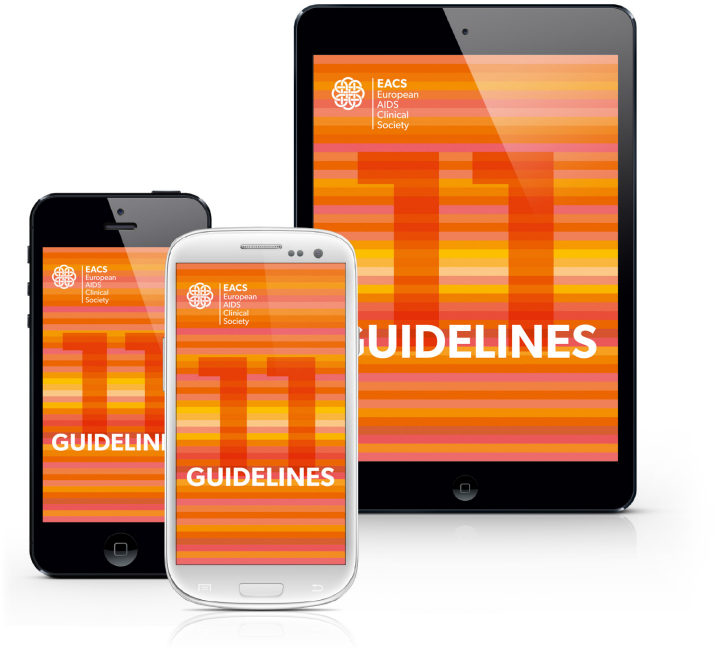
EACS Guidelines
v11.0



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HIV TREATMENT

Initial Combination Regimen for ART-naïve Adult PLWH

ONLY 2 CATEGORIES

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	

Alternative regimens	
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner
TAF/FTC or TDF/XTC + RPV or TAF/FTC/RPV or TDF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food

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Initial Combination Regimen for ART-naïve Adult PLWH

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	

NEW

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Initial Combination Regimen for ART-naïve Adult PLWH

Alternative regimens	
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner
TAF/FTC or TDF/XTC + RPV or TAF/FTC/RPV or TDF/FTC/RPV	CD4 count > 200 cells/μL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food

~~ABC/3TC + RAL qd or bid~~
~~TDF/FTC/EVG/c~~
~~TAF/FTC/EVG/c~~
~~ABC/3TC +EFV~~
~~ABC/3TC + ATV/c or ATV/r~~
~~ABC/3TC + DRV/c or DRV/r~~
~~TAF/FTC or TDF/FTC or TDF/3TC + ATV/c or ATV/r~~
~~RAL 400 mg bid + DRV/c or DRV/r~~

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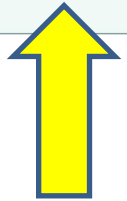
Initial Combination Regimen for ART-naïve Adult PLWH

If the person has acquired HIV while receiving PrEP: In this situation, change PrEP to a triple-drug ART regimen including a third drug with a high barrier to resistance (preferably DRV/b, DTG or BIC) plus two nucleoside analogues without interrupting antiretrovirals.

1 NRTI + INSTI		
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	II (Weight increase (DTG)) V (3TC/DTG not after PrEP failure)



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Switch Strategies for Virologically Suppressed Persons

Dual therapies

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is

a) no historical resistance and
b) HBV immunity or if non-immune concomitant HBV Vaccination

Dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b
Long-acting CAB + RPV bi-monthly injections

NEW

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

Switch Strategies for Virologically Suppressed Persons

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Dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b
Long-acting CAB + RPV bi-monthly injections

~~3TC+ATV/R~~

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

Virological Failure

Section has been updated including new wording for treatment recommendations in the presence of resistance mutations

In case of demonstrated resistance mutations	General recommendations:
	Use at least 2 and preferably 3 active drugs in the new regimen (including active drugs from previously used classes) based on resistance mutations present in current and earlier genotypic analyses
	* If genotype shows only limited NRTI mutation(s) e.g. M184V and/or 1-2 TAMs(iii): new regimen can include 2 NRTIs (3TC or FTC plus another NRTI with at most low level resistance) and either 1 active PI/b (i.e. DRV/b) or BIC or DTG (RAL, EVG/c or NNRTI not recommended) * If genotype shows multiclass resistance (i.e. ≥ 2 classes): new regimen will usually use - at least 1 fully active PI/b (i.e. DRV/b) or 1 fully active 2nd generation INSTI (BIC, DTG) - plus 1 or 2 drugs remaining fully active despite resistance to other drugs from the class (i.e. 1 or 2 NRTIs and/or DOR) - and/or from a class not used previously i.e. INSTI, NNRTI, PI/b, assessed by genotypic testing * When a 2-3 drugs active regimen cannot be constructed with NRTI, NNRTI, PI/b and INSTI, a drug with a new mechanism of action such as fostemsavir or ibalizumab can be added to obtain such a 2-3 drugs active regimen

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Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy

"The decision of ART regimen should be discussed with the person and individualized taking into account tolerability, possible adherence issues, as well weighed against potential risk coming from ART exposure or suboptimal pharmacokinetics in pregnancy"

Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy

Recommended regimens	
2 NRTIs + INSTI (PREFERRED)	
ABC/3TC + DTG or ABC/3TC/DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy HLA-B*57:01 negative HBsAg negative
TDF/XTC or TAF/FTC + DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy. TAF/FTC not recommended in first 14 weeks of pregnancy
TDF/XTC or TAF/FTC + RAL 400 mg bid	TAF/FTC not recommended in first 14 weeks of pregnancy
2 NRTIs + PI/r	
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food TAF/FTC not recommended in first 14 weeks of pregnancy

NEW

NEW

NEW

NEW

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Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy

Alternative regimens	
2 NRTIs + INSTI	
ABC/3TC + RAL 400 mg bid	HBsAg negative HLA-B*57:01 negative
2 NRTIs + NNRTI	
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner TAF/FTC not recommended in first 14 weeks of pregnancy
TDF/XTC or TAF/FTC + RPV or TDF/FTC/RPV or TAF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food TAF/FTC not recommended in first 14 weeks of pregnancy
2 NRTIs + PI/r	
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food

~~ATV, ZDV and LPV/r~~

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ART in TB/HIV Co-infection

Suggested timing of ART initiation in TB/HIV co-infection

ART should be started as soon as possible (within two weeks of initiating TB treatment) regardless of CD4 count

NEW

However, if TB meningitis signs and symptoms are present ART initiation may be delayed. See When to start ART in PLWH with Opportunistic Infections (OIs)

Pre-exposure Prophylaxis (PrEP)

Whole section has been updated

The following procedures are recommended:

- Documented negative fourth generation HIV test a week prior to starting PrEP. In case of suspicion of acute HIV-infection, an RNA test on plasma should also be performed, page 15. During PrEP, a fourth generation HIV test should be repeated at one month and then every 3 months. In stable long-term users who are on 6 monthly prescriptions an interim third generation test that can be performed without a visit to clinic is acceptable
- PrEP should be changed to triple-drug ART without interruption in case of early clinical signs of HIV seroconversion or a positive HIV diagnostic test which may necessitate referral for evaluation to an HIV unit, see ART initiation page 12
- PrEP may continue during pregnancy and breastfeeding if the risk of acquiring HIV persists

NEW

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Pre-exposure Prophylaxis (PrEP)

Whole section has been updated

3. PrEP regimen

- TDF/FTC 300*/200 mg 1 tablet qd. In both men and women PrEP should be taken for 7 days before the first exposure and stopped 7 days after the last exposure
- A trial with daily TAF/FTC in MSM and transgender women has shown non inferiority to daily TDF/FTC. No data are available in other high risk groups
- For men only, PrEP may be dosed 'on demand' (double dose of TDF/FTC 2-24 hours before each sexual intercourse, followed by two single doses of TDF/FTC, 24 and 48 hours after the first drug intake; no data for TAF/FTC so far). There are no efficacy data with on demand PrEP with TDF/FTC in women

NEW

Acknowledgements

HIV Treatment	
Chair: José Arribas	**Madrid, Spain**
Vice-Chair: Jean-Michel Molina	**Paris, France**
Young scientist: Rosa De Miguel Buckley	**Madrid, Spain**
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Drug-drug interactions

Catia Marzolini
for the Drug-Drug interactions EACS Guidelines panel

Part III

Drug-drug interactions and other prescribing issues in PLWH

- Drug-drug interactions between **ARVs** and **non-ARVs**
- Drug-drug interactions between **Analgesics** and ARVs
- Drug-drug interactions between **Anticoagulants/Antiplatelet Agents** and ARVs
- Drug-drug interactions between **Antidepressants** and ARVs
- Drug-drug interactions between **Antihypertensives** and ARVs
- Drug-drug interactions between **Anti-malarial Drugs** and ARVs
- **Drug-drug interactions between Anti-tuberculosis Drugs and ARVs** **NEW**
- **Drug-drug interactions between Anxiolytics and ARVs** **NEW**
- Drug-drug interactions between **Bronchodilators** (for COPD) and ARVs
- Drug-drug interactions between **Contraceptives** and ARVs
- Drug-drug interactions between **Corticosteroids** and ARVs
- **Drug-drug interactions between COVID-19 Therapies and ARVs** **NEW**
- **Drug-drug interactions between Hormone Replacement Therapy (HRT) and ARVs** **NEW**
- Drug-drug interactions between I**mmunosuppressants** (for SOT) and ARVs
- Drug-drug interactions between **Pulmonary Antihypertensives** and ARVs
- Drug-drug interactions between **Viral Hepatitis Drugs** and ARVs
- Administration of ARVs in PLWH with **Swallowing difficulties**
- Dose adjustment of ARVs for **Impaired hepatic function**
- Dose adjustment of ARVs for **Impaired renal function**
- Selected non-ARV drugs requiring dosing dosage adjustment in renal insufficiency
- Prescribing in elderly PLWH
- Selected top 10 drug classes to avoid in older PLWH
- Dosage recommendations for hormone therapy when used at high doses for gender transitioning

Major updates to DDI tables

+ **FOSTEMSAVIR** : (produg converted to temsavir)

temsavir mainly metabolized by hydrolysis, contribution of CYP3A4
no inhibitory or inducing effects on CYPs or UGTs
inhibition of BCRP, OATP1B1/3

➔ **temsavir does mostly not impact the PK of comedications except BCRP/OATP substrates**

examples: statins, ethinylestradiol, grazoprevir

➔ **strong inhibitors of CYP3A4: no clinically relevant increase in temsavir concentrations**

➔ **moderate inducers of CYP3A4: no clinically relevant reduction in temsavir concentrations**

➔ **strong inducers of CYP3A4: contraindicated as substantial reduction in temsavir concentrations**

QT interval prolongation at supra-therapeutic doses

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DDI between ARVs and non-ARVs

