 months to 3 years)  3.5-5 kg: 100 mg QD  5-7.5 kg: 150 mg QD  7.5-10 kg: 200 mg QD  ≥ 3 years  10-15 kg: 200 mg QD  15-20 kg: 250 mg QD  20-25 kg: 300 mg QD  25-32.5 kg: 350 mg QD  32.5-40 kg: 400 mg QD  ≥40 kg: 600 mg QD  Tablets:  ≥40 kg: 600 mg QD | EFV 200mg tablets (scored)  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: 1 tablet QD  14-19.9 kg: 1.5 tablets QD  20-24.9 kg: 1.5 tablets QD  EFV 200 mg tablets  25 - 34.9 kg: 2 tablets QD |
| Nevirapine (NVP) | ≥ birth/15 days | WHO: First line in children <2 weeks  Alternative in children ≥2 weeks  PENTA: First line in children <3 years if unexposed to NVP perinatally and with three NRTI (ABC,3TC, ZDV)  Alternative in children ≥3 years old  DHHS: First line in children aged <2 weeks  Alternative in children 2 weeks to <3 years | Immediate release: tablets: 200 mg  Oral suspension: 10 mg/ml  Extended release (XR) tablet: 100 mg, 400mg | ALL doses of NVP are QD for 14 days then BD (lead-in)  Immediate release (tablets or suspension):  Dosed on BSA:  150-200 mg/m2  Dosed on Weight:  ≥1 month to <8 years: 7 mg/kg (lead-in with 4mg/kg)  >8 years: 4 mg/kg BD (lead in with 4 mg/kg QD)  Extended release tablets (no lead-in with XR tablets) (≥3 years):  0.58-0.83 m2: 200 mg QD  0.84-1.16m2: 300 mg QD  ≥1.17m2: 400mg QD (all patients must initiate therapy with immediate-release formulations for 14 days). | ALL doses of NVP are QD for 14 days then BD (lead-in)  Immediate release (tablets or suspension):  Dosed on BSA:  ≥1 month to <8 years: 150-200 mg/m2  ≥8 years: 120-150 mg/m2  Extended release tablets (no lead-in with XR tablets):  6 to <18 years  0.58-0.83 m2: 2x100 mg QD  0.84-1.16 m2: 3x100 mg QD  ≥1.17 m2: 1x 400 mg QD  Children aged < 1 month; (not FDA approved)  Gestational age 34 – 37 weeks: 4 mg/kg BD for the first week, increasing to 6 mg/kg BD thereafter  Gestational age ≥37 weeks: 6 mg/kg BD | NVP 50 mg tablets (dispersable)  3-5.9 kg: 1 tablet BD  6-9.9 kg: 1.5 tablets BD  10-13.9 kg: 2 tablets BD  14-19.9 kg: 2.5 tablets BD  20-24.9 kg: 3 tablets BD  NVP 200mg tablets  25-34.9 kg: 1 tablet BD  For children <4 weeks of age:  NVP liquid 10 mg/mL  2-3 kg: 1.5 mL BD  3-4 kg: 2 mL BD  4-5 kg: 3 mL BD |
| Rilpivirine (RPV) | ≥12 years/≥12 years | WHO/PENTA:  Not included  DHHS:  Alternative in children >12 years old | Film coated tablet 25 mg | Not recommended in children | Film coated tablet  ≥12 years and 35 kg or more: 25 mg QD | No dose in annex |
| Protease inhibitors (PIs) | Licensing restrictions | Guideline status | Available formulation | Dose from PENTA Guideline1 | Dose from DHHS guideline2 | Dose from WHO dosing annex 20183 |
|  | EMA / FDA |  |  |  |  |  |
| Atazanavir (ATV) | ≥ 3 months (≥ 5 kg)/ ≥ 3 months (≥ 5 kg | WHO:  Alternative in children ≥3 months for 2nd line  PENTA:  First line for children >6 years  DHHS:  First line in children ≥3 years | Oral powder formulation: 50 mg/sachet  Capsules: 150 mg, 200 mg, 300 mg | Boosted atazanavir (≥6 years):  Capsules  15-20 kg: 150 mg + 100 mg ritonavir (RTV) QD  20-40 kg: 200 mg + 100 mg RTV QD  ≥40 kg: 300 mg QD + 100 mg RTV QD | Boosted atazanavir:  (ART naïve and experienced)  Oral powder: (≥ 3 months)  5 to <15 kg: 200 mg + 80 mg RTV QD  15 to <25 kg:250 mg +80 mg RTV QD  Capsules: (≥ 6 years)  15 to <35 kg: 200 mg + RTV 100 mg QD  >35 kg: 300 mg + RTV 100 mg QD  Unboosted atazanavir:(>13 years)  ART naïve only  400 mg QD | ATV 100 mg capsules  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: 2 capsules + 100 mg RTV QD  14-19.9 kg: 2 capsules + 100 mg RTV QD  20-24.9 kg: 2 capsules + 100 mg RTV QD  ATV 200 mg capsules  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: 1 capsule + 100 mg RTV QD  14-19.9 kg: 1 capsule + 100 mg RTV QD  20-24.9 kg: 1 capsule + 100 mg RTV QD  ATV 300 mg tablet  25-34.9 kg: 1 tablet QD |
| Darunavir (DRV) | ≥ 3 years (≥ 15 kg)/  ≥ 3 years (≥ 10 kg) | WHO:  alternative in children ≥3 years for 3rd line  PENTA:  Alternative in children 3 to <12 years  First line in children >12 years  DHHS:  First line in children 3 to <6 years as BD regimen. Alternative in children 6 to <12 years (due to availability of other QD regimens at this age).  First line in children >12 years old as QD regimen | Oral suspension: 100 mg/ml  Tablets: 75 mg, 150 mg, 300 mg, 400 mg, 600 mg, 800 mg. | ART-naïve or ART-experienced:  Child dosing liquid: (≥3 years, ≥10 kg):  10-11 kg: 200 mg BD + 32mg RTV BD  11-12 kg: 220 mg BD + 32mg RTV BD  12-13 kg: 240 mg BD + 40mg RTV BD  13-14 kg: 260 mg BD + 40mg RTV BD  14-15 kg: 280 mg BD + 48mg RTV BD  15-30 kg: 380 mg BD + 50mg RTV BD  30-40 kg: 460 mg BD + 60mg RTV BD  ≥40 kg: 600 mg BD + 100mg RTV BD  Child dosing tablets (≥3 years):  15-30 kg: 375 mg BD + 50 mg RTV BD  30-40 kg: 450 mg BD + 60 mg RTV BD  ≥40 kg: 600 mg BD + 100 mg RTV BD | ART-naïve or ART-experienced:  Suspension (≥3 years, ≥10 kg):  10 to <11 kg: 200 mg BD + 32 mg RTV BD  11 to <12 kg: 220 mg BD + 32 mg RTV BD  12 to <13 kg: 240 mg BD + 40 mg RTV BD  13 to <14 kg: 260 mg BD + 40 mg RTV BD  14 to <15 kg: 280 mg BD + 48 mg RTV BD  Suspension/tablets (≥3 years, ≥15 kg):  Twice-daily  15 to <30 kg: 375 mg DRV + 48 mg RTV BD  30 to <40 kg: 450 mg DRV + 60 mg RTV BD  No darunavir resistance-associated mutations  ≥40 kg: 800 mg DRV + 100 mg RTV QD  With ≥1 DRV resistance-associated mutations  ≥40 kg: 600 mg DRV + 100 mg RTV BD | DRV 75 mg tablet  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: 5 tablets BD  20-24.9 kg: 5 tablets BD  DRV 400 mg tablet  25-34.9 kg: 1 tablet BD  DRV 150 mg tablet  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: 4 tablets QD  20-24.9 kg: 4 tablets QD  DRV 600 mg tablet  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: 1 tablet QD  20-24.9 kg: 1 tablet QD  25-34.9 kg: 1 tablet QD  DRV liquid 100 mg/mL  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: 2.5 mL BD  20-24.9 kg: .3.5 mL BD  25-34.9 kg: -  RTV with QD DRV: 100 mg RTV tablet  RTV with BD DRV:  <15 kg: 0.5 mL RTV liquid 80 mg/mL (40 mg)  15-30 kg: 25 or 50 mg RTV tablets |
| Lopinavir (LPV) | ≥2 weeks | WHO:  Alternative regimen for children for whom an approved DTG dose is available. First line in children for whom an approved DTG dose is not available.  PENTA:  First line for children <6 years  Alternative for children >6 years  DHHS:  First line in children 14 days to <3 years  Alternative in children 3 to <12 years | Oral solution:  LPV/r 80/20 mg/ml  Tablets:  LPV/r 100/25 mg, 200/50 mg | Oral solution:  Dosed on BSA:  14 days to <6 months: 300/75 mg/m2 BD (max 400/100 BD)  6 months to <18 years: 230/57.5 mg/m2 BD (max 400/100 BD)  Dosed on weight:  14 days to <6 months: 16/4 mg/kg BD (max 400/100 BD)  6 months to <18 years: 10/2.5 mg/kg BD (max 400/100 BD)  Tablets:  15 to <25 kg: 200/50 mg BD  25 to <35 kg: 300/75 mg BD  >35 kg: 400/100 mg BD  With EFV/NVP:  Oral solution:  6 months to <18 months: 300/75 mg/m2 BD  Tablet:  15 to <20 kg: 200/50 mg BD  20 to <30 kg: 300/75 mg BD  30 to <45 kg: 400/100 mg BD  >45 kg: 500/125 mg BD | Oral solution:  Dosed on BSA:  ART-naïve or ART-experienced:  14 days to <12 months: 300/75 mg/m2 BD (max 400/100 BD)  ART naïve only:  1 to <18 years: 230/57.5 mg/m2 BD (max 400/100 BD)  Dosed on weight:  14 days to <12 months: 16/4 mg/kg BD (max 400/100 BD)  1 to <18 years:  <15 kg: 13/3.25 mg/kg  >15 kg: 10/2.5 mg/kg BD (max 400/100 BD)  Tablets:  Target mg/m2 230 mg/m2 (ART-naïve only):  15 to <20 kg: 200/50 mg BD  20 to <25 kg: 200/50 mg BD (230 mg/m2)  25 to <30 kg: 300/75 mg BD  30 to <35 kg: 300/75 mg BD  35 to 45 kg: 400/100 BD  >45 kg: 400/100 mg BD  Target mg/m2 300 mg/m2:  15 to <20 kg: 200/50 mg BD  20 to <25 kg: 300/75 mg BD (300 mg/m2)) 25 to <30 kg: 300/75 mg BD  30 to <35 kg: 400/100 BD  35 to 45 kg: 400/100 BD  >45 kg: 400/100 mg BD or 500/100 BD  With EFV/NVP:  12 months to <18 years: 300/75 mg/m2 BD | LPV/r 100/25 mg tablet  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: 2 tablets AM, 1 tablet PM  14-19.9 kg: 2 tablets BD  20-24.9 kg: 2 tablets BD  25-34.9 kg: 3 tablets BD  LPV/r 40/10 mg pellets  3-5.9 kg: 2 tablets BD  6-9.9 kg: 3 tablets BD  10-13.9 kg: 4 tablets BD  14-19.9 kg: 5 tablets BD  20-24.9 kg: 6 tablets BD  LPV/r liquid 80/20 mL  3-5.9 kg: 1 mL BD  6-9.9 kg: 1.5 mL BD  10-13.9 kg: 2 mL BD  14-19.9 kg: 2.5 mL BD  20-24.9 kg: 3 mL BD  For children 2 to <4 weeks of age:  2-3 kg: 0.6 mL BD  3-4 kg: 0.8 mL BD  4-5 kg: 1 mL BD |
| InSTI | Licensing restrictions | Guideline status | Available formulation | Dose from PENTA Guideline | Dose from DHHS guideline | Dose from WHO dosing annex 20183 |
|  | EMA / FDA |  |  |  |  |  |
| Dolutegravir (DTG) | ≥ 6 years (≥15 kg) /≥ 30 kg | WHO: First line in children for whom an approved dose is available  PENTA:  Alternative regimen children >12 years  DHHS:  First line in children >30 kg | Solid film coated Tablets: 50 mg, 25 mg, 10 mg | Without integrase resistance:  ≥ 12 years and ≥40 kg: 50mg QD  With integrase resistance: 50 mg BD | InSTI naïve  Tablets:  30 kg to <40 kg: 35 mg QD  >40 kg: 50 mg QD  (InSTI naïve with UGT1a/Cyp3A inducers)  >40 kg: 50 mg BD  (InSTI experienced or with suspected INTSI resistance)  >40 kg: 50 mg BD | DTG 25 mg tablets  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: -  20-24.9 kg: 2 tablets QD\*  DTG 50 mg tablets  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: -  20-24.9 kg: 1 tablet QD\*  25-34.9 kg: 1 tablet QD |
| Elvitegravir  (EVG) | >12 years old | WHO/PENTA:  not included  DHHS:  First line in children >12 years  Alternative in children 6 to <12 years | Film coated tablets: 150 mg  (150/150/200/10 EVG/cobicistat/3TC /TAF) | Not recommended in children | Adult film coated tablet:  >25 kg: 150 mg (1 tablet) | No dose in annex |
| Raltegravir (RTG) | Birth/Birth | WHO:  Preferred regimen for neonate  Alternative for older children for whom an approved DTG dose is not available  PENTA:  Alternative regimen children >12 years  DHHS:  First line in children from birth to <6 years  Alternative in children >6 years | Film coated tablet: 400 mg, 600mg  Chewable tablet: 25 mg, 100 mg *scored*  Granules for Suspension: 20 mg/ml  NB. Suspension and chewable tabs are not bioequivalent to film-coated tabs. | Child dosing chewable tab:  11 to <14 kg: 75 mg BD  14 to <20 kg: 100 mg BD  20 to <28 kg: 150 mg BD  28 to <40 kg: 200 mg BD  ≥40 kg: 300 mg BD  Film coated tab (≥6 years and >25 kg or ≥12 years):  400 mg BD | Oral suspension:  Birth to < 1 week:  2 to <3 kg: 4 mg QD  3 to <4 kg: 5 mg QD  4 to <5 kg: 6 mg QD  1 to < 4 weeks  2 to < 3 kg: 8 mg BD  3 to < 4 kg: 10 mg BD  4 to < 5 kg: 15 mg BD  Aged ≥4 weeks:  3 to <4 kg: 25 mg BD  4 to <6 kg: 30 mg BD  6 to <8 kg: 40 mg BD  8 to <11 kg: 60 mg BD  11 to <14 kg: 80 mg BD  14 to <20 kg: 100 mg BD    Child dosing chewable tab:  11 to <14 kg: 75 mg BD  14 to <20 kg:100 mg BD  20 to <28 kg: 150 mg BD  28 to <40 kg: 200 mg BD  ≥40 kg: 300 mg BD  Film coated tab (≥6 years and >25 kg or ≥12 years):  400 mg BD | RTG 25 mg tablets (chewable)  3-5.9 kg: 1 tablet BD  6-9.9 kg: 2 tablets BD  10-13.9 kg: 4 tablets BD  14-19.9 kg: 5 tablets BD  20-24.9 kg: 6 tablets BD  RTG 100 mg tablets (chewable)  3-5.9 kg: -  6-9.9 kg: -  10-13.9 kg: -  14-19.9 kg: 1 tablet BD  20-24.9 kg: 1.5 tablets BD  RTG 400 mg tablet  25-34.9 kg: 1 tablet BD  RTG liquid 10 mg/mL  3-5.9 kg: 3 mL BD  6-9.9 kg: 5mL BD  10-13.9 kg: 8mL BD  14-19.9 kg: 10 mL BD  20-24.9 kg: -  For children <1 weeks of age:  2-3 kg: 0.4 mL QD  3-4 kg: 0.5 mL QD  4-5 kg: 0.7 mL QD  For children 1 to <4 weeks of age:  2-3 kg: 0.8 mL BD  3-4 kg: 1 mL BD  4-5 kg: 1.5 mL BD |

