Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
INSTIs (alpha order)	**All INSTIs**	• Well-tolerated	• Possible ↑wt in adults, esp. Black/African American women • Potential for multiple drug interactions due to hepatic metabolism • Oral absorption can be reduced by simultaneous admin. w/ polyvalent cations
	BIC	• Once daily • Can give w/ or w/o food • Avail. as FDC • Higher barrier to resistance vs. RAL	• FDC tab **not recommended** in hepatic impairment or est. CrCl <30 mL/min • CNS side effects, esp. sleep disturbances; depression and suicidal ideation rare, usually in pts w/ psychiatric dz hx • CYP3A4 and UGT1A1 substrate, potential for drug interactions • Inhibits tubular secretion of creatinine; incr. SCr w/o affecting glomerular fxn; generally benign
	DTG	• Once daily • Can give w/ or w/o food • Avail. as FDC • Single-agent DTG avail. in several strengths, small tab size • Avail. as dispersible tab for susp • Higher barrier to resistance vs. RAL	• UGT1A1 substrate, potential for drug interactions • CNS side effects, esp. sleep disturbances; depression and suicidal ideation rare, usually in pts w/ psychiatric dz hx • Inhibits tubular secretion of creatinine; incr. SCr w/o affecting glomerular fxn; generally benign

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	RAL	• Can give w/ or w/o food • Avail. as tab, chew tab, and granules for susp • Chewable tabs can be crushed/mixed w/ various liquids for infants ≥4 wk old and ≥3 kg • Favorable lipid profile	• Lower barrier to resistance vs. boosted PI-, BIC-, or DTG-based regimens • UGT1A1 substrate, potential for drug interactions • Depression and suicidal ideation rare, usually in pts w/ psychiatric dz hx • Incr. in CK, myopathy, and rhabdomyolysis have been reported • Potential for rare allergic rxn/hepatitis • Granule form requires multistep prep; requires caregiver instruction • Higher pill burden than other INSTI-based regimens; no FDC form
NNRTIs (alpha order)	**All NNRTIs**	• Long half-life • Lower risk of dyslipidemia/fat maldistribution vs. PIs • PI-sparing • Lower pill burden for children taking solid form; easier to use vs. PI-based regimens	• Prevalence of NNRTI-resistant strains in ART-naïve pts; low barrier to resistance; single mutation can confer resistance, w/ cross-resistance between EFV and NVP • Rare but serious, life-threatening skin rash, incl. SJS, and hepatic toxicity (greatest risk w/ NVP), although none of these have been reported in neonates • Potential for multiple drug interactions due to hepatic metabolism

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	DOR	• Once daily • Avail. as FDC • Can give w/ or w/o food • Maintains antiviral activity in the setting of some NNRTI mutations • Favorable lipid profile • Not assoc w/ wt gain vs. boosted DRV or EFV	• Neuropsych AEs (fewer compared w/ EFV) • Contraindicated w/ strong CYP3A inducers • Potential for CYP3A4 drug interactions • Tx-emergent DOR resistance mutations may confer resistance to some NNRTIs
	EFV	• Once daily • Avail. as FDC • Potent ARV activity • Can give w/ food (except high-fat meals); recommended to take on empty stomach • May open capsules, add to food	• Neuropsych AEs incl. dizziness, abnormal dreams, HA, depression, suicidality, insomnia, somnolence; HS dosing recommended to reduce CNS effects • Rash (generally mild); QT prolongation; dyslipidemia • Potential for CYP3A4 drug interactions • No commercially avail. liquid form • Limited dosing data for children <3 yo • No dosing data for children <3 mo
	NVP	• Liquid form avail. • Dosing info for young infants avail. • Can give w/ or w/o food • ER form allows once-daily dosing in older children	• Reduced virologic efficacy in young infants, regardless of peripartum NVP exposure • ↑incidence of rash/HSR vs. other NNRTIs • ↑rate of serious hepatic toxicity vs. EFV • Decreased virologic response vs. EFV • BID dosing needed in children w/ BSA <0.58 m^2 • Lower resistance barrier