	Non-ARV drugs	ATVlc	ATVlr	DRVlc	DRVlr	LPVlr	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG
Cardiovascular drugs	atorvastatin	↑822%	↑	↑290%	↑	↑490%	↓2%	↓43%	↓37%	↓	↑4% D10%	↑	↔	↔	↔	↔	↔
	fluvastatin	↑	↑	↑	↑	↔	↔	↑	↑	↔	↔	↑	↔	↔	↔	↔	↔
	pravastatin	↑	↑	↑	↑81%	↑33%	↔	↓44%	↓	↔	↔	↔	↔	↔	↔	↔	↔
	rosuvastatin	↑242%	↑213%	↑93%	↑48%	↑108%	↔	↔	↔	↔	↔	↑69%	↔	↔	↔	↔	↔
	simvastatin	↑	↑	↑	↑	↑	↔	↓68%	↓	↓	↔	↑	↔	↔	↔	↔	↔
	amlodipine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
	diltiazem	↑a	↑a	↑	↑	↑a	E	↓69%	↓E	↓	E	E	E	E	↔	E	↔
	metoprolol	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	verapamil	↑a	↑a	↑	↑	↑a	E	↓	↓E	↓	E	E	E	E	↔	E	↔
	warfarin	↑	↑ or ↓	↑	↓	↓	↔	↑ or ↓	↑	↑ or ↓	↔	↔	↔	↔	↔	↔	↔
CNS drugs	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↔	↔	↔
	carbamaze-pine	↑D	↑D	↑D	↑	↑D c	D	↓27% D36%	D	↓D	D	D	D	D	D	D	D49%
	citalopram	↑a,b	↑a,b	↑	↑	↑a,b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	diazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
	lamotrigine	↔	↓32% d	↔	↓	↓50%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔
	midazolam (oral)	↑	↑	↑	↑	↑	↓18%	↓	↓	↓	↔	↔	↑18%	↑15%	↑10%	↔	↔
	mirtazapine	↑b	↑b	↑	↑	↑b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↔	↔	↔
	phenytoin	D	↓D	D	↓D	↓D c	D	↓D	D	D	D	D	D	D	D	D	D e
	pimozide	↑	↑	↑	↑	↑	↔	↑	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	sertraline	↑	↓	↑	↓49%	↓b	↔	↓39%	↓	↓	↔	↔	↔	↔	↔	↔	↔
	triazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
Anti-infectives	clarithromycin	↑E a,b	↑E a,b	↑E	↑	↑ a,b	↑	↓39%	↓39% E42%	↓31% E26%	E b	E a,b	E	E	↔	E b	↔
	fluconazole	↑? a,b	↔ a,b	↑?	↔	↔ a,b	↑	↔	E86%	E100%	E b	E a,b	↔	↔	↔	E b	↔
	itraconazole	↑Eb	↑Eb	↑E	↑E	↑Eb	↑	↓39%	↓E	↓61%	E b	Eb	E	E	↔	E b	↔
	rifabutin	↑D f	↑ g	↑D f	↑ g	↑ g	D50% h	↓38% i	↓17% D37%	↑17%	D42%	D30%	k	D38%	↔	D	↔
	rifampicin	D	D72%	D	D57%	D75% m	D82%	D26%	D	D58%	D80%	D82%	D	D75%	D59%	D	D54% n
	voriconazole	↑↓ Eb	↑↓ Db	↑E	↓	↑↓ Eb	↑	↓E	↑14% E36%	↓E	E	E	E	E61%	↔	E	↔
	antacids	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	D	D	↔	D
	PPIs	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	↔	↔
	H2 blockers	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	↔	↔

Major updates to DDI tables

+ **CABOTEGRAVIR** : metabolism by UGT1A1 (major), UGT1A9 (minor)
no inhibitory or inducing effects on CYPs or UGTs
inhibition of OAT1/3

Oral administration

- ➔ **cabotegravir does mostly not impact comedications except sensitive OAT substrates**
- ➔ **strong inhibitors: minimal effect on cabotegravir concentrations**
- ➔ **moderate inducers: minimal effect on cabotegravir concentrations**
- ➔ **strong inducers: contraindicated as substantial reduction in cabotegravir levels**
- ➔ **divalent cations: similarly to other INSTIs, oral cabotegravir is subject to chelation**

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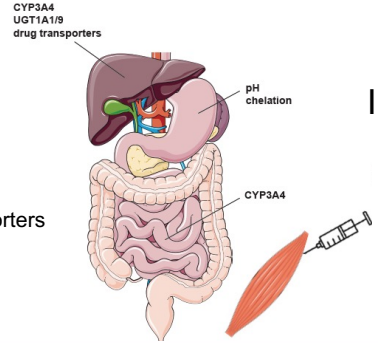
DDI between ARVs and non-ARVs

	Non-ARV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG
Cardiovascular drugs	atorvastatin	↑822%	↑	↑290%	↑	↑490%	↓2%	↓43%	↓37%	↓	↑14% D10%	↑	↔	↔	↔	↔	↔
	fluvastatin	↑	↑	↑	↑	↔	↔	↑	↑	↔	↔	↑	↔	↔	↔	↔	↔
	pravastatin	↑	↑	↑	↑81%	↑33%	↔	↓44%	↓	↔	↔	↔	↔	↔	↔	↔	↔
	rosuvastatin	↑242%	↑213%	↑93%	↑48%	↑108%	↔	↔	↔	↔	↔	↑69%	↔	↔	↔	↔	↔
	simvastatin	↑	↑	↑	↑	↑	↔	↓68%	↓	↓	↔	↑	↔	↔	↔	↔	↔
	amlodipine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
	diltiazem	↑a	↑a	↑	↑	↑a	E	↓69%	↓E	↓	E	E	E	E	↔	E	↔
	metoprolol	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	verapamil	↑a	↑a	↑	↑	↑a	E	↓	↓E	↓	E	E	E	E	↔	E	↔
	warfarin	↑	↑ or ↓	↑	↓	↓	↔	↑ or ↓	↑	↑ or ↓	↔	↔	↔	↔	↔	↔	↔
CNS drugs	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↔	↔	↔
	carbamaze-pine	↑D	↑D	↑D	↑	↑D c	D	↓27% D36%	D	↓D	D	D	D	D	D	D	D49%
	citalopram	↑a,b	↑a,b	↑	↑	↑a,b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	diazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
	lamotrigine	↔	↓32% d	↔	↓	↓50%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔
	midazolam (oral)	↑	↑	↑	↑	↑	↓18%	↓	↓	↓	↔	↔	↑18%	↑15%	↑10%	↔	↔
	mirtazapine	↑b	↑b	↑	↑	↑b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↔	↔	↔
	phenytoin	D	↓D	D	↓D	↓D c	D	↓D	D	D	D	D	D	D	D	D	D e
	pimozide	↑	↑	↑	↑	↑	↔	↑	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔
	sertraline	↑	↓	↑	↓49%	↓b	↔	↓39%	↓	↓	↔	↔	↔	↔	↔	↔	↔
	triazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔
Anti-infectives	clarithromycin	↑E a,b	↑E a,b	↑E	↑	↑ a,b	↑	↓39%	↓39% E42%	↓31% E26%	E b	E a,b	E	E	↔	E b	↔
	fluconazole	↑? a,b	↔ a,b	↑?	↔	↔ a,b	↑	↔	E86%	E100%	E b	E a,b	↔	↔	↔	E b	↔
	itraconazole	↑Eb	↑Eb	↑E	↑E	↑Eb	↑	↓39%	↓E	↓61%	E b	Eb	E	E	↔	E b	↔
	rifabutin	↑D f	↑ g	↑D f	↑ g	↑ g	D50% h	↓38% i	↓17% D37%	↑17%	D42% j	D30%	k	D38%	↔	D	↔
	rifampicin	D	D72%	D	D57%	D75% m	D82%	D26%	D	D58%	D80%	D82%	D	D75%	D59%	D	D54% n
	voriconazole	↑↓ Eb	↑↓ Db	↑E	↓	↑↓ Eb	↑	↓E	↑14% E36%	↓E	E	E	E	E61%	↔	E	↔
	antacids	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	D	D	↔	D
	PPIs	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	↔	↔
	H2 blockers	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	↔	↔

DDIs with oral vs im cabotegravir/rilpivirine

Oral administration

- chelation with divalent cations
- change in gastric pH
- Inhibition/induction CYP/drug transporters



Intramuscular administration

- chelation with divalent cations
- change in gastric pH
- Inhibition/induction CYP/drug transporters

Examples of medications interacting with the oral but not the intramuscular administration of RPV
Antacids; famotidine; lansoprazole; liraglutide; omeprazole; orlistat; pantoprazole; rabeprazole; ranitidine

Examples of medications interacting with the oral but not the intramuscular administration of CAB
Antacids; calcium; iron; magnesium; multivitamins containing divalent cations; orlistat; strontium ranelate

Intramuscular administration: → DDIs at the gastrointestinal level are avoided
→ DDIs at the hepatic level can still occur (magnitude of DDIs with inducers is not mitigated)

➔ **moderate and strong inducers are contraindicated with cabotegravir/rilpivirine LA**

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DDIs with COVID19 therapies

Drug-drug Interactions between COVID-19 Therapies and ARVs

	COVID-19 Therapy	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
Antiviral Drugs and mAbs	bamlanivimab/ etesevimab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	casirivimab/ imdevimab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	remdesivir	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Immune Therapies	anakinra	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	baricitinib	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	canakinumab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	convalescent plasma	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	COVID-19 vaccines	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	dexamethasone (low dose*)	↑a	↑a	↑a	↑a	↑a	Db	↓c	↓c	↓c	Dd	D	De	↔	↔	D	↔	↑a	↔	D	↔
	hydrocortisone	↑a	↑a	↑a	↑a	↑a	↔	↓c	↓c	↓c	↔	↔	↔	↔	↔	↔	↔	↑a	↔	↔	↔
	methyl-prednis-olone	↑a	↑a	↑a	↑a	↑a	↔	↓c	↓c	↓c	↔	↔	↔	↔	↔	↔	↔	↑a	↔	↔	↔
	ruxolitinib	↑f	↑f	↑f	↑f	↑f	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↑f	↔	E	E
	sarilumab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	tocilizumab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

Refer to the DDI table between anticoagulants/antiplatelet agents and ARVs for COVID patients receiving anticoagulants.

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Dosing recommendations with low dose dexamethasone

b Consider increasing DOR to 100 mg bid during treatment for COVID-19 and for approximately 2 weeks after the end of treatment.

c Doubling the dose of dexamethasone, hydrocortisone or methylprednisolone is recommended.

d Dexamethasone is a dose dependent CYP3A4 inducer and may decrease RPV concentrations. Although the level of induction at the dose recommended for COVID (6 mg/day) is likely to be relatively modest, it is advised either using hydrocortisone (IV, 200 mg/day) or, alternatively, giving dexamethasone but doubling the dose of RPV to 50 mg qd. This dose should be maintained for 2 weeks after the end of treatment as any reduction in RPV concentrations may persist for up to 14 days after stopping dexamethasone.

e Consider using MVC at a dose of 600 mg bid with dexamethasone in the absence of a PI or other potent CYP3A4 inhibitors. Consider decreasing MVC to 150 mg bid with dexamethasone in presence of a PI or strong CYP3A4 inhibitor. These dose adjustments should be considered during treatment for COVID-19 and for approximately 2 weeks after the end of treatment.