\*: At the time of writing, this dose is based on predicted exposures derived from PK results from the Odyssey4,5 and IMPAACT 10936 trials  
EMA: European Medicines Agency

FDA: US-Food and Drug Administration

PENTA: Pediatric European Network for treatment of Aids

DHHS: Department of Health and Human Services

WHO: World Health Organization

NRTI: nucleoside (/nucleotide) reverse transcriptase inhibitors

NNRTI: non-nucleoside reverse transcriptase inhibitors

PI: protease inhibitors

InSTI: integrase strand transfer inhibitors  
VL: viral load

PM: in the evening  
AM: in the morning

QD: dosed once daily  
 BD: dosed twice daily  
 QDS: dosed four times daily (dosed every 6 hours)  
Scp: Scoop (a scoop measuring 40 mg of pediatric TDF granules)

Table 2. Pharmacokinetic studies of NNRTIs in HIV infected pediatric patients

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Efavirenz (EFV)** | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | | **Population** | | | **Age (years, unless stated differently)** | | | **BSA (m2)** | | | **Weight (kg)** | | | **Suppression rates**  **(%)** | | **AUC** | | **C trough (mg/l)** | | **Cmax (mg/l)**  **Or C mid-dose interval**  **(CMDI)** |
| EFV once-daily |  | |  | | |  | | |  | | |  | | |  | | AUC0-24 (h\*mg/L) | |  | |  |
| Star et al 2002.7,8 | EFV Liquid formulation in combination with nelfinavir QD  Dose = (subject weight in kg/70)0.7 x 720 mg  Mean dose: 284 mg/day | | N=488  ART naive and experienced  3 to <10 years old | | | Median (range):  5.1 (3.1 – 9.6) 8 | | | Not reported | | | Not reported | | | 63% VL <400 copies/mL at week 48  58% VL <50 copies/mL  At week 48 | | Mean (SD):  68.818 (±32.831)9 | | Mean (SD):  1.768 (1.294)8 | | Mean (SD):  4.483 (1.831)8 |
| Von Hentig et al. 2006.9 | EFV capsules QD  Dose ranged between 375 and 480 mg/m2 (12.5 and 17.0  mg/kg body weight) | | N=11,  NNRTI naive children  4 to <10 years old  Weighing >13 kg | | | Median (range):  8.7 ( 4.3 - 12.0) | | | Median (range)  1.01 (0.72 – 1.51) | | | Median (range):  25 (16 -50) | | | 80% VL <50 copies/mL10 | | Mean (range):  63.608 (44.222 – 82.989) | | Mean (range):  1.293 (0.889 -1.697) | | Mean (range):  5.552 (3.951-7.153) |
| Ren et al 2007.11 | EFV capsule formulation QD  13to <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 | | N=15,  Information on prior ART use was not reported  3-15 years, weighing >10 kg | | | Median (SD):  7.2 (2.7) | | | Not reported | | | Median (SD):  19.4 (4.2) | | | 67% VL <50 copies/mL after at least 6 months of ART | | Not reported | | Median (IQR):  1.18 (0.46–  1.70) | | Median (IQR)  **CMDI**:  1.58 (0.67-2.20) |
| Fletcher et al. 200812 | EFV capsules dosed in combination with nelfinavir QD  Initial dose:  child dose (mg/day) =(child weight in kg/70 kg) 0.7 × 600 mg/day. Rounded off to the nearest 25 mg increment dose.  Median dose (SD) [CV%]  Week 2:  12 mg/kg (1.4)[12%]  Week 56:  13 mg/kg (5) [36%] | | N=50,  At week 2  N=34,  At week 56 (after dose adjustment)  3 to <16 years at initiation, NNRTI and PI based ART-naive. | | | Median (range):  Week 2  7 (3-16)  Week 56  8 (5–17) | | | Median (range):  Week 2  0.9 (0.6-2.1)  Week 56  1 (0.7 - 2.0) | | | Median (range):  Week 2  24 (13.4-98.0)  Week 56  26.2 (16.6–93.7) | | | 81% VL <400 copies/mL at week 48  70% VL <50 copies/mL at week 48 | | Median (SD)[CV%]:  Week 2  60 (58) [77%]  Week 56  60 (33) [59%] | | Median (SD)[CV%]:  Week 2  1.45 (2.16)  [103.1%]  Week 56  1.30 (1.27) [77.3%] | | Median (SD)[CV%]  Cmax:  Week 2  4.09 (2.67) [58.3]  Week 56  4.55 (1.73) [39.5] |
| Wintergerst et al. 200813 | EFV dose median(range):  Dose in mg  300 mg (200–800)  Dose in mg/kg  13.3 (9.7–22.5)  EFV capsule formulation QD  13to <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 | | N=33,  ART experienced and naive children  No age or weight limit reported. | | | Median (range):  8.2 (2.1–16.7) | | | Not reported | | | Median (range):  24 (12–62) | | | 81.1% VL <50 copies/mL treated under TDM  (intend to treat) | | Not reported | | Not reported | | Not reported |
| Hirt et al. 200914 | EFV capsules 200 mg  EFV capsule formulation QD  13 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  Average dose:  250 mg | | N=48,  ART naive  30 months to <15 years old  Weighing at least 10 kg | | | Median (range):  6.35 (2.77–14.70) | | | Not reported | | | Median (range):  16.4 (11–37) | | | 86% VL <400 copies/mL with AUC >49h\*mg/L  At week 8  50% VL <400 copies/mL with AUC <49h\*mg/L  At week 8 | | Median (no range reported):  65.2 | | Median (no range reported):  1.64 | | Median Cmax (no range reported):  3.71 |
| Ren et al. 200915 | EFV capsule formulation QD  13to <15 kg: 200 mg  15 to <20 kg: 250mg  20 to <25 kg: 300 mg  25 to <32.5 kg: 350 mg  32.5 to <40 kg: 400 mg  >40 kg: 600 mg  After rifampicin-based therapy  Dose mg/kg Median (IQR):  14.0 (12.8–14.5) | | N= 15,  Receiving EFV based therapy after TB treatment with rifampicin,  aged 3–15 years and weighing >10 kg | | | Median (IQR):  7.1 (5.7–9.2) | | | Not reported | | | Median (IQR):  20.5 (17.3–24.8) | | | 81.1% VL <50 copies/mL treated under TDM  (intend to treat) | | Not reported | | Median (IQR):  0.86 (0.61–3.56) | | Median (IQR)  **CMDI**:  1.23 (0.85 -4.18) |
| Pavia-Ruz et al. 201516 | EFV Oral solution 30 mg/ml (QD)  EFV capsule sprinkles QD,  Dose Oral solution  Groups 1-3  <10 kg: 390 mg  10 <17 kg: 600 mg  Groups 4  10 to <15 kg: 360 mg  15 to <20 kg: 390 mg  20 to <25 kg: 450mg  25 to <32.5 kg: 510 mg  32.5 to <40 kg: 630mg  >40 kg: 720 mg  Dose capsule sprinkles:  Groups 1-2  <10 kg: 300 mg  10 to <17 kg: 400 mg  Group 3  <10 kg:400 mg  10 to <17 kg: 600 mg  Group 4  <10 kg: 150 mg  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: 600mg | | N=37,  ART naive and experienced  3 months to <6 years  Group 1: N=15 (3 -<6 months)  Group 2: N=10 (26 months - <2 years)  Group 3: N=4 (2 -<3 years)  Group 4: N=8 (3 -<6 years) | | | Median (IQR):  All children  0.663 (0.430–2.324)  Group 1:  0.392 (0.334–0.441)  Group 2:  0.825 (0.608–1.851)  Group 3:  2.313 (2.198–2.660)  Group 4:  3.922 (3.543–4.786) | | | Not reported | | | Not reported | | | 77.8% Vl <400 copies/mL at week 48  63.0% VL <50 copies/mL at week 48 | | Median (CV%):  Oral solution  Group 1:  130 (98%)  Group 2:  71.4 (49%)  Group 3:  93.8 (68%)  Group 4:  131 (98%)  Capsule sprinkles  Group 1:  353 (68%)  Group 3 (N=1):  742 (N/A) | | Median (CV%):  Oral solution  Group 1:  0.391 (141%)  Group 2:  0.445 (57%)  Group 3:  0.648 (7%)  Group 4:  1.185 (111%)  Capsule sprinkles  Group 1:  2.229 (103%)  Group 3 (N=1):  5.650 (N/A) | | Median (CV%) Cmax::  Oral solution  Group 1:  3.790 (76%)  Group 2:  1.998 (51%)  Group 3:  2.167 (68%)  Group 4:  2.632 (83%)  Capsule sprinkles  Group 1:  10.543 (45%)  Group 3 (N=1):  14.400 (N/A) |
| Moore et al. 201717 | ~1600mg \*(weight in kg/70)0.7  rounded for weight  band dosing  Dose increased after week 2 PK exposure measurement if below target range.  capsule formulation QD | | N=47,  Aged 3 to 36 months  ART naive  Group:  1A: N=22  1B: N=16  2A: N=7  2B: N=2  Group 1: Extensive metabolizers  Group 2: Slow metabolizers  Group A: aged 3-24 months  Group B: aged 24 – 36months | | | Median (IQR):  All children  19 months (13–27)  Group 1: 19 (13- 27)  Group2: 20 (18-26) | | | Not reported | | | Not reported | | | 82% [95% CI (68 - 92)] VL< 400 copies/mL and <1 log10 decrease in VL from baseline | | Median (IQR):  Extensive metabolisers  Group 1A:  108.58  (58.85- 135.92)  Group 1B:  106.84  (35.55- 132.17)  Poor metabolizers  Group 2A:  490.20  (339.48- 650.25)  Group 2B:  83.11  (63.71-102.50) | | Median (IQR):  Extensive metabolisers  Group 1A:  1.80  (1.01- 2.48)  Group 1B:  2.63 (0.83- 3.74)  Poor metabolizers  Group 2A:  20.78  (12.29- 24.25)  Group 2B:  3.11  (2.18- 4.03) | | Median (IQR) Cmax::  Extensive metabolisers  Group 1A  9.19  (6.02, 10.72)  Group 1B  7.53  3.49, 10.25  Poor metabolizers  Group 2A  21.85  18.37, 33.39  Group 2B  4.78  4.48, 5.07 |
| Adult data8 | EFV 600 mg QD | |  | | |  | | |  | | |  | | |  | | Mean (SD):  58.148 (23.013) | | Mean (SD):  1.768 (1.010) | | Mean (SD):  4.072 (1.168) |
| **Nevirapine (NVP)** | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | | | **Population** | | | | **Age (years, unless stated differently)** | | **BSA (m2)** | **Weight(kg)** | | | **Suppression rates**  **(%)** | | | **AUC** | | **Ctrough**  **(mg/L)** | | **Cmax (mg/L)** |
| NVP twice-daily |  | | |  | | | |  | |  |  | | |  | | | AUC0-12 (h\*mg/L) | |  | |  |
| Chokephaibulkit et al. 2005 18 | Median dose (SD)  164 (27) mg/m2 BD  In adult fixed dose combination tablets containing 200mg NVP | | | ART naive and experienced children taking adult fixed dose combination  N=34 (14 ART naive) | | | | Median (range):  8.4 (3–15) | | Not reported | Not reported | | | Naive:  92% VL <400 copies/mL after 26 weeks  Experienced: Not reported | | | Median (range):  78.4  (50 – 306.6) | | Median (range):  Cmin  5.98 (2.57-24.37) | | Not reported |