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	RPV	• Once daily • Avail. as FDC	• Don't use if HIV VL >100K copies/mL • Must take w/ ≥500-kcal meal at same time daily (may affect adherence) • Potential for CYP3A4 drug interactions • Oral absorption ↓ w/ incr. gastric pH; use w/ PPIs contraindicated • Low resistance barrier • Depression, HA, rash, QTc prolongation
PIs (alpha order)	**All PIs**	• NNRTI-sparing • Clinical, virologic, immunologic efficacy well-documented • Higher barrier to resistance vs. NNRTIs and RAL; PI resistance requires multiple mutations • When combined w/ dual-NRTI backbone, targets HIV at 2 steps of replication (inhibits viral RT and protease)	• Metabolic complications (dyslipidemia, fat maldistribution, insulin resistance) • Potential for multiple drug interactions due to hepatic metabolism • ↑pill burden vs. NRTI-/NNRTI-based regimens for pts taking solid forms • Poor palatability of liquid preps (may affect adherence) • Most PIs require RTV/COBI boosting; thus, more drug interactions

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	Boosted ATV	• Once daily • Powder form avail. • ATV has less effect on TG, total cholesterol levels vs. other PIs (however, RTV boosting is assoc w/ these)	• No liquid form • Admin. w/ food • Indirect hyperbilirubinemia is common but asymptomatic. Scleral icterus may be distressing, affect adherence • Cholelithiasis, nephrolithiasis, PR interval prolongation • Use w/ caution w/ preexisting conduction system defects (can prolong PR interval) • RTV/COBI assoc w/ many drug interactions • Absorption ↓ when given w/ acid-lowering agents • COBI inhibits tubular secretion of creatinine; incr. SCr w/o affecting glomerular fxn; generally benign
	Boosted DRV	• Once daily in children ≥12 yo • Liquid form avail. • DRV requires a boosting agent • Avail. as FDC	• Pedi pill burden high w/ current tablet dose forms • Admin. w/ food • Must be boosted to achieve adequate plasma concentrations • Contains sulfa moiety (cross-sensitivity w/ sulfonamides unknown) • Hyperlipidemia, incr. transaminases • RTV/COBI assoc w/ many drug interactions • Can only be used once daily in absence of certain PI-associated resistance mutations • COBI inhibits tubular secretion of creatinine; incr. SCr w/o affecting glomerular fxn; generally benign

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	LPV/r	• LPV is the only PI avail. coformulated w/ RTV in liquid and tab forms • Tabs may be given w/o regard to food, but better tolerated w/ meal/snack	• Poor palatability of liquid form (bitter), although palatability of FDC better than RTV alone • Give liquid form w/ food • RTV assoc w/ many drug interactions • Should not be given to infants before postmenopausal age of 42 wk and postnatal age ≥14 days • Use w/ caution if preexisting conduction system defects (can prolong PR and QT interval)
Dual-NRTI backbones (alpha order)	**ABC + (3TC or FTC)**	• Palatable liquid forms • Can give w/ or w/o food • Avail. as FDC	• Risk of ABC HSR; perform HLA-B*5701 screening before initiating ABC tx • ABC has been assoc w/ CV dz and cardiac events in some, but not all, observational studies in adults
	FTC/TAF for kids ≥6 yo	• Once daily • Small tab size • Lower risk of TFV-associated renal and bone toxicity w/ TAF vs. w/ TDF in adults • Avail. as FDC • Active against HBV; recommended dual-NRTI option for pts w/ coinfection	• Limited safety/efficacy data of this combo in children • ↑lipid levels

Advantages & Disadvantages of ARV Components Recommended for Initial Tx in Children[1]

class	ARV	advantages	disadvantages
	TDF + (3TC or FTC)	• Once-daily dosing for TDF • Resistance slow to develop • Lower risk of mitochondrial toxicity vs. other NRTIs • Can give w/ or w/o food • Avail. as lower-strength tabs/oral powder for use in younger children • Avail. as FDC • Active against HBV; recommended dual-NRTI option for pts w/ coinfection	• Limited pedi experience • Potential bone and renal toxicity
	ZDV + (3TC or FTC)	• Extensive pedi experience • Coformulations of ZDV/3TC avail. (Combivir, generic) for children ≥30 kg • Palatable liquid forms • Can give w/ or w/o food • FTC avail. as palatable liquid form for once-daily admin.	• Bone marrow suppression w/ ZDV • Lipoatrophy w/ ZDV • ZDV requires bid dosing

[1] Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Table 8. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/regimens-recommended-initial-therapy-antiretroviral-naive-children. Accessed July 31, 2024.