COVID-19 Drug Interactions

www.covid19-druginteractions.org

DDIs with Anti-tuberculosis Drugs

Drug-drug Interactions between Anti-tuberculosis Drugs and ARVs

Anti-tuberculosis drugs		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
First line and second line drugs	amikacin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a
	bedaquiline	↑ b	↑ b	↑	↑	↑62% b	↔	↓18%	↓	↑3%	↔ b	↔ b	↔	↔	↔	↔ b	↔	↑	↔	↔	↔
	capreomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ c	↔	↔	↔	↑ E a
	clofazimine	↔ b	↔ b	↔	↔	↔ b	E	↔	↔	↔	E b	E b	E	E	↔	↔ b	↔	↔	↔	↔	↔
	cycloserine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	delamanid	d	d	d	d	d	↔	↔ e	↔	↔	↔ f	↔ f	↔	↔	↔	↔ f	↔	d	↔	↔	↔
	ethambutol	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	ethionamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	isoniazid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	kanamycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a
	moxifloxacin	↑ b	↓ b	↔	↓	↓ b	↔	↓	↓	↔	↔ b	↔ b	↔	↔	↔	↔ b	↔	↔	↔	↔	↔
	para-aminosali-cylic acid	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↑E
	pyrazinamide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	rifabutin	↑ D g	↑h	↑ D g	↑h	↑h	D50% i	↓38% j	D37%	↑17%	D42% k	D30%	I	D38%	↔	D	↔	↑ D g	E19%	Dm	↔
	rifampicin	D	D72%	D	D57%	D75% n	D82%	D26%	D	D58%	D80%	D82%	D o	D75%	D59%	D	D54% p	D	D40% q	Dm	D12%
	rifapentine	D	D	D	D	D	D	D	D	D	D	D	D o	D	D	D	D r	D	D	Dm	↔
	streptomycin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ a

m Rifamycins decrease TAF exposure when given 25 mg qd therefore the label recommends to use TAF 25 mg bid. However, the intracellular tenofovir diphosphate (active entity) concentrations are likely to be higher than those observed with TDF even without rifampicin [1] suggesting that usage of TAF 25 mg qd may be acceptable.

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Alignment with WHO HIV treatment guidelines released in July 2021

Other updates to DDI tables

EACS tables are linked to DDIs websites and have been revised to include all updates made to the websites in the past year. >30 comedications were included to existing tables.

HIV Drug Interactions

www.hiv-druginteractions.org

HEP Drug Interactions

www.hep-druginteractions.org

Drug-drug Interactions between Viral Hepatitis Drugs and ARVs

Viral hepatitis drugs		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
HCV DAAs	elbasvir/ grazoprevir	↑	↑376% ↑958%	↑	↑66% ↑650%	↑271% ↑1186%	↓4% ↑7%	↓54% ↓83%	↓	↓	↑7% ↓2%	↔ ↑	↔	↔	↔	↔	↓2% ↓19%	↑118% ↑436%	↓19% ↓11%	↔	↓7% ↓14%
	glecaprevir/ pibrentasvir	↑	↑553% ↑64%	↑	↑397%	↑338% ↑146%	↔	↓	↓	↓	E 84%	↑	E	E	↔	↔	↔	↑205% ↑57% E47%	E47%	↔	E29%
	sofosbuvir	↔	↔	↑	↑34%	↔	↔	↓6%	↔	↔	↑9%	↑	↔	↔	↔	↔	↔	↔	↓5% D27%	↔	↓6%
	sofosbuvir/ ledipasvir	↑a	↑8% ↑113%a	↑a	↑34% ↑39%a	↔a	↑4% ↓8%	↓6% ↓34%a	↔	↔	↑10% ↑8%a	↑	E	↑7% ↓13%	↔	↔	↔	↑36% ↑78%a	↓5% ↓9% D~20%	E32%	E a
	sofosbuvir/ velpatasvir	↔a	↑22% ↑142%a	↔a	↓28% ↓16%a	↓29% ↑2%a	↔	↓3% ↓53%	↓	↓	↑16% ↓1%	↑	E	↔	↔	↔	↓8% ↓9%	↑a	↑24% ↓2%	↔	E a
	sofosbuvir/ velpatasvir/ voxilaprevir	↑	↑40% ↑93% ↑331%	↑a	↓28% ↓5% ↑143%b	↑	↔	↓	↓	↓	↔	↑	E	↑9% ↓4% ↓9%	↔	↔	↔	↑22% ↑16% ↑171%a	↔	E	E a
HDV	Bulevirtide	↑	↑	↑	↑	↑	E	↑	↑	↔	E	↔	E	↔	↔	E	↔	↑	↔	↔	↔

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Prevention and Management of Co-morbidities Guidelines V11.0

EACS Guidelines V11.0

- Co-morbidities Guidelines largest section of the EACS Guidelines
- 57 pages of guidance spanning 17 major themes
- Incorporates principles of shared care
- Challenges of COVID19

Frailty / Ageing	Type 2 diabetes mellitus
Opioid addiction	Dyslipidaemia
Cancer	Lifestyle Interventions
Cardiovascular Disease	Hypertension
Renal disease	Liver disease
Obesity / weight gain	Sexual and reproductive health
Respiratory disease	Travel
Organ transplant	Mental health and cognitive impairment
Bone health / vit D / fractures	

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Mental Health – Anxiety Disorders

Screening and diagnosis of anxiety		
Who?	**How to screen?**	**How to diagnose?**
Consider screening all PLWH recommended at each clinic visit (in view of the high prevalence of anxiety) **Populations at particularly high risk** • Positive history of anxiety disorders in family • Anxious personality • Alcohol excess • As part of investigation of cognitive impairment, see page 104 • Multiple stressful life events (particular relevance during COVID-19 pandemic)	**Generalised Anxiety Disorder-2 (GAD-2) Screening tool**[i]**:** 'Over the last 2 weeks, how often have you been bothered by the following problems?' • Feeling nervous, anxious or on edge • Not being able to stop or control worrying **Score each question and calculate sum:** 0. Not at all 1. Several days 2. More than half the days 3. Nearly every day	**If GAD-2 cut-off score of ≥ 3**, ask the following questions to diagnose General Anxiety Disorder: • excessive anxiety for more days than not over 6 months • difficulty controlling worry • associated with at least three of these symptoms (restlessness, fatigue, difficulty concentrating, irritability, muscle tension, sleep disturbances) • significant life impairment • not attributable to another substance or medical condition • not being better explained by another medical disorder Seek expert advice to diagnose panic disorders, social phobia and PTSD Rule out hyperthyroidism, hypoglycemia and hyperadrenocorticism. Exclude caffeine excess and use of stimulants (such as cocaine, crystal meth, amphetamines)

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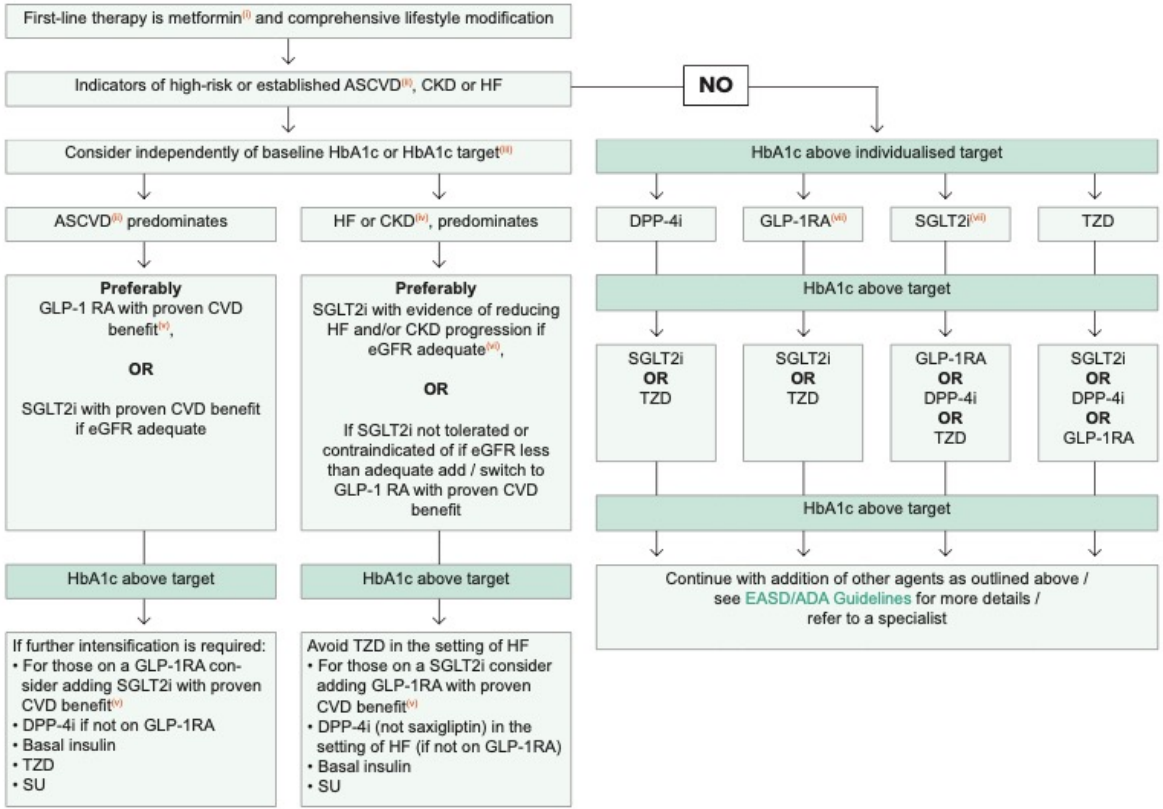
Diabetes mellitus