| King et al. 2005 19 | Capsule and liquid formulation  120 mg/m2 BD,  Median dose mg/kg (range):  4.4 (2.2–5.5) | | | N=20 (PK study: N=10)  5 months – 21 years old  ART experienced and virologically suppressed | | | | Median (range):  7.0 (0.4–20.8) | | Not reported | Median (range):  22.8 (8–126.4) | | | 28% retained VL <400 copies/mL | | | Median (range):  41.8 (25.4–102.4) | | Median (range):  2.2 (1.4–7.6) | | Median (range):  5.1 (3.1–10.9) |
| L’Homme et al. 200820 | Mean (range):  370 (317, 486) mg/m2/day  3 to <6 kg: 100 mg NVP In two doses  6 to <10 kg: 150 mg NVP in two doses  10 to <15 kg: 200 mg NVP in two doses  15 to <20 kg: 250 mg NVP in two doses  20 to <25 kg: 300 mg NVP in two doses  25 to <30 kg: 400 mg NVP in two doses | | | 3 to <6 kg: N=2  6 to <10 kg: N=13  10 to <15 kg: N=9  15 to <20 kg: N=19  20 to <25 kg: N=12  25 to <30 kg: N=10  Naive children  Aged 3 months to <14 years | | | | Mean (range):  All children:  6.9 (0.5, 14.9)  3 to <6 kg:  0.8 (0.7, 0.8)  6 to <10 kg:  1.3 (0.5, 4.2)  10 to <15 kg:  5.2 (2.2, 6.8)  15 to <20 kg:  7.0 (4.8, 12.6)  20 to <25 kg:  10.2 (7.7, 13.5)  25 to <30 kg:  12.9 (10.2, 14.9) | | Not reported | Mean (range):  All children:  16.0 (3.4, 29.0)  3 to <6 kg:  4.3 (3.4, 5.2)  6 to <10 kg:  7.7 (6.0, 9.8)  10 to <15 kg:  11.2 (10.0, 13.0)  15 to <20 kg:  16.5 (15.0, 19.0)  20 to <25 kg:  21.5 (20.0, 24.0)  25 to <30 kg:  27.0 (25.0, 29.0) | | | 78% VL <250 copies/mL at week 4821 | | | Mean (range) [SD]:  All children  94.4 (32.1, 232) [39.4]  3 to <6 kg:  76.1 (40.4, 112)  6 to <10 kg:  102 (55.3, 232)  10 to <15 kg:  80.8 (42.0, 158)  15 to <20 kg:  90.6 (61.3, 141)  20 to <25 kg:  85.9 (41.3, 169)  25 to <30 kg:  118 (32.1, 208) | | **Mean C12** (range) [SD]:  All children  6.0 (1.4, 16.9) [3.0]  3 to <6 kg:  5.7 (1.8, 9.7)  6 to <10 kg:  6.4 (3.5, 16.9)  10 to <15 kg:  5.0 (2.2, 10.5)  15 to <20 kg:  5.6 (3.2, 8.9)  20 to <25 kg:  5.6 (2.9, 11.0)  25 to <30 kg:  7.9 (1.4, 14.9) | | Mean(range) [SD]:  All children  10.0 (3.8, 22.5) [3.8]  3 to <6 kg:  8.5 (5.3, 11.7)  6 to <10 kg:  10.7 (5.6, 22.5)  10 to <15 kg:  9.1 (4.1, 16.8)  15 to <20 kg:  9.6 (6.5, 15.3)  20 to <25 kg:  9.0 (4.1, 17.6)  25 to <30 kg:  12.0 (3.8, 21.2) |
| Pollock et al. 200922 | TRIOMUNE 30 (200 mg NVP)  Receiving tablets to achieve  8 mg NVP/kg/day  Dose (range in mg/kg)  <8 kg: 50mg in two doses  (>6.2) (n=1)  8 to <12 kg: 100 mg in two doses  (8.3-12.5) (n=10)  12 to <18 kg: 150 mg in two doses  (8.3-12.5) (n=7)  18 to <22 kg:200 mg in two doses  (9.1-11.1) (n=1)  22 to <28 kg: 250 mg in two doses  (8.9-11.4) (n=4)  28 to <32 kg:300 mg in two doses  (9.4-10.7) (n=10)  32 to <38 kg:  350mg in two doses  (9.2-10.9) (n=1)  >38 kg: 400 mg in two doses (<10.5) (n=3) | | | N=37,  ART naive and experienced,  Malnourished children: N=25  Normal weigh children: N=12  0 to 16 years | | | | Median (range):  All children:  4.4 (0.7, 16.0)  Malnourished:  2.6 (0.7, 14.7)  Normal weight:  6.3 (0.8, 16.0) | | Median (range):  All children:  0.52 (0.25, 1.23)  Malnourished:  0.40 (0.25, 0.96)  Normal weight:  0.62 (0.32, 1.23) | Median (range):  All children:  12.3 (3.9, 38.9)  Malnourished:  7.8 (3.9, 24.0)  Normal weight:  15.9 (6.3, 38.9) | | | 54% VL<400 copies/mL | | | Median (range):  All children:  -  Malnourished:  60.082 (35.328–166.629)  Normal weight:  79.861 (43.922–14.6376) | | Median (range):  All children:  -  Malnourished:  5.084 (1.645–8.489)  Normal weight:  5.881 (2.305–9.097) | | Median (range):  All children:  -  Malnourished:  6.719 (3.401–18.947)  Normal weight:  9.483 (5.099–22.453) |
| Chokephaibulkit et al. 201123 | Generic FDC tablets vs liquid, dosed to achieve  300–400mg NVP/m2/day | | | N-=42,  Thai children  Clinically stable on NVP treatment  5 months to <13 years  Children were randomized 1:1 to start with either Liquid formulation or generic FDC with NVP/ZDV/3TC and crossed over to the other formulation after PK analysis. After, PK analysis was done with the new formulation.  6 to <8 kg: N=6  8 to <16 kg: N=12  16 to <23 kg: N=12  23 to <30 kg: N=12 | | | | Median (range):  All children  6 years (0.5–12) | | Not reported | Median (range):  All children  19 kg (6–29) | | | Not reported | | | Geometric Mean (90%CI):  Liquid:  81.88 (74.59-89.89)  Generic FDC tablet  68.88 (62.13–76.36) | | Geometric Mean (90%CI):  Liquid:  4.94 (4.32–5.65)  Generic FDC tablet  4.19 (3.66–4.81) | | Geometric Mean (90%CI):  Liquid:  8.39 (7.75–9.08)  Generic FDC tablet  7.67 (7.04–8.34) |
| Fillekes et al. 201224 | FDC tablet 50 mg NVP  Median (IQR) NVP dose  348 (326385) mg/m2 | | | N=15,  Children >1 month old  weighing 3 to <6 kg | | | | Median (IQR):  4.8 (4.2, 8.4) months | | Not reported | Median (IQR):  5.3 (4.3, 5.5) | | | Not reported | | | Median (IQR) [CV]:  70 (56, 104) [31] | | Median (IQR) [CV]:  4.3 (2.9, 6.9) [2.8] | | Median (IQR) [CV]:  7.5 (6.2, 10) [2.6] |
| Gopalan 201725 | Lead-in dose: 120-150 mg/m2 QD  Therapeutic dose (after week 2): 120-150 mg/m2 BD. | | | N=20,  ART experienced and naive initiating NVP therapy  2 to <18 years | | | | Median (IQR):  9 (6 -11) | | Not reported | Not reported | | | 70% VL <200 copies/mL | | | Not reported | | Median (IQR):  Week1:  4.8 (3.5- 6.1)  Week 2:  3.4 (2.1 -7.9)  Week 4:  8 (5.6 -10.7) | | Not reported |
| Adult data26 | NVP 200 mg BD | | |  | | | |  | |  |  | | |  | | | Median (range):  54.5 (48.0–71.8) | | Median (range):  3.73 (3.20–5.08) | | Median (range):  5.7 (5.00–7.44) |
| NVP Once-daily |  | | |  | | | |  | |  |  | | |  | | | AUC0-24 (h\*mg/L) | |  | |  |
| Giaquinto 201427 | NVP extended release (NVP-XR) Versus  NVP immediate release (NVP-IR)  Dosed to achieve  14 mg/kg/day for children <8 years old  and  8 mg/kg/day for children >8 years old | | | N= 45  Virologically suppressed on NVP-immediate release formulation  Aged 3 to <18 years old  3 to <6 years: N=16  6 to <12 years: N=16  12 to <18 years: N=17 | | | | Not reported | | 100% remained virally suppressed  (VL <50 copies/mL) after 48 weeks28 | Not reported | | | Not reported | | | Geometric mean:a  NVP-XR:  112.61  NVP-IR:  124.58  Ratio XR:IR % (90%CI) [CV]:  90.39  (82.39–99.17)  [26.8] | | Geometric mean:a  NVP-XR:  3.474  NVP-IR:  3.814  Ratio XR:IR % (90%CI) [CV]:  91.08  (82.28–100.81)  [29.5] | | Geometric mean:a  NVP-XR:  6.055  NVP-IR:  7.055  Ratio XR:IR % (90%CI) [CV]:  85.82  (75.90–97.03)  [36.2] |
| Adult data29 | NVP-XR 400mg QD | | |  | | | |  | |  |  | | |  | | | Median (IQR)  101.8 (92.6–145.3) | | Geometric mean: 2.88 (2.33–4.09) | | Geometric mean: 6.69 (5.95–8.64) |
| **Rilpivirine (RPV)** | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | **Population** | | | **Age (years, unless stated differently)** | | **BSA (m2)** | | **Weight (kg)** | | | | **Suppression rates**  **(%)** | | | **AUC** | | **Ctrough**  **(mg/L)** | | **Cmax (mg/L)** | |
| RPV once-daily |  |  | | |  | |  | |  | | | |  | | | AUC0-24 (h\*mg/L) | |  | |  | |
| Crauwels et al. 201430  Group 1: >12 to ≤15  Group 2:>15 to ≤18 | Adult tablets  25 mg RPV QD | Group 1: N=12  Group 2: N=13  Aged 12 to <18 years weighing >32 kg | | | Median (range):  15 (13–17) | | Not reported | | Median (range):  44 (35–58) | | | | Not reported | | | Geometric mean (range):  All children:  1.750 (0.887–3.573)  Group 1:  1.488  Group2:  2.032 | | Geometric mean (range):  All children:  0.0636 (0.0328–0.1620)  Group 1:  0.0553  Group2:  0.0722 | | Geometric mean (range):  All children:  0.1023 (0.0485–0.1820)  Group 1:  0.085  Group2:  0.1212 | |
| Foca et al. 201631  Group 1: RPV  Group 2: RPV +DRV/r | Adult tablets  RPV 25 mg QD  Combined with or without DRV/r | Group 1: N=15,  Group 2: N=14  ART naïve and experienced  12 to <24 years old | | | Median (range):  Group 1:  20.4 (12.4 - 22.8)  Group 2:  19.7(14.6 - 22.9) | | Median (range):  Group 1:  1.8 (1.3 - 3.9)  Group 2:  1.7 (1.5 - 2.2) | | Median (range):  Group 1:  69.3 (38.4,115.6)  Group 2:  60.2 (49.5, 95.0) | | | | Not reported | | | Geometric mean  (90% CI):  Group 1:  2.38 (1.92-2.94)  Group 2:  6.74 (4.89-9.28) | | Geometric mean  (90% CI):  Group 1:  0.07 (0.03-0.10)  Group 2:  0.23 (0.17-0.32) | | Geometric mean  (90% CI):  Group 1:  0.14 (0.12, 0.18)  Group 2:  0.39 (0.27, 0.57) | |
| Lombaard et al. 201632 | Adult tablets  RPV 25 mg QD | N=34,  ART naive adolescents  Aged 12 to <18 years | | | Median (range):  14.5 (12–17) | | Not reported | | Median (range):  45.2 (33–93) | | | | Week 48  Baseline VL <100.000 copies/mL (N=28)  N (%, 90% CI):  22 (79, 63-94)  Baseline VL >100.000 copies/mL (N=8)  N (%, 90% CI): 4 (50, 15-85)  Baseline VL <100.000 (N=28): 79% (63-94) VL <50 copies/mL at Week 48  Baseline VL >100.000 (N=8):  50% (15-85) VL <50 copies/mL at Week 48 | | | Mean (SD):  2.391 (0.991) | | Mean (SD):  0.0835 (0.0387) | | Not reported | |
| Adult data33 | 25 mg QD |  | | |  | |  | |  | | | |  | | | Median (range):  2.204 (0.482-8.601)  Mean (SD):  2.397 (1.032) | | Median (range):  0.074 (0.001-0.300)  Mean (SD):  0.080 (0.037) | | Mean (no range reported): 0.220 mg/L | |

