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EACS Treatment Guidelines V10.0
An introduction to the 2019 Major Revisions

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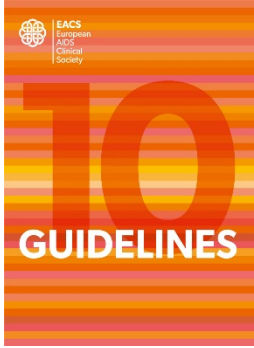
Presenter Disclosure Information



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- No participation in Speakers Bureau ever
- No stocks or stock options of pharmaceutical or biotech companies ever
- No participation in Satellite Meetings since 2011
- No participation in Advisory Boards since 2014

COI mandatory for everyone involved in the EACS Guidelines

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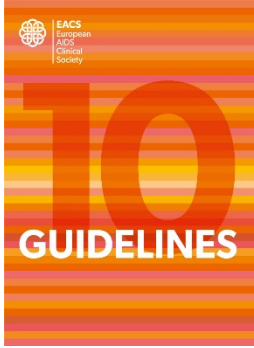
Aims of the EACS Guidelines



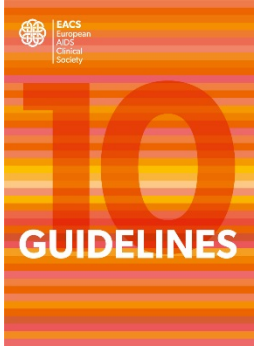
The scope of the EACS guidelines is to

Provide easy accessible recommendations to clinicians centrally involved with the care of PLWH

Cover a large and geographically diverse area

Not to be considered as a full overview of all aspects of HIV-infection, but rather as a continuously updated overview of the most relevant clinical issues in HIV with emphasis on co-morbidities

Summary of Changes from v9.1. to v10.0



ART section

- What to start with, pages 12-13
  - New recommendation favouring unboosted INSTI with high genetic barrier (DTG or BIC) as third agent for treatment-naïve PLWH initiating treatment
  - 2 NRTIs + DOR included in recommended regimens
  - When indicated, TDF/3TC has been added as a backbone
  - Dual therapy with DTG + 3TC has been upgraded to recommended regimens
- Primary HIV infection, page 14
  - High genetic barrier INSTI or PI/b recommended for initial therapy if resistance testing is not available
- Switch strategies for virologically suppressed persons, page 15
  - DTG + 3TC has been included in dual therapies supported by large clinical trials
  - DRV/b + RPV has been included as dual therapy option supported by small trials
  - Monotherapy with PI/b not recommended
- Treatment of pregnant women living with HIV or women considering pregnancy, page 17
  - Whole section has been updated with treatment guidance regarding different scenarios (Tables 1, 2 and 3)
- ART in TB/HIV co-infection, page 20.
  - New tables have been included (ART in TB/HIV co-infection and DDIs)
- Post-exposure prophylaxis (PEP), page 22
  - TAF/FTC, RAL qd and BIC have been included as possible drugs to include in a PEP regimen
- Pre-exposure prophylaxis (PrEP), page 23
  - TAF/FTC has been included as alternative in MSM and transgender women

DDI section

- All tables have been updated with most recent data on DDIs and the ... page 39
- ... ment for renal and hepatic insufficiency, pages 40, 42, 43
- ... Monotherapy when ... provides guidance on dosage adjustments to overcome DDIs with ARVs page 49
- Two new tables: "Top 10 Drug Classes to Avoid in Elderly PLWH" and "Non-HIV Drugs Requiring Dosage Adjustment in Renal Insufficiency" have been developed to prevent inappropriate prescribing in elderly PLWH, pages 45, 47, 48

DDI and other prescribing issues in PLWH - a new individual section

Co-morbidity section

- All tables have been updated with the addition of BIC and DOR and older ARVs (including older PIs, ddI and d4T) have been removed from all sections apart from that on lipoatrophy, pages 57, 67, 74-76, 78, 87, 90-91 and 94
- A comment has been included on use of e-cigarettes in the lifestyle intervention section, page 53
- Screening for kidney disease recommends the use of albumin/creatinine ratio for glomerular disease and protein/creatinine ratio for screening for and diagnosing ARV-related tubulopathy, pages 64-66
- There are updated targets for lipids and a change in threshold for ART modification from 20% 10-year risk of CVD to 10% 10-year risk of CVD, page 54 and 60
- Blood pressure targets have been updated, pages 54-55
- The medical management of hypertension has been updated to include amended drug sequencing suggestions and recommendations on drugs to use, page 56
- There is an additional 4th step in the work-up of liver disease in PLWH to include risk stratification based on risk prediction tools and transient elastography and an updated algorithm for surveillance of varices, page 69
- There is a minor update for the screening guidance for HCC in non-cirrhotic PLWH with HBV, pages 8, 52, 71 and 95
- In the sexual health section, there is a statement about U=U, including how this information affects options for conception for PLWH and their partners and screening for menopause, page 80
- In the section on depression, there is a statement on the impact of depression on overall well-being, page 84
- In the cognitive guidelines, recommendations for modification of ART are based on either CSF resistance testing or on likely ART toxicity, page 88