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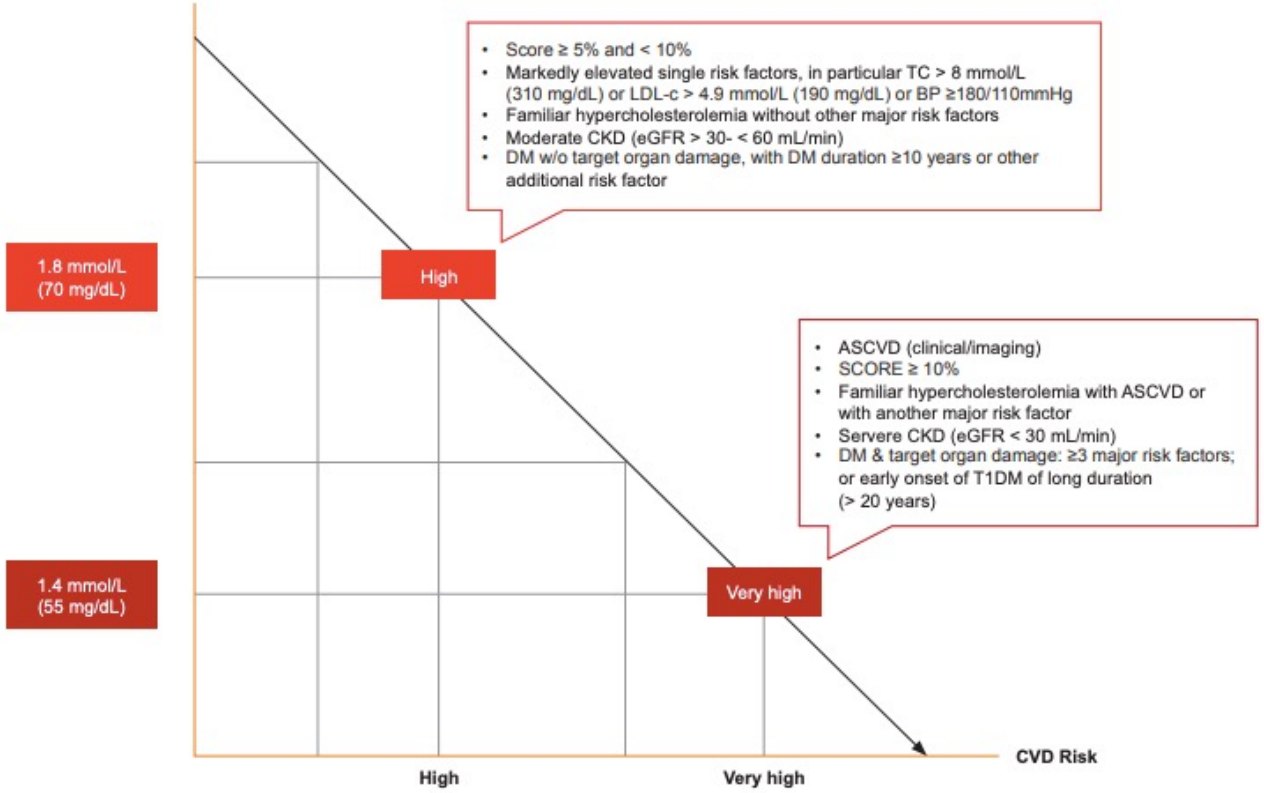
Treatment of dyslipidaemia – LDL goals



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Obesity / Weight Gain

- Evolving area
- More detailed guidance
- Targeted treatment goals
- Lifestyle, behavioural, pharmacological and surgical management options

	Weight Gain	Obesity	Comments
Definition	It is a physiological phenomenon associated with aging. Body weight of an average European adult is estimated to increase by 0.3 - 0.5 kg per year Definition is lacking. An increase > 5% of weight is often used, as opposed to the magnitude of weight loss recommended in lifestyle interventions as initial treatment of cardiometabolic conditions	BMI-based definitions (WHO): Overweight: BMI 25 to < 30 kg/m² Class I obesity: BMI 30 to < 35 kg/m² Class II obesity: BMI 35 to < 40 kg/m² Class III obesity: BMI ≥ 40 kg/m² For Asian populations, overweight is defined as BMI 23 to 27.5 kg/m² and obesity ≥ 27.5 kg/m²	Weight gain and obesity represent a continuum associated with negative health
Consequences	Increased risk of DM, hypertension, dyslipidemia, and CVD	Body Image disturbance Increased risk of DM, hypertension, CVD some cancers, obstructive sleep apnea, cholecystitis, erectile dysfunction, non-alcoholic fatty liver disease, osteoarthritis, depression, and neurocognitive impairment	
Contributing factors	Older age Sedentary lifestyle Altered sleep pattern Intake of excess or poor-quality calories (e.g., saturated fats, processed sugars) Excess alcohol consumption Some medications (e.g., psychotropic drugs, steroids, anti-diabetic drugs) Endocrine disorders (e.g., GH deficiency, hypothyroidism, Cushing's syndrome, hypogonadism)		
Impact of ART	Initiation of ART in PWH increases weight as part of a return-to-health phenomenon INSTI and TAF may induce greater weight gain than other ARVs		See Adverse effects of ARVs and drug classes
Aim of intervention	Emphasise the importance of behaviour goals rather than weight loss goals An objective of 5 - 10% weight loss may have benefits on: • ↑ 5% HDL cholesterol • ↓ 5 mmHg systolic and diastolic BP in hypertension • ↓ 0.5% (decrease 2.55 mmol/mol) HbA1c in DM • Improving sleep apnoea		
Management	Motivation to change: Discuss support systems (e.g. family, friends), motivating factors, and barriers to change Discuss benefits of making changes Set realistic and achievable lifestyle changes		
Lifestyle recommendations	Consider behavioral intervention (motivational interviewing, stimulus control or cognitive restructuring) along with self-monitoring; intensify behavioral intervention if several unsuccessful weight loss attempts		See Lifestyle Interventions
General principles	Treat underlying or associated conditions There are several drugs specifically recommended for those with a BMI ≥ 30 kg/m² or ≥ 25 kg/m² and weight-related complications (DM, hyper¬tension) (e.g. orlistat, phentermine/topiramate, lorcaserin, naltrexone/bupropion, liraglutide). These drugs should be prescribed by an endocrinologist or obesity expert. All of them may have adverse effects and drug-drug interactions with ART		Consider TDM (therapeutic drug monitoring) in obese PLWH. ↑ risk of virological failure with long acting CAB/RPV in obese PWH
Bariatric surgery		Medical devices or endoscopic procedures (e.g intragastric balloon, aspiration therapy, endoscopic sleeve gstrroplasty) or bariatric surgery should be considered in persons with a BMI ≥ 40 kg/m² or ≥ 35 kg/m² with obesity-related comorbidities refractory to serious attempts at lifestyle changes and should be coordinated through an established, specialist-led obesity programme.	Consider therapeutic drug monitoring and drug dose adjustment post-bariatric surgery

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Approach to screening for Frailty

Older PLWH ≥ 50 years

At diagnosis and once a year in the follow-up

SCREENING FOR FRAILTY
walking speed or Short Physical Performance Battery (SPPB) or FRAIL Scale (FS)

NEGATIVE

Walk speed ≥ 1.2 m/s or SPPB 12 or FS 0 points

walk speed 0.8 - 1.2m/s or SPPB 10-11 or FS 1-2 points

POSITIVE

Walk speed ≤ 0.8 m/s or SPPB ≤ 9 or FS 3-5 points

> 1 geriatric syndromes:
falls, cognitive impairment, depression, polypharmacy, functional impairment

No

Usual follow-up

Diet and exercise recomendations

Yes

DIAGNOSE FRAILTY

Physical Function, Frailty and Geriatric Syndromes Assessment integrated in the Comprehensive Geriatric Asessment (CGA)
by a health practitioner with specific training in frailty assessment

Care Plan integrated in the global approach

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Acknowledgements

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- Franck Boccara
- Fatima Brañas
- Susanne Dam Nielsen
- Giada Sebastiani

Incoming Chair: Alan Winston

Young Scientist: Aoife Cotter

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  - Drug-drug interactions
  - Viral Hepatitis Co-infections
  - Opportunistic Infections and COVID19
  - Paediatric HIV Treatment

- Governing Board

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Clinical Management and Treatment of Viral Hepatitis Co-infections in PLWH

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Other: None

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Summary of Changes

- **Simplified HCV treatment option:**
  - If pangenotypic regimens are foreseen, HCV genotype determination is not mandatory before starting treatment
- **Treamtent of recently acquired Hepatitis C:**
  - Immediate treatment recommended to reduce onward transmission[1]
- **HCV treatment options**
  - Table with alternative treatment options was removed
- **HDV infection**
  - Bulevirtide added as treatment option for HDV-infection

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[1] Boesecke et al, NEAT recommendations, AIDS 2020

DAA treatment options

Preferred DAA HCV treatment options (except for persons pre-treated with Protease or NS5A inhibitors)				
HCV GT	Treatment regimen	Treatment duration & RBV usage		
		Non-cirrhotic	Compensated cirrhotic	Decompensated cirrhotics CTP class B/C
1 & 4	EBR/GZR	12 weeks[i]		Not recommended
	GLE/PIB	8 weeks	8-12 weeks[ii]	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV[ix]
	SOF/LDV +/- RBV	8-12 weeks without RBV[iii]	12 weeks with RBV[iv]	12 weeks with RBV[ix]
2	GLE/PIB	8 weeks	8-12 weeks[ii]	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV[ix]
3	GLE/PIB	8 weeks[v]	8-12 weeks[ii,v]	Not recommended
	SOF/VEL +/- RBV	12 weeks[vi]	12 weeks with RBV[vii]	12 weeks with RBV[ix]
	SOF/VEL/VOX	-	12 weeks	Not recommended
5 & 6	GLE/PIB	8 weeks	8-12 weeks[ii]	Not recommended
	SOF/LDV +/- RBV	12 weeks +/- RBV[viii]	12 weeks with RBV[iv]	12 weeks with RBV[ix]
	SOF/VEL	12 weeks		12 weeks with RBV[ix]

For HCV treatment options to be used if preferred options are not available, please see version 10.1 of the EACS Guidelines

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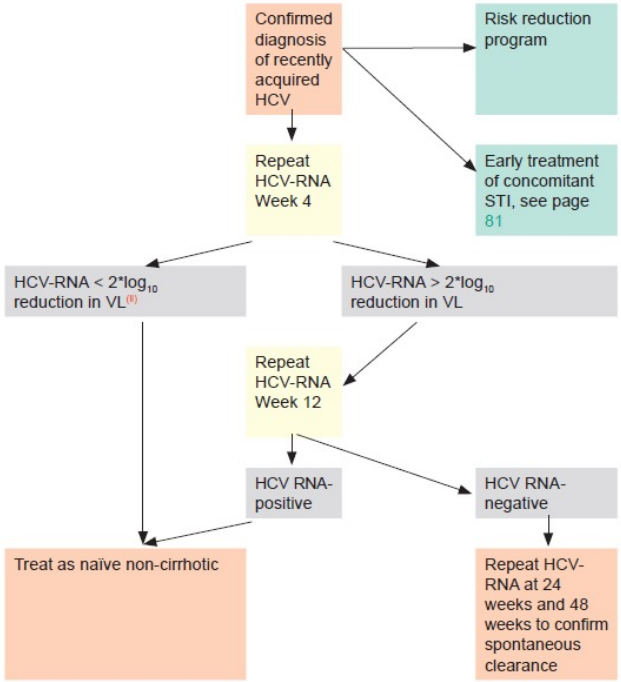
Recently acquired HCV infection

1. DAA based HCV treatment immediately after diagnosis is recommended in PLWH with ongoing risk behavior
2. If immediate treatment is not indicated, the algorithm below should be used



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Thanks

Viral Hepatitis Co-infections	
Chair: Andri Rauch	**Bern, Switzerland**
Vice-Chair: Christoph Boesecke	**Bonn, Germany**
Young scientist: Charles Béguelin	**Bern, Switzerland**
Juan Berenguer	Madrid,Spain
Sanjay Bhagani	London, United Kingdom
Raffaele Bruno	Pavia, Italy
Svilen Konov	London, United Kingdom
Karine Lacombe	Paris, France
Stefan Mauss	Düsseldorf, Germany
Luís Mendão	Lisbon, Portugal
Lars Peters	Copenhagen, Denmark
Massimo Puoti	Milan, Italy
Jürgen K. Rockstroh	Bonn, Germany