a: geometric mean calculated on 45 children in the intensive PK substudy  
AUC: area under the concentration-time curve  
BSA: body surface area  
Ctrough: concentration at the end of the dosing interval  
Cmax: maximum concentration in the dosing interval  
Cmdi: concentration at mid-dose interval  
IQR: inter quartile range  
95% CI: 95% confidence interval  
CV%: coefficient of variation  
SD: standard deviation  
QD: dosed once daily  
BD: dosed twice daily  
XR: extended release formulation  
IR: immediate release formulation  
VL: viral load

Table 3. Pharmacokinetic studies of protease inhibitors in HIV infected pediatric patients.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Atazanavir (ATV)** | | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | **Population** | | | | **Age (years, unless stated differently)** | | | **BSA (m2)** | | **Weight (kg)** | | **Suppression rates**  **(%)** | | **AUC** | | | **Ctrough**  **(mg/L)** | | | **Cmax (mg/L)** | |
| ATV once daily |  |  | | | |  | | |  | |  | |  | | AUC0-24 (h\*mg/L)  (calculated as AUC (12) \*2) | | |  | | |  | |
| Kiser et al 2011 34  IMPAACT 1020 | **Powder formulation**  IMP1: 310 mg/m2 (boosted)    IMP3a: 310 mg/m2 (boosted)  **Capsules**  IMP3b: 205 mg/m2 (boosted)  IMP5: 205 mg/m2 (boosted)  IMP6: 620 mg/m2 (**un**boosted) | N=195 (172 evaluable PK)  **Powder formulation**  3 to 6 months (n=11)  (IMP0)  91 days - <2 years old (n=17)  (IMP1)  2 to 13 years (n=21)  (IMP3)  **Capsules**  2 years to 13 years (n=21)  (IMP3)  13 years to <21 years, boosted (n=14)  (IMP5)  13 years to <21 years, **un**boosted (n=21)  (IMP6)  64% American, 36% South-African  PI experienced (42%) & naive | | | | Median(range):  Total  8.7 years (0.3–21.3)  Median (IQR):  IMP0: 0.4 (0.1)  IMP1: 1.3 (0.9)  IMP3a: 4.5 (1.8)  IMP3b: 8.8 (4.2)  IMP5: 17.1 (2.4)  IMP6: 14.6 (2.9) | | | Median(range):  Total  0.98m2 (0.27–2.32)  Median (IQR):  IMP0: 0.32 (0.02)  IMP1: 0.42 (0.06)  IMP3a: 0.64 (0.13)  IMP3b: 0.98 (0.32)  IMP5: 1.73 (0.55)  IMP6: 1.54 (0.29) | | Median (range):  Total  26.6 (4.3–121.9)  Median (IQR):  IMP0: 6.2 (0.5)  IMP1: 8.5 (1.4)  IMP3a: 15 (4.1)  IMP3b: 28.8 (12.5)  IMP5: 62.3 (34.9)  IMP6: 52 (18.8) | | 58.5% at week 48  (69.5% of ART naive, 43.3% of ART experienced patients were <400 copies/ml at 48 weeks after initiation) | | Median (IQR):  IMP0:  38.928 (42.778)  IMP1:  44.243 (41.664)  IMP3a:  52.199 (37.148)  IMP3b:  45.680 (20.028)  IMP5:  42.835 (18.910)  IMP6:  51.781 (25.659) | | | Median (IQR):  IMP0:  0.596 (0.672)  IMP1:  0.482 (0.433)    IMP3a:  0.947 (0.759)  IMP3b:  0.575 (0.469)  IMP5:  0.885 (0.799)  IMP6:  0.510 (0.516) | | | Median (IQR):  IMP0:  4.952 (4.706)  IMP1:  6.501 (5.865)    IMP3a:  5.593 (3.397)  IMP3b:  5.013 (2.301)  IMP5:  4.095 (2.616)  IMP6:  7.006 (3.399) | |
| Bunupuradah 2014 35 | 200 mg ATV / 100mg RTV  + TDF/FTC | N = 18 Thai children  Aged 6-18 years  PI experienced & naive  ATV taken with TDF | | | | Median (IQR):13 years (11-14) | | | Median (range):  1.21 m2 (0.96-1.35): | | median (range):  35 (25-42) | | 75% at week 48 | | Geometric Mean (SD):  35.05 (1.06) | | | Geometric Mean (SD):  0.31 (1.13) | | | Geometric Mean (SD):  3.93 (1.06) | |
| Cressey 2016 36 | 400 mg ATV QD  &  600 mg ATV  QD | ATV 400: N= 18 (14 African, American, 1 White, 3 Hispanic)  ATV 600: N= 6  (4 African American, 1 white, 1 Hispanic)  Adolescents 6 to < 24 years old  With min BSA: >0.85 m2 | | | | Median (95%CI):  ATV 400 mg:  20.3 (6-23)  ATV 600 mg:  16.9 (13-23) | | | Median (CI 95%):  ATV 400 mg:  1.79 (0.85–2.29) m2  ATV 600:  1.72 (1.43-2.1) m2 | | Median (95%CI):  ATV 400:  70 (22-111) kg  ATV 600:  65 (45-86) kg | | ATV 400 mg: 82% < 200 copies/ml  ATV 600 mg:  80% <200 copies/ml | | Geometric Mean (95% CI):  ATV 400:  19.9 (14.1-28.1)  ATV 600:  29.3 (13.7-62.9) | | | Geometric Mean (95% CI):  ATV 400: 0.18 (0.09-0.36)  ATV 600:  0.13 (0.03-0.61) | | | Geometric Mean (95% CI):  ATV 400: 2.6 (1.8–3.7)  ATV 600:  4.0 (1.9–8.1) | |
| Sevinsky et al.37  PRINCE I & PRINCE II | **ATV powder formulation**  5 to <10 kg: 150/80 ATV/r [n=43] (group 1)  5 to <10 kg: 200/80 ATV/r [n=10] (group 2)  10 to <15 kg: 200/80 ATV/r [n=37] (group 3)  15 to <25 kg: 250/80 ATV/r [n=48] (group 4)  25 to <35 kg: 300/100 ATV/r [n=8] (group 5) | Children 3 months – <6 years: PRINCE I  Children 3 months to <11 years  Prince II  Total amount of children involved in the study: 146 (used to inform on group age and weight parameters)  (62.3% ART-experienced)  56.8% Black/African American  Involved in PK study: 88  (used to inform on AUC, Ctrough and Cmax) | | | | Age in months Median (range):  All children  41 (3–120)  Group 1:  6.0 (3–25)  Group 2:  4.0 (3–30)  Group 3:  35.0 (15–54)  Group 4:  61.5 (34–115)  Group 5:  86.5 (79–120) | | | Not reported | | Median (range):  Group 1:  6.9 (5.4-9.7)  Group 2:  6.9 (6.0–9.9)  Group 3:  12.5 (10.4–14.8)  Group 4:  17.6 (15.0–24.8)  Group 5:  26.0 (25.1–34.9) | | ART naive: 79% <400copies/ml at week 48  ART-experienced: 62% <400 copies/ml at week 48 | | Geometric Mean (CV%)  Group 1:  32.503 (61%)  Group 2:  39.519 (54%)  Group 3:  50.305 (67%)  Group 4:  55.687 (45%)  Group 5:  44.329 (63%) | | | Geometric Mean (CV%):  Group 1:  0.336 (76%)  Group 2:  0.550 (60%)  Group 3:  0.572 (111%)  Group 4:  0.686 (68%)  Group 5:  0.468 (104%) | | | Geometric Mean (CV%):  Group 1:  4.131 (55%)  Group 2:  4.466 (59%)  Group 3:  5.197 (53%)  Group 4:  5.394 (46%)  Group 5:  4.210 (52%) | |
| Adult refrence data38 | 400/100 mg QD |  | | | |  | | |  | |  | |  | | GM (CV%):  46.073 (66%) | | | GM (CV%):  0.636 (97%) | | |  | |
| **Darunavir (DRV)** | | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | | | **Population** | | | **Age (years, unless stated differently)** | | | **Weight (kg)** | | **Suppression rates**  **(%)** | | **AUC** | | | **Ctrough (mg/l)** | | | **Cmax (mg/L)** | | |
| DRV/r twice-daily |  | | |  | | |  | | |  | |  | | AUC0-24 (h\*mg/L)  (calculated as AUC (12)\*2) | | |  | | |  | | |
| Blache et al. 200939,40  (DELPHI) | DRV tablets +ritonavir liquid (<40 kg) or capsules (>40 kg)  11-19 mg/kg darunavir BD  With 2.5 mg/kg ritonavir BD | | | N = 76, (as reported for PK results)  6-12 years: N=24  12-17 years: N=76  (as reported in baseline demographics)  Weighing >20 kg  ART experienced | | | Mean (range not reported)  14 | | | Not reported | | 59% VL<400 copies/mL  48% VL<50 copies/mL | | Mean (range):  123.3 (71.9–201.5)  6-12 years:  112.8 (range not reported)  12 to <18 years:  132.8 (range not reported) | | | Mean (range):  3.7 (1.8–7.2)  6-12 years: 3.3  (range not reported)  12 to <18 years: 4.1  (range not reported) | | | Not reported | | |
| Chokephaibulkit et al. 201241 | DRV tablets + ritonavir capsules  20 to <30 kg: 375/100 DRV/r BD  30 to <40 kg:450/100 DRV/r BD  >40 kg:600/100 DRV/r BD | | | N=19,  Thai children >7 years, >20 kg  20% ART experienced  20 to <30 kg: N=12  30 to <40 kg: N=2  >40 kg: N=5 | | | Median (range):  13 (7-16) | | | Median (range):  29.4 (20–67.6) | | Not reported | | Median (CV%):  All children  120.6 (2\*60.3)  20 to <30 kg:  117.0 (85%)  (2\*58.5)  30 to <40 kg:  117.0 (18%)  (2\*58.5)  >40 kg:  131.6 (44%)  (2\* 65.8)) | | | Median (CV%):  All children  3.1 (76%)  20 to <30 kg:  3.0 (96%)  30 to <40 kg:  3.2 (60%)  >40 kg:  3.1(44%) | | | Median (CV%):  All children  8.3 (55%)  20 to <30 kg:  8.1 (65%)  30 to <40 kg:  8.2 (1%)  >40 kg:  9.0 (46%) | | |
| Violari et al. 201542,43  ARIEL trial | Oral suspension  Part I  20/3mg/kg DRV/r BD  10 to <15 kg, 15 to <20 kg  Part II  25/3mg/kg DRV/r BD  10-15 kg  375/50mg DRV/r BD  15-20 kg | | | N= 21  3 to <6 years old  ART experienced  Part I  10 to <15 kg n=10b  15 to <20 kg n=14b  Part II  10 to <15 kg n=9b  15 to <20 kg n=12b | | | Median (range):  4.4 (3.0, 6.0) a | | | Median (range):  14.9 (12, 20) a | | 71.4% VL<50 copies/mL | | Mean (SD):  Overall  78.5 (25.1)  Part I  10 to <15 kg (20/3mg/kg): 137.4  (2\*68.7 (25.5)) b  15 to <20 kg (20/3mg/kg): 158.0 (2\*79.0(31.4))b  Part II  10 to <15 kg (25/3mg/kg): 190.8  (2\*95.4 (33.4)) b  15 to <20 kg (375/50mg drv/r): 163.2  (2\*81.6 (33.7))b | | | Part I  10 to <15 kg 4.429  (2.064) b  15 to <20 kg 4.848 (2.526) b  Part II  10 to <15 kg 6.414  (2.637)b  15 to <20 kg 5.027 (2.828) b | | | Not reported | | |
| Adult refrence data40,44 | 600/100 mg DRV/r BD | | |  | | |  | | |  | |  | | Median (range):  111.632 (64.874-355.360) | | | Median (range):  3.307  (1.517-13.198) | | | Mean (CV%):  8,390 (21%)44 | | |
| DRV/r once-daily |  | | |  | | |  | | |  | |  | | AUC0-24 (h\*mg/L) | | |  | | |  | | |
| Flynn et al. 201445  DIONE trial | DRV tablet + ritonavir tablet  >40 kg: 600/100 QD | | | N=12,  Aged 12 to <18 years  Weighing >40 kg  ART naive patients | | | Median (range):  14.4 (12.6-17.3) | | | Median (range):  50.5 (40.0-61.6) | | 92% VL <50 copies/mL at week 24  83% VL <50 copies/mL at week 48 | | Median (SD):  80.7 (23.6) | | | Median (SD):  1.93 (0.87) | | | Not reported | | |
| Chokephaibulkit et al. 201446 | DRV tablet + ritonavir tablet  20-30 kg: 450/100 mg QD  30-40 kg: 600/100 mg QD  >40 kg: 900/100 mg QD | | | N= 8,  Thai children  Eligible 6 to <18 years (≥11years were enrolled)  Weighing >40kg  ART naive patients | | | Median (range):  16 (11.0-18.9) | | | - | | 75% VL <50 copies/mL at week 48 | | Median (range):  51.2 (20.7-117.7) | | | Median (range):  0.70 (0.2-2.4) | | | Median (range):  5.88 (2.36–10.5) | | |
| Violari et al. 201542  ARIEL trial | DRV oral suspension + ritonavir oral suspension  <15 kg: 40/7 mg/kg QD  >15 kg: 600/100 mg QD | | | N=10,  Aged 3 to < 6 years  ART experienced | | | Median (range):  4.4 (3.0-6.0) | | | Median (range):  14.9 (12-20) | | Not reported | | Median (SD):  115 (40.6) | | | Not reported | | | Not reported | | |
| Larson et al. 201647 | DRV/r (formulation not reported)  >40 kg: 800/100 mg DRV/r QD | | | N= 16,  Eligible 9 to <24 years (≥ 13.7 years were enrolled)  >40kg  ART experienced but without DRV RAM. | | | Median (range):  20.1 (13.7-23.2) | | | Median (range):  66.7 (40.0-92.3) | | Not reported | | Median (range):  57.9 (49.6-67.6) | | | Median (range):  1.0 (0.8-1.3) | | | Median (range):  5.5 (4.6–6.5) | | |
| Bastiaans et al. 201848  DAPHNE trial | DRV/r tablet  15-30 kg: 600/100 mg QD  30-40 kg: 675/100 mg QD  >40 kg: 800/100 mg QD | | | N=12,  Aged 6 to <12 years  Weighing >15 kg  ART experienced but without DRV RAM. | | | Median (range):  8.9 (6.3-11.7) | | | Median (range):  26.6 (22.4-45.0) | | 91% VL <50 copies/mL at 11.6 months | | Median (CV%):  63.1 (33%) | | | Median (CV%):  1.5(44%) | | | Median (CV%):  5.6 (34%) | | |
| Adult refrence data40,49 | 800/100 mg QD | | |  | | |  | | |  | |  | | Median (range):  87.854  (45.000-219.240) | | | Median (range):  2.041  (0.368-7.242) | | | Mean (CV%):  7.460 (20.3)49 | | |
| **Lopinavir (LPV)** | | | | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Intended dose and formulation** | | **Population** | | **Age (years, unless stated differently)** | | | **BSA (m2)** | | | | **Weight (kg)** | | **Suppression rates**  **(%)** | | **AUC** | | | **Ctrough (mg/l)** | | | **Cmax (mg/L)** |
| LPV twice-daily |  | |  | |  | | |  | | | |  | |  | | AUC0-12 (h\*mg/L) | | |  | | |  |
| Sáez-Llorens 200350 | LPV Oral solution  230/57.5 mg/m2 LPV/r BD  300/75mg/m2 LPV/r BD  Co administrated with and without NVP | | N=44  ART naïve children  6 months to <12 years  N= 66, ART experienced (co administrated NVP) | | **Mean** (Range):  ART Naïve (no NVP)  4.8 months (6-10.2)  ART experienced (with NVP)  5.7 months (8 -12.6) | | | Not reported | | | | Not reported | | 79% had VL <400  copies/mL at Week 48 | | Mean (SD)  230/57.5 No NVP:  72.6 (31.1)  230/57.5 With NVP:  51.6 (27.8)  300/75 No NVP:  116.4 (57.1)  300/75 With NVP:  85.8 (36.9) | | | Mean (SD)  230/57.5 No NVP:  3.35(2.14)  230/57.5 With NVP:  1.80 (1.68)  300/75 No NVP:  6.53 (4.57)  300/75 With NVP:  3.56 (3.45) | | | Mean (SD)  230/57.5 No NVP:  8.16 (2.94)  230/57.5 With NVP:  6.71 (3.32)  300/75 No NVP:  12.45 (5.77)  300/75 With NVP:  10.04 (3.26) |
| Rosso et al. 200651 | Oral solution  230/57.5 mg/m2 BD | | N=21  ART naïve | | Median (range):  7.43 (3.50–13.46) | | | Not reported | | | | Median (range):  24.9 (8.3–39.0) | | 100% VL <400 copies/mL at 24 weeks | | Not reported | | | Median (IQR):  7.90 (5.45-9.77) | | | Median (IQR)  14.60 (10.83–15.98) |
| Verweel et al. 200752 | Soft gel capsule and oral solution  230/57.5 mg/m2 BD | | N= 23  ART naïve, with PI mutations, and PI experienced (with no previous virological failure) | | Median (range):  5.6 (0.4-13.2 | | | Median (range):  0.75 (0.30–1.31) | | | | Median (range):  18.1 (5.4–43.9) | | Naïve:  97% VL <50 copies/mL at 48 weeks  PI resistance at baseline:  66% VL <50 copies/mL  At 48 weeks  Pi experienced without prior  virological failure:  100% VL <50 copies/mL | | Mean (SD):  75.3 (33.7) | | | Mean (SD):  3.68 (2.48) | | | Mean (SD):  9.33 (3.27) |
| Chadwick et al. 200853 | LPV Oral solution  300/75 mg/m2 LPV/r BD | | N=18  ART naïve c  Aged 6 weeks to <6 months | | Median (SD):  3.4 months (1.4) | | | Median (SD):  0.31(0.05) | | | | Median (SD):  5.5(1.5) | | 53% had VL<400  copies/mL at week 24 | | Median (SD):  67.52(37.94) | | | Median (SD):  2.37(2.7) | | | Not reported |
| La Porte 200954 | Soft gel capsule and oral solution 230/57.5 mg/m2 BD | | N= 6  Virologically suppressed on LPV BD | | Median (range):  9.8 (5.8-15.5) | | | Median (range):  0.98 (0.73–1.54) | | | | Not reported | | Not reported | | Median (range):  161.8 (46.6–271.8) | | | Median (range):  5.7 (1.7–9.7) | | | Median (range):  9.8 (3.4-15.2) |