New young scientist: Kathrin van Bremen, Bonn Germany

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Part VI Opportunistic Infections and COVID-19

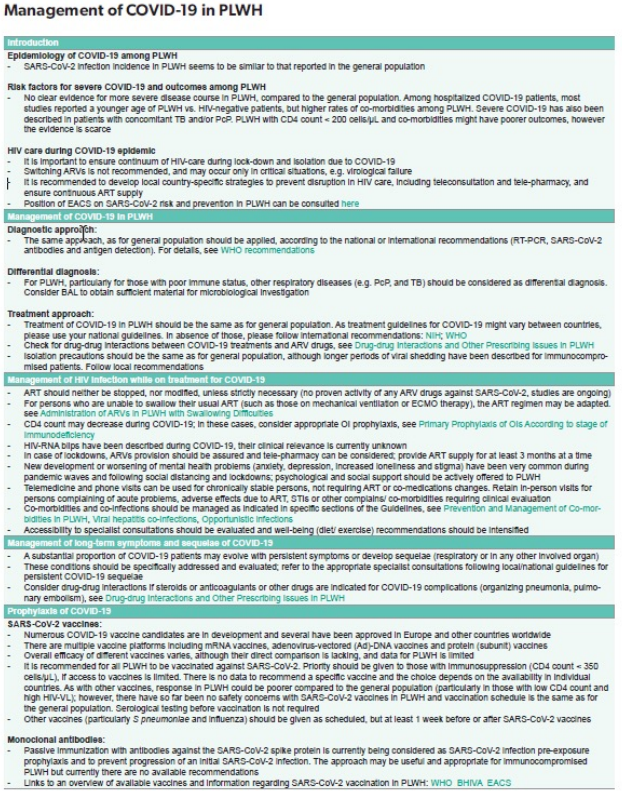
Ole Kirk for the Opportunistic Infection EACS guidelines panel

Changes

- New section on COVID-19
- Table on when to start ART in PLWH with OIs
- Table on primary Prophylaxis of OIs According to Stage of Immunodeficiency
- Prophylaxis and treatment of *Pneumocystis jirovecii* Pneumonia (PcP)
- TB section
- Minor revisions in text for individual OIs

New COVID-19 section

- **NOT COVID treatment guidelines**
- Introduction
- Management of COVID-19 in PLWH
- Management of HIV infection while on treatment for COVID-19 and during the pandemic
- Management of long-term symptoms and sequelae of COVID-19
- Prophylaxis of COVID-19
  - vaccines and monoclonal antibodies



Management of COVID-19 in PLWH

Introduction

Epidemiology of COVID-19 among PLWH
- SARS-CoV-2 infection incidence in PLWH seems to be similar to that reported in the general population

Risk factors for severe COVID-19 and outcomes among PLWH
- No clear evidence for more severe disease course in PLWH, compared to the general population. Among hospitalized COVID-19 patients, most studies reported a younger age of PLWH vs. HIV-negative patients, but higher rates of co-morbidities among PLWH. Severe COVID-19 has also been described in patients with concomitant TB and/or PcP. PLWH with CD4 count < 200 cells/µL and co-morbidities might have poorer outcomes, however the evidence is scarce

HIV care during COVID-19 epidemic
- It is important to ensure continuum of HIV-care during lock-down and isolation due to COVID-19
- Switching ARVs is not recommended, and may occur only in critical situations, e.g. virological failure
- It is recommended to develop local country-specific strategies to prevent disruption in HIV care, including teleconsultation and tele-pharmacy, and ensure continuous ART supply
- Position of EACS on SARS-CoV-2 risk and prevention in PLWH can be consulted here

Management of COVID-19 in PLWH

Diagnostic approach:
- The same approach, as for general population should be applied, according to the national or international recommendations (RT-PCR, SARS-CoV-2 antibodies and antigen detection). For details, see WHO recommendations

Differential diagnosis:
- For PLWH, particularly for those with poor immune status, other respiratory diseases (e.g. PcP, and TB) should be considered as differential diagnosis. Consider BAL to obtain sufficient material for microbiological investigation

Treatment approach:
- Treatment of COVID-19 in PLWH should be the same as for general population. As treatment guidelines for COVID-19 might vary between countries, please use your national guidelines. In absence of those, please follow international recommendations: NIH; WHO
- Check for drug-drug interactions between COVID-19 treatments and ARV drugs, see Drug-drug Interactions and Other Prescribing Issues in PLWH
- Isolation precautions should be the same as for general population, although longer periods of viral shedding have been described for immunocompromised patients. Follow local recommendations

Management of HIV infection while on treatment for COVID-19
- ART should neither be stopped, nor modified, unless strictly necessary (no proven activity of any ARV drugs against SARS-CoV-2, studies are ongoing)
- For persons who are unable to swallow their usual ART (such as those on mechanical ventilation or ECMO therapy), the ART regimen may be adapted. see Administration of ARVs in PLWH with Swallowing Difficulties
- CD4 count may decrease during COVID-19; In these cases, consider appropriate OI prophylaxis, see Primary Prophylaxis of OIs According to stage of Immunodeficiency
- HIV-RNA blips have been described during COVID-19, their clinical relevance is currently unknown
- In case of lockdowns, ARVs provision should be assured and tele-pharmacy can be considered; provide ART supply for at least 3 months at a time
- New development or worsening of mental health problems (anxiety, depression, increased loneliness and stigma) have been very common during pandemic waves and following social distancing and lockdowns; psychological and social support should be actively offered to PLWH
- Telemedicine and phone visits can be used for chronically stable persons, not requiring ART or co-medications changes. Retain in-person visits for persons complaining of acute problems, adverse effects due to ART, STIs or other complains/ co-morbidities requiring clinical evaluation
- Co-morbidities and co-infections should be managed as indicated in specific sections of the Guidelines, see Prevention and Management of Co-morbidities in PLWH, Viral hepatitis co-infections, Opportunistic infections
- Accessibility to specialist consultations should be evaluated and well-being (diet/ exercise) recommendations should be intensified

Management of long-term symptoms and sequelae of COVID-19
- A substantial proportion of COVID-19 patients may evolve with persistent symptoms or develop sequelae (respiratory or in any other involved organ)
- These conditions should be specifically addressed and evaluated, refer to the appropriate specialist consultations following local/national guidelines for persistent COVID-19 sequelae
- Consider drug-drug interactions if steroids or anticoagulants or other drugs are indicated for COVID-19 complications (organizing pneumonia, pulmonary embolism), see Drug-drug Interactions and Other Prescribing Issues in PLWH

Prophylaxis of COVID-19

SARS-CoV-2 vaccines:
- Numerous COVID-19 vaccine candidates are in development and several have been approved in Europe and other countries worldwide
- There are multiple vaccine platforms including mRNA vaccines, adenovirus-vectored (Ad)-DNA vaccines and protein (subunit) vaccines
- Overall efficacy of different vaccines varies, although their direct comparison is lacking, and data for PLWH is limited
- It is recommended for all PLWH to be vaccinated against SARS-CoV-2. Priority should be given to those with immunosuppression (CD4 count < 350 cells/µL). If access to vaccines is limited. There is no data to recommend a specific vaccine and the choice depends on the availability in individual countries. As with other vaccines, response in PLWH could be poorer compared to the general population (particularly in those with low CD4 count and high HIV-VL); however, there have so far been no safety concerns with SARS-CoV-2 vaccines in PLWH and vaccination schedule is the same as for the general population. Serological testing before vaccination is not required
- Other vaccines (particularly *S pneumoniae* and influenza) should be given as scheduled, but at least 1 week before or after SARS-CoV-2 vaccines

Monoclonal antibodies:
- Passive immunization with antibodies against the SARS-CoV-2 spike protein is currently being considered as SARS-CoV-2 infection pre-exposure prophylaxis and to prevent progression of an initial SARS-CoV-2 infection. The approach may be useful and appropriate for immunocompromised PLWH but currently there are no available recommendations
- Links to an overview of available vaccines and information regarding SARS-CoV-2 vaccination in PLWH: WHO BHIVA EACS

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When to start ART & primary prophylaxis

Table on when to start ART in PLWH with OIs

- Removal of CD4 threshold and of comment on CMV end organ disease
- Inclusion of comment on TB meningitis (delay of ART initiation for 4 weeks, but can be initiated within the first 2 weeks if CD4 < 50 (100) cells/μL)

Table on primary Prophylaxis of OIs According to Stage of Immunodeficiency

- Inclusion of strategy for management of positive cryptococcal serum antigen and CD4 count <100 cells/μL

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Pneumocystis jirovecii Pneumonia

Secondary prophylaxis:

- **Can be interrupted when** CD4 count >100 cells/μL and HIV-VL undetectable over 3 months

Treatment:

- Wording changed regarding addition of **caspofungin or other echinocandins** to standard treatment for moderate-severe PcP: **can be considered, but not mandatory**

Tuberculosis I

Treatment for fully susceptible TB:

- An alternative shorter regimen of **rifapentine, isoniazid**, **pyrazinamide** and **moxifloxacin** for 2 months, followed by **rifapentine**, **isoniazid** and **moxifloxacin** for 2 months can be used, if **rifapentine** is available

Reference to see Drug-drug Interactions between Anti-tuberculosis Drugs and ARVs

Tuberculosis II

Text for resistant TB revised (aligned with WHO guidelines from 2020)

- definition of XDR-TB
- all oral regimens for MDR-/XDR-TB

- and shorter (6-12 months) courses in selected groups of MDR-/XDR-TB

Drug choices	
Each empiric regimen should be reassessed and modified if needed once drug sensitivity results become available	
Group A: **Include all three drugs**	• **levofloxacin** or **moxifloxacin** • **bedaquiline** • **linezolid**
Group B: **Add one or both drugs**	• **clofazimine** • **cycloserine** or **terizidone**
Group C: **Add to complete the regimen and when drugs from Groups A and B cannot be used**	• **ethambutol** • **delamanide** • **pyrazinamide** • **amikacin** (or **streptomycin** – only if susceptible) • **imipenem–cilastatin** or **meropenem** with **amoxicillin/clavulanic acid** • **ethionamide** or **prothionamide** • **para-aminosalicylic acid**

Acknowledgements

Opportunistic Infections and COVID-19

Chair: Ole Kirk	**Copenhagen, Denmark**
Vice-Chair: Paola Cinque	**Milan, Italy**
Young scientist: Daria Podlekareva	**Copenhagen, Denmark**
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Gerd Fätkenheuer	Cologne, Germany
Hansjakob Furrer	Bern, Switzerland
José M. Miro	Barcelona, Spain
Cristiana Oprea	Bucharest, Romania
Anton Pozniak	London, United Kingdom
Alain Volny-Anne	Paris, France

Other panels (HIV Treatment, Comorbidity and Drug-Drug Interactions), especially young scientists Rosa De Miguel Buckley and Aoife Cotter