| Puthanakit 2009 55 | Oral solution  **Low dose mg LPV/r: \***  8 to 16.9 kg: 120/30 n= (3)  17 to 19.9 kg: 144/36 n= (1)  20 to 24.9 kg: 160/40 n= (4)  25- 29.9 kg: 200/50 n= (1)  30 to34.9 kg: 240/60 n= (1)  >35 kg: 280/70 n= (2)  **Standard dose: \***  8 to 16.9 kg: 160/40 n= (2)  17 to 19.9 kg: 200/50 n= (0)  20 to 24.9 kg: 240/60 n= (5)  25 to 29.9 kg: 280/70 n= (2)  30 to34.9 kg: 320/80 n= (0)  >35 kg: 400/100  n= (3) | | N=22  Aged 2 to <18 years  Low dose: n=11  Standard dose: n=11  ART naïve **Thai** children | | Median (IQR):  All children:  9.5 (7.0–12.3)  Standard dose:  9.6 (8.4-14.7)  Low dose:  8.6 (6.7-11.8) | | | Median (IQR):  All children:  0.9 (0.8–1.1)  Standard dose:  0.9 (0.8–1.2)  Low dose:  0.8 (0.7–1.1) | | | | Median (IQR):  Standard dose:  24 (20-37)  Low dose:  21 (17-31) | | Low dose efficacy:  100% VL <50 copies/mL at 48 weeks  Standard dose efficacy:  75% VL <50 copies/mL at 48 weeks | | Median (range)[%CV]:  Low dose:  83.1 (56.0–112.9) [35%]  Standard dose  117.6 (74.0–128.5) [32%] | | | Median (range)[%CV]:  Low dose:  3.4 (2.7–5.4) [46%]  Standard dose  4.9 (2.7–8.0) [54%] | | | Median (range)[%CV]:  Low dose:  10.1 (7.1–13.7) [33%]  Standard dose  11.9 (10.6–14.4) [25%] |
| Chadwick et al. 200956 | LPV Oral solution  300/75 mg/m2 LPV/r BD | | N=9  ART Naïve children  Aged 14 days to <6 weeks  Weighing >2.5kg | | Median (SD):  5.7 weeks (0.8) | | | Median (SD):  0.27(0.04) | | | | Median (SD):  4.7(0.88) | | 71% had VL <400 copies/mL at week 48 for cohort57 | | Median (SD):  36.6(14.8) | | | Median (SD):  2.22 (1.34) | | | Median (SD):  4.76 (1.84) |
| Chadwick et al. 201157 | LPV Oral solution  300/75 mg/m2 LPV/r BD | | N=20  aged <6 months old  ART Naïve children | | Median (range):  12.4 months (12.0-15.5) | | | Median (range):  0.43(0.33-0.50) | | | | Not reported | | 71% had VL <400 copies/mL at week 48 | | Median (IQR):  99.1 (82.4-124.5)  (for children starting ART at age 14 days to <6 weeks)  112.0 (95.0-148.8)  (for children starting ART at age 6 weeks to <6 months) | | | Not reported | | | Not reported |
| Chokephaibulkit et al. 2012 58 | Adult tablets  230/57.5 mg/m2 BD | | N=6  Virologically suppressed | | Median (range):  13.1 (9.3–17.7) | | | Not reported | | | | Median (range):  40.8 (26.8–50.3) | | Children where virologically suppressed (baseline) | | Median (range):  172 (125–201) | | | Median (range):  4.2 (2.0–6.5) | | | Median (range):  8.8 (7.4–9.8) |
| Bastiaans et al 201459 | Pediatric tablets (100/25mg)  ≥15 to ≤25kg: 200/50 mg  >25 to ≤35kg: 300/75 mg  >35kg: 400/100 mg | | N=53  ART experienced  Mixed ethnicities | | Median (IQR):  Whole group:  11.0 (8.8–14.7)  ≥15 to ≤25:  7.4 (6.8–8.8)  >25 to ≤35:  10.9 (10.1–13.9)  >35:  15.0 (13.7–15.7) | | | Not reported | | | | Median(IQR):  All children:  31.0 (23.6–40.0)  ≥15 to ≤25:  20.5 (19.3–23.5)  >25 to ≤35:  30.2 (29.1–32.1)  >35:  41 (38.3–49.5) | |  | | GM (95% CI):  All children:  106.9 (97.8–116.9)  ≥15 to ≤25:  104.1 (84.9–127.5)  >25 to ≤35:  116.9 (100.6–135.8)  >35:  101.9 (89.1–116.6) | | | GM (95% CI):  All children:  4.9 (4.14–5.80)  ≥15 to ≤25:  4.2 (3.07–5.78)  >25 to ≤35:  5.1 (3.53–7.36)  >35:  5.4 (4.16–6.97) | | | GM (95% CI):  All children:  12.0 (11.1–12.9)  ≥15 to ≤25:  12.2 (10.4–14.5)  >25 to ≤35:  13.0 (11.4–14.8)  >35:  11.0 (10.0–12.2) |
| Lyall et al. 2015 60  (PENTA 18) | Pediatric tablets (100/25mg)  ≥15 to ≤25 kg: 200/50 mg  >25 to ≤35 kg: 300/75 mg  >35 kg: 400/100 mg | | N=26  Suppressed for at least 24 weeks on LPV/r containing therapy  Mixed ethnicity  ≥15 to ≤25: N=7  >25 to ≤35: N=8  >35: N=11 | | Median (IQR):  Whole group:  12.8 (8.7, 14.7)  ≥15 to ≤25:  7.1 (6.7, 8.7)  >25 to ≤35:  10.6 (9.5, 15.0)  >35:  14.3 (13.5, 15.4) | | | Not reported | | | | Median (IQR):  All children:  32.1 (24.1, 41.0)  ≥15 to ≤25:  19.4 (19.0, 23.1)  >25 to ≤35:  30.7 (29.8, 32.1)  >35:  42.0 (38.5, 49.5) | | 8% rebound at 48 weeks | | GM (95% CI) **AUC0-24 (double AUC0-12)**:  All children:  223.9 (194.8, 257.4)  ≥15 to ≤25:  232.1 (153.3, 351.4)  >25 to ≤35:  256.8 (209.3, 315.2)  >35:  198.1 (159.8, 245.5) | | | GM (95% CI):  All children:  5.69 (4.58, 7.07)  ≥15 to ≤25:  4.92 (2.65, 9.16)  >25 to ≤35:  6.65 (5.22, 8.47)  >35:  5.57 (3.73, 8.32) | | | GM (95% CI):  All children:  5.69 (4.58, 7.07)  ≥15 to ≤25:  4.92 (2.65, 9.16)  >25 to ≤35:  6.65 (5.22, 8.47)  >35:  5.57 (3.73, 8.32) |
| Adult refrence data61 | Adult tablets  400/100 mg/m2 LPV/r BD | |  | |  | | |  | | | |  | |  | | Median(SD):  92.6 (36.7) | | | Median(SD):  5.5 (2.7) | | | Mean (SD):  9.8 (3.7) |
| Once-daily LPV/r |  | |  | |  | | |  | | | |  | |  | | AUC0-24 (h\*mg/L) | | |  | | |  |
| Rosso 200651 | 460/115 mg/m2 QD | | N=7  ART naïve | | Median (range):  8.67 (3.83–14.98) | | | Not reported | | | | Median (range)  24.9 (8.3–39.0) | | 100% VL <400 at 24 weeks | | Not reported | | | Median (IQR):  1.59 (0.77-6.85) | | | Median (IQR):  11.80 (11.15-16.35) |
| Van der Lee 200662 | 460/115 mg/m2 QD | | N=19  Virologically suppressed on LPV BD  Pre-treatment status unknown | | Median (range):  4.5 (1.4-12.9) | | | Median (IQR):  0.76 (0.58–1.08) | | | | Median (IQR):  19.8 (13.6-30.0) | | - | | Median (SD):  149.8 (58.8) | | | Mean (SD):  2.88 (3.74)  (53% of children Ctrough <1.0mg/L) | | | Mean (SD): 10.77 (2.90) |
| Van der Flier 200763 | Adult tablets (200/50 mg)  460/115 mg/m2 QD | | N=15  Aged 4 to <15 years  ART experienced without relevant mutations  Virologically suppressed on LPV BD | | Median (range):  8.7 (4.4-15.0) | | | Median (range):  1.12 (0.79-1.56) | | | | Median (range):  33.8 (19.1–56.8) | | 100% VL <50 copies/mL after 24 weeks | | Mean (SD):  217.9 (44.9) | | | Mean (SD):  3.1 (2.4) | | | Mean (SD):  14.8 (2.4) |
| La Porte 200954 | Soft gel capsule and oral solution 460/115mg/m2 QD | | N= 7  Virologically suppressed on LPV BD | | Median (range):  9.8 (5.8-15.5) | | | Median (range):  0.98 (0.73–1.54) | | | | Not reported | | Viral load of one patient blipped to 666 copies/mL but regained viral suppression | | Median (range):  214.6 (114.2-289.2) | | | Median (range):  3.4 (0.6-7.4) | | | Median (range): 13.5 (8.3-17.5) |
| Chokephaibulkit et al. 2011 58 | Adult tablets (200/50 mg)  460/115 mg/m2 QD | | N=6  Virologically suppressed on LPV BD | | Median (range):  13.1 (9.3–17.7) | | | Not reported | | | | Median (range):  40.8 (26.8–50.3) | | 100% VL <40 copies/mL at 48 weeks | | Median (range):  200 (95–228) | | | Median (range):  3.9 (0.2–7.3) | | | Median (range):  12.1 (8.5–15.0) |
| Lyall et al. 2015 60  (PENTA 18) | Pediatric tablets (100/25 mg)  ≥15 to ≤25: 200/50 mg  >25 to ≤35: 300/75 mg  >35: 400/100 mg | | N=26  Suppressed for at least 24 weeks on LPV/r containing therapy  Mixed ethnicity  ≥15 to ≤25: N=7  >25 to ≤35: N=8  >35: N=11 | | Median (IQR):  Whole group:  12.8 (8.7, 14.7)  ≥15 to ≤25:  7.1 (6.7, 8.7)  >25 to ≤35:  10.6 (9.5, 15.0)  >35:  14.3 (13.5, 15.4) | | | Not reported | | | | Median (IQR):  Whole group:  32.1 (24.1, 41.0)  ≥15 to ≤25:  19.4 (19.0, 23.1)  >25 to ≤35:  30.7 (29.8, 32.1)  >35:  42.0 (38.5, 49.5) | | 8% rebound at 48 weeks | | GM (95% CI)  Whole group:  160.9 (138.4, 187.0)  ≥15 to ≤25:  172.6 (121.3, 245.7)  >25 to ≤35:  159.3 (120.6, 210.5)  >35:  155.0 (116.8, 205.6) | | | GM (95% CI):  Whole group:  5.69 (4.58, 7.07)  ≥15 to ≤25:  4.92 (2.65, 9.16)  >25 to ≤35:  6.65 (5.22, 8.47)  >35:  5.57 (3.73, 8.32) | | | GM (95% CI):  Whole group:  14.0 (12.7, 15.6)  ≥15 to ≤25:  15.5 (12.4, 19.4)  >25 to ≤35:  15.0 (12.2, 18.5)  >35:  12.5 (10.7, 14.7) |
| Adult refrence data61,64 | 800/200 mg/m2 LPV/r QD | |  | |  | | |  | | | |  | |  | | Mean (SD):  154.1 (61.4) | | | Mean (SD):  Cmin  1.7 (1.6) | | | Mean (SD):  11.8 (3.7) |

a: based on data from Violari et al. 93  
b: based on data from FDA pharmacology review94  
c: not reported which children were used for PK study  
AUC: area under the concentration-time curve  
BSA: body surface area  
Ctrough: concentration at the end of the dosing interval  
Cmax: maximum concentration in the dosing interval  
ART: antiretroviral therapy  
PI: protease inhibitor  
DRV RAM: darunavir resistance associated mutations   
IQR: inter quartile range  
95% CI: 95% confidence interval  
CV%: coefficient of variation  
SD: standard deviation  
GM: geometric mean  
QD: dosed once daily  
BD: dosed twice daily  
VL: viral load  
IMP: IMPAACT study group (1-6)

Table 4. Pharmacokinetic studies of integrase inhibitors and TAF in HIV infected pediatric patients

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Dolutegravir (DTG)** | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose DTG and formulation** | | **Population** | | | **Age (years, unless stated differently)** | | **Weight (kg)** | | | **Suppression rates %**  **(95%CI)** | | | **AUC** | | **Ctrough (mg/l)** | | **Cmax (mg/L)** | |
| DTG once-daily |  | |  | | |  | |  | | |  | | | AUC0-24 (h\*mg/L) | |  | |  | |
| Viani et al. 201565 IMPAACT P1093 | Film coated tablets (FCT)  15 to <20 kg: 20 mg QD  20 to <30 kg: 25 mg QD  30 to <40 kg: 35 mg QD  >40 kg: 50 mg QD  Cohort 1: (FCT) | | Aged 12 to <18: N=23  ART experienced  Weighing >15 kg  **Fasted** | | | Median (range):  12 to <18 years  14.6 (12.2-17.9) | | Median (range):  12 to <18 years old  50.8 (37.1-91.4) | | | 12 to <18 years:  74% (52-90) <400  copies/mL at week 48  61% (39-80) <50  copies/mL at week 48 | | | Median (range):  12 to <18 years  52.9 (13.1-85.0) | | Median (range):  12 to <18 years  1.14 (0.21-2.12) | | Median (range):  12 to <18 years  4.01 (1.15-6.08) | |
| Viani et al 201466 | Film coated tablets (FCT)  20 to <30 kg: 25 mg QD  30 to <40 kg: 35 mg QD  >40 kg: 50mg QD  Cohort 2: (FCT) | | Aged 6 to <12:  N=11  Cohort 2A: 6 to <12 years  Cohort 2B: 6 to <12 years  ART experienced  Weighing >15 kg  **Fasted** | | | Median (range):  6 to <12 years:  10 (8-11) | | Median (range):  6 to <12 years:  30.0 (18-54) | | | 6 to <12 years:  78.3% (56.3-92.5)  <400 copies/mL at week 48  73.9% (51.6-89.8)  <50 copies/mL at week 48 | | | Median (range):  6 to <12 years:  50.46 (46%) | | Median (range):  6 to <12 years:  0.92 (89%) | | Median (range):  6 to <12 years:  Not reported | |
| Ruel et al. 20186 IMPAACT P1093 | Dispersible tablets (DT)  3 to <6 kg: 5 mg QD  6 to <10 kg: 10 mg QD  10 to <14 kg: 15 mg QD  14 to <20 kg: 20 mg QD  20 to <20 kg: 25mg QD | | N=30,  ART experienced  4 weeks to 2 years:  Weighing >3 kg  **Fasted** | | | Median (range):  Cohort 3 -DT:  0.34 (0.28-0.39)  Cohort 4 -DT:  1.2 (0.9-1.9)  Cohort 5 -DT:  4.0 (2.1-5.9) | | Not reported | | | 4 weeks to 2 years:  81% VL <400 copies/mL at week 48 | | | Geometric mean (CV%) :  Cohort 3 -DT:  61 (44%)  Cohort 4 -DT:  51 (38%)  Cohort 5 -DT:  40 (36%) | | Geometric mean (CV%):  Cohort 3 -DT:  1.207 55(%)  Cohort 4 -DT:  0.711 (60%)  Cohort 5 -DT:  0.461 (59%) | | Not reported | |
| Bollen et al. 4 Odyssey | Film coated tablets  14 to <20 kg: 20 mg QD  20 to <25 kg: 25 mg QD | | Aged <18 years  Weighing 14 to <25 kg  14 to <20 kg: n=19  20 to <25 kg: n=14  **Fasted** | | | Median (IQR):  14 to <20 kg: 6.2 (5.1-7.4)  20 to <25 kg: 9.5 (7.6-10.6) | | Median (IQR):  14 to <20 kg:  17 (16.0-18.6)  20 to <25 kg:  23.4 (22.9-23.9) | | | Not reported | | | Geometric mean (CV%):  14 to <20 kg:  39.6 (32%)  20 to <25 kg:  30.1 (41%) | | Geometric mean (CV%):  14 to <20 kg:  0.48 (67%)  20 to <25 kg:  0.29 (97%) | | Geometric mean (CV%):  14 to <20 kg:  4.03 (31%)  20 to <25 kg:  3.20 (40%) | |
| Turkova et al.5 Odyssey | Film coated tablets  25 to <30 kg: 25 mg QD (PK1)  25 to <30 kg: 50 mg QD (PK2)  30 to <40 kg: 35 mg QD (PK1)  30 to <40 kg: 50 mg QD (PK2) | | Aged <18 years  Weighing 25 to <40 kg  25 to <30 kg: n=18  30 to < 40 kg: n=10  **Fasted** | | | Median (range):  25 to <30 kg:  10.7 (7.5-17.9)  30 to <40 kg:  11.2 (9.8-17.8) | | Median (range):  25 to <30 kg:  27.5 (25.0-30.7)  30 to <40 kg:  31.0 (29.9-38.2) | | | Not reported | | | Geometric mean (CV%):  25 to <30 kg (25mg):  33.1(23%)  25 to <30 kg (50mg):  58.7 (27%)  30 to <40 kg (35mg):  40.3 (35%)  30 to <40 kg (50mg):  53.5 (32%) | | Geometric mean (CV%):  25 to <30 kg (25mg):  0.38 (48%)  25 to <30 kg (50mg):  0.75 (42%)  30 to <40 kg (35mg):  0.45 (63%)  30 to <40 kg (50mg):  0.63 (49%) | | Geometric mean (CV%):  25 to <30 kg (25mg):  3.16 (24%)  25 to <30 kg (50mg):  5.41 (25%)  30 to <40 kg (35mg):  3.98 (28%)  30 to <40 kg (50mg):  5.22 (25%) | |
| Bollen et al. (Ref.)  Odyssey (CROI 2019) | Film coated tablets (FCT) and Dispersible tablets (DT)  20 to <25 kg: 50 mg FCT QD  20 to <25 kg: 30 mg DT QD | | Aged <18 years  Weighing 20 to <25 kg  20 to <25 kg FCT: n=7  20 to <25 kg DT: n=8  **Fasted** | | | Median (range):  20 to <25 kg FCT:  9.7 (8.1-11.7)  20 to <25 kg DT:  8.6 (6.8-11.3) | | Median (range):  20 to <25 kg FCT:  22.4 (20.5-24.5)  20 to <25 kg DT:  21.8 (20.3-22.7) | | | Not reported | | | Geometric mean (CV%):  20 to <25 kg FCT:  62.8 (30%)  20 to <25 kg DT:  71.8 (28%) | | Geometric mean (CV%):  20 to <25 kg FCT:  0.77 (51%)  20 to <25 kg DT:  0.71 (74%) | | Geometric mean (CV%):  20 to <25 kg FCT:  6.07 (29%)  20 to <25 kg DT:  7.42 (25%) | |
| Adult refrence data67 | 50 mg DTG QD | | **Fasted** | | |  | |  | | |  | | | GM (CV%):  43.4 (20%) | | GM (CV%):  0.83 (26%) | | GM (CV%):  3.34 (16%) | |
| **Raltegravir (RTG)** | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | **Population** | | | **Age (years, unless stated differently)** | | | | **Weight (kg)** | | | **Suppression rates**  **(%)** | | | **AUC** | | **Ctrough (mg/l)** | | **Cmax (mg/L)** |