Guidelines Chair Georg Behrens & Guidelines Coordinator Lene Ryom

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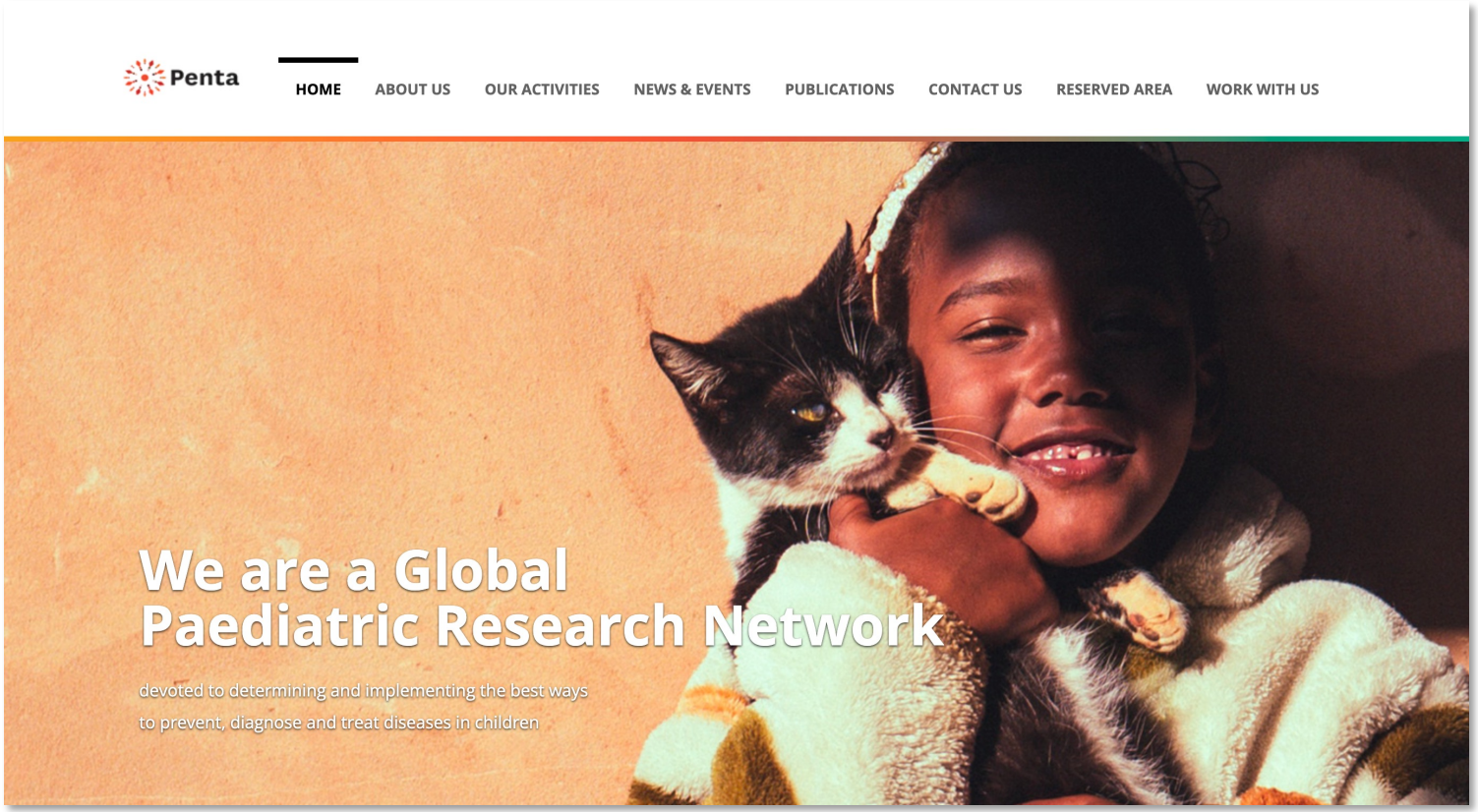
Paediatric ART Panel

Alasdair Bamford for the EACS Peadiatric ART Panel



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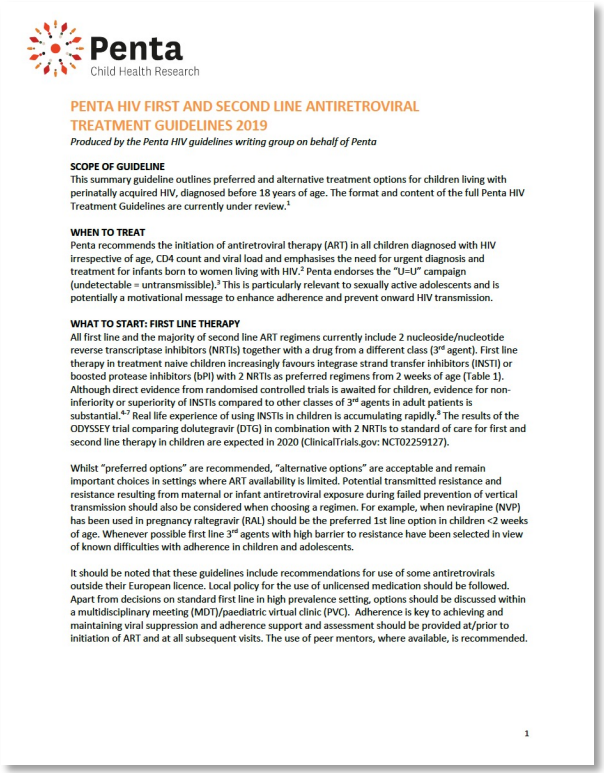
Penta

https://penta-id.org/



Penta
Child Health Research

PENTA HIV FIRST AND SECOND LINE ANTIRETROVIRAL TREATMENT GUIDELINES 2019

Produced by the Penta HIV guidelines writing group on behalf of Penta

SCOPE OF GUIDELINE

This summary guideline outlines preferred and alternative treatment options for children living with perinatally acquired HIV, diagnosed before 18 years of age. The format and content of the full Penta HIV Treatment Guidelines are currently under review.[1]

WHEN TO TREAT

Penta recommends the initiation of antiretroviral therapy (ART) in all children diagnosed with HIV irrespective of age, CD4 count and viral load and emphasises the need for urgent diagnosis and treatment for infants born to women living with HIV.[2] Penta endorses the "U=U" campaign (undetectable = untransmissible).[3] This is particularly relevant to sexually active adolescents and is potentially a motivational message to enhance adherence and prevent onward HIV transmission.

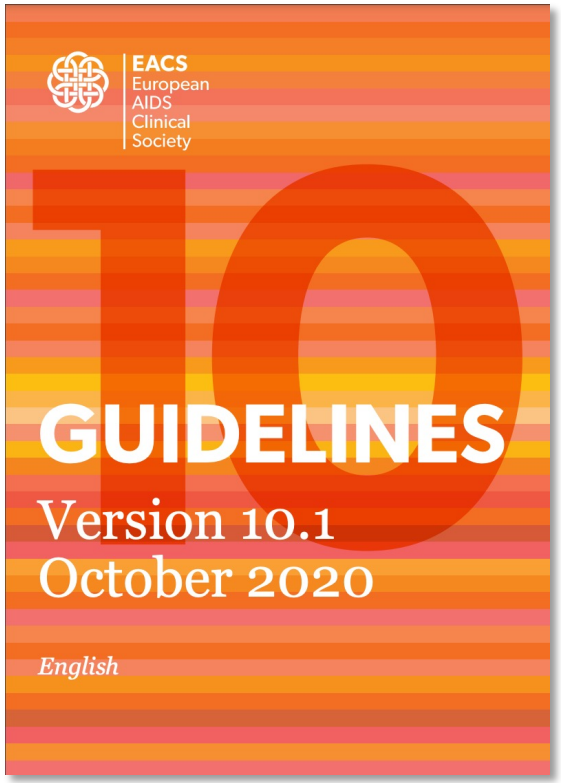
WHAT TO START: FIRST LINE THERAPY

All first line and the majority of second line ART regimens currently include 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) together with a drug from a different class (3rd agent). First line therapy in treatment naive children increasingly favours integrase strand transfer inhibitors (INSTI) or boosted protease inhibitors (bPI) with 2 NRTIs as preferred regimens from 2 weeks of age (Table 1). Although direct evidence from randomised controlled trials is awaited for children, evidence for non-inferiority or superiority of INSTIs compared to other classes of 3rd agents in adult patients is substantial.[4-7] Real life experience of using INSTIs in children is accumulating rapidly.[8] The results of the ODYSSEY trial comparing dolutegravir (DTG) in combination with 2 NRTIs to standard of care for first and second line therapy in children are expected in 2020 (ClinicalTrials.gov: NCT02259127).

Whilst "preferred options" are recommended, "alternative options" are acceptable and remain important choices in settings where ART availability is limited. Potential transmitted resistance and resistance resulting from maternal or infant antiretroviral exposure during failed prevention of vertical transmission should also be considered when choosing a regimen. For example, when nevirapine (NVP) has been used in pregnancy raltegravir (RAL) should be the preferred 1st line option in children <2 weeks of age. Whenever possible first line 3rd agents with high barrier to resistance have been selected in view of known difficulties with adherence in children and adolescents.

It should be noted that these guidelines include recommendations for use of some antiretrovirals outside their European licence. Local policy for the use of unlicensed medication should be followed. Apart from decisions on standard first line in high prevalence setting, options should be discussed within a multidisciplinary meeting (MDT)/paediatric virtual clinic (PVC). Adherence is key to achieving and maintaining viral suppression and adherence support and assessment should be provided at/prior to initiation of ART and at all subsequent visits. The use of peer mentors, where available, is recommended.

1



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Paediatric HIV Treatment

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Gareth Tudor-Williams	London, United Kingdom
Anna Turkova	London, United Kingdom
Alla Volokha	Kyiv, Ukraine
Wave representative:	
Justyna D. Kowalska	Warsaw, Poland

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Penta

Table 1. Preferred and Alternative First Line Options in Children and Adolescents Living with HIV

	Backbone		3rd Agent (in alphabetical order)	
Age	**Preferred**	**Alternative**	**Preferred**	**Alternative**
0 - 4 weeks	ZDV[i] + 3TC	-	LPV/r[ii, iii] NVP[iii] RAL[iii]	-
4 weeks - 3 years	ABC[iv] + 3TC[v]	ZDV[i] + 3TC[vi] TDF[vii] + 3TC	DTG[viii]	LPV/r NVP RAL
3 - 6 years	ABC[iv] + 3TC[v]	TDF + XTC[ix] ZDV + XTC[ix]	DTG	DRV/r EFV LPV/r NVP RAL
6 - 12 years	ABC[iv] + 3TC[v] TAF[x] + XTC[ix]	TDF + XTC[ix]	DTG	DRV/r EFV EVG/c RAL
> 12 years	ABC[iv] + 3TC[v] TAF[x] + XTC[ix]	TDF + XTC[ix]	BIC[xi] DTG	DRV/b EFV[xii] RAL[xii] RPV[xii]