| RTG twice-daily |  |  | | |  | | | |  | | |  | | | AUC0-24 (h\*mg/L) | |  | |  |
| Nachmann et al. 201468 | Chewable tablet (CT)  Film-coated tablet (FCT)  Group 1: FCT  Group 2A: FCT  Group 2B: CT  Group3: CT  FCT: 400mg BD (children weighing at least 25 kg)  CT: 6 mg/kg BD maximum of 300 mg/day | N=96  ART experienced and naive,  Aged 2 to <19 years  N (N in intensive PK sub-study)  12 to <19 years FCT (Group 1): N=59 (11)  6 to <12 years FCT (Group 2A): N=4 (11)  6 to <12 years CT (Group 2B): N=13 (10)  2 to <6 years CT (Group 3): N=20 (12) | | | Mean (SD):a  Group 1: 15.2 (1.9)  Group 2A: 10 (1.4)  Group 2B: 8.8 (1.6)  Group3: 3.2 (1.2) | | | | Mean:b  Group 1: 43.55  Group 2A: 34.54  Group 2B: 36.36  Group 3: 14.24  Median (CV%):a  Group 1: 39.8 (30.8%)  Group 2A: 32.4 (23.2%)  Group 2B: 35.1 (31.3%)  Group3: 13.4 (15.7%) | | | 79.1% VL <400 copies/ mL or >1 log10 decline from baseline at week 48  73.6% VL <400 copies/mL at 48 weeks  57.1% VL<50 copies/mL at week 48 | | | Median (CV%):b  Film coated tablets:  Group 1:  7.4 (97.6%)  Group 2A:  6.7 (120.4%)  Chewable tablets:  Group 2B:  10.5 (33.6%)  Group 3:  7.3 (58.6%) | | Median (CV%):b  Film coated tablets:  Group 1:  0.1376 (78.3%)  Group 2A:  0.1075 (220.5%)  Chewable tablets:  Group 2B:  0.0434 (87.6%)  Group 3:  0.0358 (55.5%) | | Median (CV%):b  Film coated tablets:  Group 1:  1384.1 (95.1%)  Group 2A:  2.247 (129.9%)  Chewable tablets:  Group 2B:  4.524 (53.3%)  Group 3:  5.143 (56.5%) |
| Nachmann et al. 201569 | Granules for suspension  Group 4: 6 mg/kg BD  Group 5: 6 mg/kg BD | N=96  ART experienced and naive,  Aged 4 weeks to <2 years  Group 4: 6 months to <2 years  Group 5: 4 weeks to <6 months | | | Not reported | | | | Mean (no range reported):  Group 4: 8.49  Group 5: 5.50 | | | 87.5% VL <400 copies/mL or >1 log10 reduction from baseline at week 48  66.7%VL<400copies/mL at week 48    45.5% VL<50copies/mL at week 48 | | | Geometric Mean (CV%)  Group 4:  8.8 (34%)  (19.8 µmol\*h)  Group 5:  9.9 (40%)  (22.3 µmol\*h) | | Geometric Mean (CV%):  Group 4:  0.0479 (52%)  (108.2 nmol/L)  Group 5:  0.0517 (68%)  (116.6 nmol/L) | | Geometric Mean (CV%):  Group 4:  4.7009 (64.8%) (10,600 nmol/L)  Group 5:  2.4832 (38.7%)  (5,600 nmol/L) |
| Clarke et al. 201770 | Oral granules for suspension  Day 1 to 7: 1.5 mg/kg QD  Day 8 to 28: 3.0 mg/kg BD  >4 weeks: 6.0 mg/kg BD | N=24  Full term infants <48 hours of age  Gestational age at birth >37 weeks  Weighing >2 kg | | | Mean (range):  38.5 weeks (37.0-40.9) | | | | Mean Birth weight:  2.93 (2.39-3.75) | | | All HIV NAT results were negative | | | Geometric mean (CV%):  1.5mg/kg QD (infants):  38.2 (38.4%)  3.0 mg/kg:  14.3 (43.3%) | | Geometric mean (CV%):  1.5mg/kg QD (infants):  0.948 (64.2%)  3.0 mg/kg:  0.176 (93.8%) | | Geometric mean (CV%):  1.5mg/kg QD (infants):  2.350 (35.0%)  3.0 mg/kg:  2.850 (41.9%) |
| Adult reference data71 | 400mg BD |  | | |  | | | |  | | |  | | | Geometric Mean  7.67  (17.3 µmol\*h) | | Geometric Mean:  0.0717  (161.6 nmol/L) | | Geometric Mean:  2.749  (6,200 nmol/L) |
| **Elvitegravir (EVG) and TAF** | | | | | | | | | | | | | | | | | | | |
| **Reference** | **Dose and formulation** | | | **Population** | | | **Age (years, unless stated differently)** | | | **Weight (kg)** | | | **Suppression rates**  **(%)** | | **AUC** | | **Ctrough (mg/l)** | | **Cmax (mg/L)** |
| EVG once-daily |  | | |  | | |  | | |  | | |  | | AUC0-24 (h\*mg/L) | |  | |  |
| Gaur et al. 201672 | EVG within FDC: 150 mg QD | | | N=24,  Virologically unsupressed (>1000 copies/mL)  Aged 12 to <18 years, | | | Median (range): 15 (12–17) | | | Median (range):  52.0 (35.0–88.8) | | | Not reported | | Mean (CV%):  23.840 (25.5%) | | Mean (CV%):  0.301 (81.0%) | | Mean (CV%):  2.230 (19.2%) |
| Natukunda et al. 201773 | EVG within FDC: 150 mg QD | | | N=23,  Virologically suppressed for more than 6 months  Aged 6 to <11 years, weighed at least 25 kg | | | Median (IQR):  10 (8–11) | | | Median (IQR):  30.5 (27.5–33.0) | | | 100% stayed suppressed VL<50 copies/mL | | Mean (CV%)  33.814 (58%) | | Mean (CV%):  0.370 (119%) | | Mean (CV%):  3.055 (39%) |
| Adult reference data73 | EVG within FDC: 150 mg QD | | |  | | |  | | |  | | |  | | Mean (CV%):  22.797 (35%) | | Mean (CV%):  0.287 (62%) | | Mean (CV%):  2.113 (34%) |
| TAF once-daily |  | | |  | | |  | | |  | | |  | | AUC0-12 (h\*mg/L) | |  | |  |
| Gaur et al. 201672 | TAF: 10 mg | | | N=24,  Aged 12–18 years, | | | Median (range): 15 (12–17) | | | Median (range):  52.0 (35.0–88.8) | | | Not reported | | Mean (CV%):  0.189 (55.8%) | | Not reported | | Mean (CV%):  0.167 (64.4%) |
| Natukunda et al. 201773 | TAF: 10 mg | | | N=23,  Virologically suppressed for more than 6 months  Aged 6–11 years, weighed at least 25 kg | | | Median (IQR):  10 (8–11) | | | Median (IQR):  30.5 (27·5–33·0) | | | 100% stayed suppressed VL<50 copies/mL | | Mean (CV%):  TAF:  0.333 (45%)  TNF:  0.440 (21%) | | Mean (CV%):  TAF:  Not available due to short half-life of TAF  TNF:  0.015 (25%) | | Mean (CV%):  0.313 (61%)  TNF:  0.026 (21%) |
| Adult reference data73 | TAF: 10 mg | | |  | | |  | | |  | | |  | | Mean (CV%)  TAF:  0.206 (72%)  TNF:  0.293 (27%) | | Mean (CV%):  TAF:  Not available due to short half-life of TAF  TNF:  0.011 (29%) | | Mean (CV%):  0.162 (51%)  TNF:  0.015 (26%) |

a: data from full cohort  
b: data from intensive PK studies only  
AUC: area under the concentration-time curve  
BSA: body surface area  
Ctrough: concentration at the end of the dosing interval  
Cmax: maximum concentration in the dosing interval  
ART: antiretroviral therapy  
IQR: inter quartile range  
95% CI: 95% confidence interval  
CV%: coefficient of variation  
SD: standard deviation  
GM: geometric mean  
QD: dosed once daily  
BD: dosed twice daily

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