Notes:

i In view of potential long-term toxicity, any child on ZDV should be switched to ABC or TAF (preferred) or TDF (alternative) once increase in age and/or weight makes licensed formulations available, see page 24

ii LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days although it may be considered if there is a risk of transmitted NVP resistance and INSTI in appropriate formulations are unavailable. In these circumstances the neonate should be monitored closely for LPV/r related toxicity, see page 24

iii If starting a non-DTG 3rd agent in the neonatal period it is acceptable to continue this option. However, when over 4 weeks and 3 kg, a switch to DTG is recommended if and when an appropriate formulation is available

iv ABC should NOT be prescribed to HLA-B*57:01 positive individuals (where screening is available). ABC is not licensed under 3 months of age but dosing data for younger children are available from the WHO and DHHS

v At HIV-VL > 100,000 copies/mL ABC + 3TC should not be combined with EFV as 3rd agent

vi If using NVP as a 3rd agent in children aged 2 weeks to 3 years, consider using 3 NRTI backbone (ABC + ZDV + 3TC) until VL consistently < 50 copies/mL

vii TDF is only licensed from 2 years of age

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x TAF is only licensed in Europe for treatment of HIV in combination with FTC from 12 years of age and 35 kg in TAF/FTC and from 6 years of age and 25 kg in TAF/FTC/EVG/c

xi BIC is a preferred first line option in adult PLWH. At time of writing it is not licensed under 18 years of age but may be considered in those aged 12-18 years following discussion at MDT/PVC

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xi BIC is a preferred first line option in adult PLWH. At time of writing it is not licensed under 18 years of age but may be considered in those aged 12-18 years following discussion at MDT/PVC

xii Due to predicted poor adherence in adolescence, PI/b are favoured as alternative first line 3rd agent options due their high barrier to resistance

Table 1. Preferred and Alternative First Line Options in Children and Adolescents Living with HIV

	Backbone		3rd Agent (in alphabetical order)	
Age	Preferred	Alternative	Preferred	Alternative
0 - 4 weeks	ZDV[i] + 3TC	-	LPV/r[ii, iii] NVP[iii] RAL[iii]	-
4 weeks - 3 years	ABC[iv] + 3TC[v]	ZDV[i] + 3TC[vi] TDF[vii] + 3TC	DTG[viii]	LPV/r NVP RAL
3 - 6 years	ABC[iv] + 3TC[v]	TDF + XTC[ix] ZDV + XTC[ix]	DTG	DRV/r EFV LPV/r NVP RAL
6 - 12 years	ABC[iv] + 3TC[v] TAF[x] + XTC[ix]	TDF + XTC[ix]	DTG	DRV/r EFV EVG/c RAL
> 12 years	ABC[iv] + 3TC[v] TAF[x] + XTC[ix]	TDF + XTC[ix]	BIC[xi] DTG	DRV/b EFV[xii] RAL[xii] RPV[xii]

Notes:

i In view of potential long-term toxicity, any child on ZDV should be switched to ABC or TAF (preferred) or TDF (alternative) once increase in age and/or weight makes licensed formulations available, see page 24

ii LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days although it may be considered if there is a risk of transmitted NVP resistance and INSTI in appropriate formulations are unavailable. In these circumstances the neonate should be monitored closely for LPV/r related toxicity, see page 24

iii If starting a non-DTG 3rd agent in the neonatal period it is acceptable to continue this option. However, when over 4 weeks and 3 kg, a switch to DTG is recommended if and when an appropriate formulation is available

iv ABC should NOT be prescribed to HLA-B*57:01 positive individuals (where screening is available). ABC is not licensed under 3 months of age but dosing data for younger children are available from the WHO and DHHS

v At HIV-VL > 100,000 copies/mL ABC + 3TC should not be combined with EFV as 3rd agent

vi If using NVP as a 3rd agent in children aged 2 weeks to 3 years, consider using 3 NRTI backbone (ABC + ZDV + 3TC) until VL consistently < 50 copies/mL

vii TDF is only licensed from 2 years of age

viii DTG is licensed from 4 weeks and 3 kg

ix XTC indicates circumstances when FTC or 3TC may be used interchangeably

x TAF is only licensed in Europe for treatment of HIV in combination with FTC from 12 years of age and 35 kg in TAF/FTC and from 6 years of age and 25 kg in TAF/FTC/EVG/c

xi BIC is a preferred first line option in adult PLWH. At time of writing it is not licensed under 18 years of age but may be considered in those aged 12-18 years following discussion at MDT/PVC

xii Due to predicted poor adherence in adolescence, PI/b are favoured as alternative first line 3rd agent options due their high barrier to resistance

What to do if preferred option becomes available ?

Switch Strategies for virologically supressed children and adolescents

- The general indications for switching when virologically suppressed are as for adult PLWH, see page 15 but with some additional considerations for children and adolescents relating to increasing age and weight, licensing, formulation availability, vulnerability to toxicity and predicted adherence issues in adolescence
- As children age and grow on suppressive ART, consideration should be given to simplification to robust once daily low pill burden regimens with optimal toxicity profiles and efficacy data. For example, in children aged less than 3 years commenced on liquid LPV/r, consider switching to once daily regimens when pill swallowing achieved or dispersible DTG is available
- If "preferred" options become available for a child as they get older then a switch to this option can be considered. However, if they are fully virologically suppressed on their current regimen with no toxicity or problems with convenience or adherence it is reasonable to remain on an alternative regimen
- Children and their carers should be involved in discussing the relative risk/benefit of switching when well and stable on an effective regimen
- Dual therapy is not recommended in first line or for simplification but can be considered on a case by case basis in adherent children and adolescents living with HIV
- Simplification to monotherapy and treatment interruptions are not recommended and are discouraged

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Table 2. Antiretroviral Formulations Useful for Pediatric and Adolescent Dosing and Administration

NRTI	
ABC	tablet (300 mg) solution (20 mg/mL)
FTC	capsule (200 mg) solution (10 mg/mL)
3TC	tablet (300, 150 mg) solution (10 mg/mL)
TDF	tablet (245, 204, 163, 123 mg) granules (33 mg/g)
ZDV	capsule (250 mg, 100 mg) solution (10 mg/mL) IV infusion: 10mg/mL (20 mL/vial)
TAF/FTC	tablet (25/200 mg and 10/200 mg)
TDF/FTC	tablet (300/200 mg)
ABC/3TC	tablet (600/300 mg)
ZDV/3TC	tablet (300/150 mg)
NNRTI	
EFV	tablet (600 mg) capsule (200, 100, 50 mg)
NVP	tablet (200 mg) prolonged release tablet (400, 100 mg) suspension (10 mg/mL)
RPV	tablet (25 mg)
TDF/FTC/EFV	tablet (300/200/600 mg)
TAF/FTC/RPV	tablet (25/200/25 mg)
TDF/FTC/RPV	tablet (300/200/25 mg)
PI	
DRV	tablet (800, 600, 400, 150, 75 mg) solution (100 mg/mL)
DRV/c	tablet (800/150 mg)
LPV/r	tablet (200/50 mg and 100/25 mg) solution (80/20 mg/mL)
RTV	tablet (100 mg) powder for oral suspension (100 mg sachet)
TAF/FTC/DRV/c	tablet (10/200/800/150 mg)
INSTI	
DTG	tablet (50, 25, 10 mg) dispersible tablets (5 mg)
RAL	tablet (600 mg, 400 mg) chewable tablets (100, 25 mg) granules for oral suspension (100 mg)
ABC/3TC/DTG	tablet (600/300/50 mg)
TAF/FTC/BIC	tablet (25/200/50 mg)
TAF/FTC/EVG/c	tablet (10/200/150/150 mg)
TDF/FTC/EVG/c	tablet (300/200/150/150 mg)

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Treatment Guidelines

- HIV
  - Treatment Guidelines
  - D3
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  - EPPICC
  - GEPPO
  - ODYSSEY (PENTA 20)
  - PANNA Study
  - REACH

Treatment Guidelines

The 2019 Penta guidelines for first and second line antiretroviral treatment are now available.

A table with guidance on dosing and use of paediatric formulations is also

produced and updated regularly by members of the Penta guidelines gro

this guidance table provides some dosing recommendations outside of c

Local policy for use of unlicensed medication and dosing should be follow

required.*

The aim of these guidelines is to provide a concise reference document t

choices for children and adolescents with perinatally acquired HIV in the

document will be updated at regular intervals by the Penta guidelines grc

data or evidence becomes available.

Antiretroviral / HIV Drug Dosing for Children and Adolescents 2021-22 - Imperial College Healthcare NHS Trust

(NOT for neonatal vertical transmission post exposure prophylaxis – see BHIVA guidelines)

OD = Once a day, BD = Twice a day, QDS = Four times a day

Agent	Recommended dosage, class side effects and contraindications & warnings	Formulations	Additional information	Intake Advice
Nucleoside Reverse Transcriptase Inhibitors (NRTI): lactic acidosis, steatosis, mitochondrial toxicity				
Lamivudine (3TC) *Also see FDCs*	**Liquid (≥3months)** 5 mg/kg BD or 10mg/kg OD (max dose 300mg/day). Well tolerated round up doses. **Tablet (14-19kg)**-->75mg BD or 150mg OD, **(>20-24kg)**-->75mg AM + 150mg PM or 225mg OD, **(≥25kg)**-->300mg OD Nausea, diarrhoea, headache, fatigue	Tab: 150mg (scored), 300mg 100mg (Zeffix) (orange) Generic tabs scored, appearance varies Liq: 10mg/ml (Epivir) (1-month expiry)	Reduce dose in renal impairment (seek advice). Tablets can be crushed and mixed with small amount of water or food.	Take with or without food
Emtricitabine (FTC) *Also see FDCs*	**≥ 4months:** 6mg/kg OD of the oral solution. (max. dose 240mg OD) **≥33kg:** Capsule 200mg OD; oral solution: 240mg OD Headache, diarrhoea, nausea, rash, skin discolouration on palms and soles	Cap: 200mg (blue/white) = 240mg liquid Liq: 10mg/ml – Fridge (Discard 45 days after opening) - not bioequivalent to caps. Liquid can be stored at room temp after opening	Reduce dose in renal impairment (seek advice). Do not give with lamivudine. Capsules contents can be dispersed in water.	Take with or without food
Abacavir (ABC) *Also see FDCs*	**Liquid: (≥3months)** 8mg/kg BD or 16mg/kg OD. Max dose: 600mg per day. Well tolerated round up doses. **Tablet: (14-19kg)**-->150mg BD or 300mg OD, **(>20-24kg)**-->150mg AM + 300mg PM or 450mg tab OD, **(≥25kg)**-->600mg OD ***Test HLA-B*5701 before starting, do not give abacavir if HLA-B*5701 +ve.*** Hypersensitivity reactions usually occur within first 6 weeks of therapy. **If occurs, not to be given again** Nausea, fever, headache, diarrhoea, rash, fatigue, respiratory symptoms	**Tab:** 300mg scored Liq: *20mg/mL (2 month expiry)*	Tablets can be crushed and mixed with small amount of water or food.	Take with or without food
Zidovudine (AZT)	**Liquid (4-9kg)**-->12mg/kg BD, **(>9-30Kg)**-->9mg/kg BD. Max dose 300mg BD. **Capsule (8-13kg)**-->100mg BD, **(14-21Kg)**-->100mg am + 200mg pm, **(22-27kg)**-->200mg BD, **(≥28kg)**-->250mg BD **IV dosing**: 80mg/m² QDS (alternatively total daily dose of 320 mg/m² may be given in 2 divided doses). Granulocytopenia and/or anaemia, nausea, headache, myopathy, hepatitis, nail pigmentation, neuropathy	Cap: 100mg, 250mg Liq: 10mg/ml (1-month expiry) IV: 10mg/ml (200mg/20ml vial)	Capsules contents can be dispersed in water.	Take with or without food
Nucleotide Reverse Transcriptase inhibitors (NtRTI): As NRTI's				
Tenofovir alafenamide fumarate (TAF)	**TAF is preferred NtRTI in all patients ≥6years & ≥25kg** Nausea, headache, dizziness, abnormal dreams, diarrhoea, vomiting, abdominal pain, flatulence, rash, fatigue	Only available as fixed-dose combinations – see below		
Tenofovir disoproxil (TD)	*All doses based on Tenofovir Disoproxil (TD)* **Tablet: (17-21kg)**-->123mg OD, **(22-27Kg)**-->163mg OD, **(28-34kg)**-->204mg OD **(≥35kg)**-->245mg OD. **Powder: (2 – 12yrs)** 6.5mg/kg OD ~ 1 scoop (scp) = 33mg (10-11kg)-->2 scp, (12-13kg)-->2.5 scp, (14-16kg)-->3 scp, (17-19kg)-->3.5 scp, (19-21kg)-->4 scp, (22-23kg)-->4.5 scp, (24-26kg)-->5 scp, (27-28kg)-->5.5 scp (29-31kg)-->6 scp, (32-33kg)-->6.5 scp, (34kg)-->7 scp, (≥35kg)-->7.5 scp Headache, nausea, vomiting, renal tubular dysfunction, bone demineralization, exacerbations of viral hepatitis on discontinuation. Important: Renal function, blood and urine monitoring.	**Tab:** TD 245mg (blue) **Fixed tab TD (TDF):** 123mg (150mg), 163mg (200mg), 204mg (250mg) (white) **Powder:** TD 33mg/1g per scoop (TDF 40mg/1g per scoop) **245mg tenofovir disoproxil (TD) = 300mg tenofovir disoproxil fumarate (TDF)**	Careful monitoring with boosted PI regimens for renal toxicity. Tablets can be cut or crushed and dispersed in water, but bitter taste. Orange juice can be used to mask taste.	Take with food. Granules should be mixed with soft food and not liquids
NRTI & NtRTI fixed dose combinations (FDCs) for use with third agent: Cross-reference with component drugs for side-effects and advice				
ABC + 3TC *Generic (Kivexa®)*	***Test HLA-B*5701 before starting, do not give abacavir if HLA-B*5701 positive*** **≥25kg**: 1 tablet OD	Tab: ABC 600mg/3TC 300mg	Do not cut/crush	Take with or without food
FTC + TAF ('F/TAF') *Descovy®*	**Licensed ≥12 years or ≥35kg** *(trial evidence from ≥6yrs & ≥25kg – refer to PVC)* ***With RTV/COB:*** 200mg/ 10mg tab OD; ***Not with RTV/COB:*** 200mg/25mg tab OD	Tab: FTC 200mg/ TAF10mg (grey) FTC 200mg/ TAF 25mg (blue)	Do not cut/crush	Take with or without food
TD + FTC *Generic (Truvada®)*	**≥35kg:** 1 tablet OD	Tab: TD 245mg/FTC 200mg	See tenofovir disoproxil information	
Integrase Inhibitors: Seek advice from a pharmacist for all integrase inhibitors if patient requires oral cations (e.g. calcium/magnesium/iron/aluminium/zinc), including multivitamin/mineral products				
Dolutegravir (DTG) *Also see FDCs*	*MUST SPECIFY FORMULATION WHEN PRESCRIBING – Film coated tablets are not bioequivalent to dispersible tablets* **Dispersible tablet: ≥4 wks (3-5kg)** –5mg OD, **(6-9kg)**-->15mg OD, **(10-13kg)**-->20mg OD, **(14-19kg)**-->25mg OD, **(≥20kg)**-->30mg OD **Film coated tablet: (14-19kg)**-->40mg OD, **(≥20kg)**-->50mg OD. **Integrase resistance:** 50mg BD *(refer to PVC)* Insomnia, mood changes, headache, hepatitis, rash, weight gain	**Film coated tablets**: 50mg tabs (yellow) (Can be cut/crushed) 25mg tabs (pale yellow) 10mg tabs (white) **Dispersible tablets for oral suspension:** 5mg tabs	With inducers of CYP3A/UGT1A e.g. EFV, NVP, rifampicin use dolutegravir 50mg BD	Take with food Avoid antacids/mineral supplements containing polyvalent cations 6 hours before & 2 hours after taking – seek advice
Raltegravir (RAL)	*MUST SPECIFY FORMULATION WHEN PRESCRIBING – Film coated tablets are not bioequivalent to sachets/chewable tablets* **≥4 wks:** 6mg/kg BD as **granules for oral suspension (up to 20kg):** max. 100mg BD or **Chewable tabs:** max 300mg BD **Sachets: (≥3kg)** –25mg BD, (4-5kg) –30mg BD, (6-7kg) –40mg BD, **(8-10kg)** –60mg BD, **(11-13kg)** –80mg BD, **(14-19kg)** –100mg BD **Chewable tablets: (11-13kg)** –3 x 25mg chewable tabs BD, **(14-19kg)** –1 x 100mg chewable tab BD **(≥0-27kg)** –1½ x 100mg chewable tabs BD, **(≥8-39kg)** –2 x 100mg chewable tabs BD, **(≥40kg)** –3 x 100mg chewable tabs BD Film coated tablet: **(≥25kg)**: 400mg BD **Once-daily formulation: (≥40kg)**: 1200mg OD (2x600mg film coated tablets) Nausea, dizziness, insomnia, mood changes, rash, pancreatitis, elevated liver enzymes	**100mg sachets for oral suspension:** Recommended dilution 10mg/ml but can be individualised if large volumes prohibitive. **Chewable tabs:** 25mg & 100mg (can be halved). **Film coated tablets:** 400mg (pink - can be cut/crushed) 600mg (yellow – do not cut/crush)	**Once-daily formulation:** Do not co-prescribe with rifampicin, unboosted atazanavir or aluminium, magnesium and calcium containing antacids or supplements Take with or without food	**Twice-daily formulations**: Avoid antacids/mineral supplements containing polyvalent cations 4 hours before & after taking – seek advice
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI): Require TDM with rifamycins				
Nevirapine (NVP)	**Lead in period for 14 days: (3-5.9kg)**-->50mg OD, **(6-9.9kg)**-->80mg OD, **(10-13.9kg)**-->100mg OD, **(14-19.9kg)**-->130mg OD, **(20-24.9kg)**-->150mg OD, **(≥25g)** 200mg OD, then if no rash or LFT abnormalities after 14 days see maintenance dose below. **Maintenance dose: (3-5.9kg)**-->50mg BD, **(6-9.9kg)**-->80mg BD, **(10-13.9kg)**-->100mg BD, **(14-19.9kg)**-->130mg BD, **(20-24.9kg)**-->150mg BD, **(≥25kg) 200mg BD *or* 400mg OD**. Convert total daily dose to OD dose if stable and fully suppressed. Rash, hepatitis, Steven-Johnson – usually within first 6 weeks, can occur up to 18weeks. **Check hepatic function at 2, 4, and 8 weeks.** Mood changes, vivid dreams (common but usually short lived), hypercholesterolemia, rash, gynaecomastia	**Tab:** 200mg Liq: 10mg/ml (Shake well, 6-month expiry) **Prolonged-release tabs:** 100mg, 400mg [Generic tablets first-line] Prolonged-release tabs not suitable for lead in period.	Normal release tabs can be cut. Do not cut prolonged-release tabs. No dose reduction in renal impairment.	Take with or without food. Some patients have reported the tablet remnant in faeces – not known to affect response.
Pharmacokinetic boosters – Not to be used as an antiretroviral alone				
Ritonavir (RTV)	**Child: For boosting other PIs see specific drug** **≥15kg: For boosting other PIs**: 100mg OD or 100mg BD e.g. with ATV or DRV Nausea, diarrhoea, flushing, rash	Tab: 100mg (white) **100mg sachets for oral suspension:** (see package insert for administration)	Do not cut/crush	Take with food
Cobicistat (COB) *Tybost®* *Also see FDCs*	**≥6 years & >25kg:** 150mg OD *Check for additional drug interactions when switching from ritonavir to cobicistat* Nausea, sleep disturbance, headache, dizziness, vomiting, diarrhoea, abdominal pain, flatulence, dry mouth, rash	Tab: 150mg (orange) Also see FDCs.	Do not cut/crush. Do not use in pregnancy – lower PI exposure (use RTV)	Take with food

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Additional sections

- Special populations:
- Adolescent girls of childbearing potential
- HBV
- HCV
- TB

- Adherence, failure and 2nd line ….
- "Virological failure (defined as **2 consecutive VL >200 copies/mL** at least 3 months apart with adherence support) is almost always due to suboptimal ART adherence, and always requires adherence assessment and support"

- Link to International Paediatric Virtual clinic email

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Second line options

Choosing a 3rd agent

Failed on first line NNRTI
- Switch to INSTI with a high barrier to resistance (i.e. DTG or BIC) or PI/b with optimised 2 NRTI
- If high VL and extensive resistance impacting on NRTIs consider using regimen with at least 2 fully active drugs (e.g. INSTI with PI/b and 2 NRTI)

Failed on first line PI/b
- If no significant resistance to PIs, consider continuation of PI/b (consider switch to DRV/b) with optimised 2 NRTI or PI/b based STR to reduce pill burden
- Consider switch to INSTI with high barrier to resistance (i.e. DTG or BIC)
- Consider INSTI or PI based single tablet FDC with 2 NRTI to reduce pill burden (e.g. DRV/c (only in the abscense of significant PI resistance), DTG or BIC where/when licensing allows)

Failed on first line INSTI
- If resistance testing demonstrates no INSTI resistance, consider switch to/continue INSTI with high barrier to resistance with optimised 2 NRTI
- Switch to PI/b with optimised 2 NRTI is also an option especially if INSTI resistance is demonstrated
- If INSTI resistance and substantial NRTI resistance, consider initial therapy with DTG (bid) + PI/b + optimised 2 NRTI ideally discussed at MDT/PVC

Optimising NRTI backbone

Optimising NRTI backbone

- If resistance testing available use results to guide choice of 2 NRTI
- If NRTI resistance is demonstrated, XTC with either TAF or TDF are the preferred options, used according to license. If TAF or TDF are not available or contraindicated then ZDV can be considered but alternatives to ZDV should be regularly assessed in order to remove from the regimen as soon as possible
- If resistance testing not available, switch to (or continue) TDF or TAF (or ZDV as per above) with 3TC or FTC (see below rationale)
- TDF or TAF are preferred in second line in combination with 3TC or FTC (even if failing on TDF or TAF)
- It is well established that M184V causes high level resistance to both FTC and 3TC. However ongoing use of either FTC or 3TC is still recommended in the presence of this mutation (especially if it minimises pill burden) as it is associated with an increased susceptibility to tenofovir and ZDV