Viral Hepatitis Co-infections section

- The chapter has been renamed "Clinical Management and Treatment of Viral Hepatitis Co-infections in PLWH", page 95
- The structure of the chapter has been reorganised: General recommendations, page 95, Treatment and Monitoring of Persons with HBV/HIV Co-infection, page 96 and Treatment and monitoring of Persons with HCV/HIV Co-infection, page 97
- HCC screening recommendations have been updated with the Co-morbidity panel, pages 8, 52, 71 and 95
- Practical points on diagnosing hepatic fibrosis have been updated and a table on cut-off values of non-invasive tests for the detection of significant fibrosis and cirrhosis have been added, pages 95 and 102
- The section on HBV reactivation has been updated, page 96
- Recommendations for persons with failure to DAA treatment have been updated, page 97
- The DAA table has been updated and split into two parts. One with preferred regimens and one with alternatives, pages 98 and 99
- The figure on management of recently acquired HCV infection has been updated, page 101
- The sections on HEV and HDV have been updated, pages 95 and 103

Opportunistic Infections section

- The table on when to start ART in the presence of opportunistic infections has been added, page 104
- A table on clinical presentation and management of Immune Reconstitution Inflammatory Syndrome (IRIS) has been added, page 104
- Treatment of the following OIs has been updated: CMV, HSV, VZV, histoplasmosis, cryptococcosis, pages 108-111
- Treatment details of Initial and recurrent genital/mucocutaneous HSV has been removed from the OIs section. A cross reference to the Sexual and Reproductive Health of Women and Men Living with HIV section was made instead, page 110
- Treatment of talaromycosis has been added, page 110
- Details on management of MDR-TB have been added to the TB section, page 115, as well as a table detailing doses for all TB drugs, major side effects and caution when using with ART, page 117

For more detailed summary of changes made from v9.1 to v10.0, please see http://www.eacsociety.org/guidelines/Details.from-version-9.1to10

EACS Guidelines are available online at http://www.eacsociety.org and in the EACS Guidelines App

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Video links

EACS Guidelines	Video lectures	Link to video lecture
Primary HIV Infection	When to Start ART Part 1	https://vimeo.com/197164442/93941a8e75
	When to Start ART Part 2	https://vimeo.com/197167665/3f00ac2634
	What ART to Start Part 1	https://vimeo.com/197374541/32232bd037
	What ART to Start Part 2	https://vimeo.com/197378793/215317ddab
Switch Strategies for Virologically Suppressed Persons	How to Change ART	https://vimeo.com/197161843/ae0c46e0be
Virological Failure	Adherence and Prevention of HIV Drug Resistance	https://vimeo.com/197381327/d7e972c0d5
Pre-exposure Prophylaxis	PrEP Part 1	https://vimeo.com/196714648/6a196a71a4
	PrEP Part 2	https://vimeo.com/196716750/a12a32989b
Adverse Effects of ARVs and Drug Classes	Adverse Effects and Monitoring	https://vimeo.com/197275138/3df1c99e55
Cancer: Screening Methods	Clinical Management of Cancers and HIV Part 1	https://vimeo.com/197398883/6cbeebb66e
	Clinical Management of Cancers and HIV Part 2	https://vimeo.com/197748761/68cc01229a
	Epidemiology of Cancers Part 1	https://vimeo.com/197749519/afea560124
	Epidemiology of Cancers Part 2	https://vimeo.com/197749948/e7e5062f2d
Prevention of CVD	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Kidney Disease: Definition, Diagnosis and Management	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Lipodystrophy: Prevention and Management	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Algorithm for Diagnosis and Management of HIV-Associated Neurocognitive Impairment (NCI) in Persons without Obvious Confounding Conditions	CNS and HIV Part 1	https://vimeo.com/197280954/e995f1c097
	CNS and HIV Part 2	https://vimeo.com/197370416/ee3655aa09
Diagnostic Procedures for HCV in Persons with HCV/HIV Co-infection	Hepatitis C and HIV Co-infection Part 1	https://vimeo.com/197259934/bc5cac91d1
	Hepatitis C and HIV Co-infection Part 2	https://vimeo.com/197261826/0462d2df0e
	Hepatitis C and HIV Co-infection Part 3	https://vimeo.com/197262690/a323b6cd72
Introduction to OIs	HIV and the Management of IRIS Part 1	https://vimeo.com/197762901/a147257ffc
	HIV and the Management of IRIS Part 2	https://vimeo.com/197765956/9b61e5d15d
	Pulmonary Infections Part 1	https://vimeo.com/197388161/dc24235ab6
	Pulmonary Infections Part 2	https://vimeo.com/197389876/7c26fb8551
	Pulmonary Infections Part 3	https://vimeo.com/197392161/f90020ae21
	CNS and HIV-related Opportunistic Infections Part 1	https://vimeo.com/197752868/34462456dd
	CNS and HIV-related Opportunistic Infections Part 2	https://vimeo.com/197758431/6b2939c62a
Diagnosis and Treatment of TB in PLWH	Tuberculosis and HIV Co-infection Part 1	https://vimeo.com/196723861/7a067d0254
	Tuberculosis and HIV Co-infection Part 2	https://vimeo.com/197161188/4e881b687c

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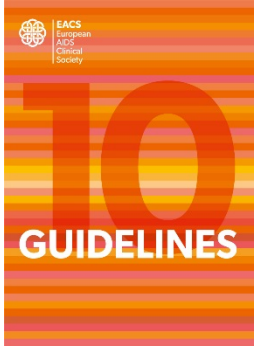
EACS European AIDS Clinical Society 10 GUIDELINES

The guidelines v10.0 consist of

- Summary of changes from v9.1 to 10.0
- Part I : Assessment
- Part II : ART
- Part III: DDI and other prescribing issues
- Part III: Co-morbidities
- Part IV: Viral hepatitis and Co-infections
- Part V : Opportunistic Infections
- References
- Video links



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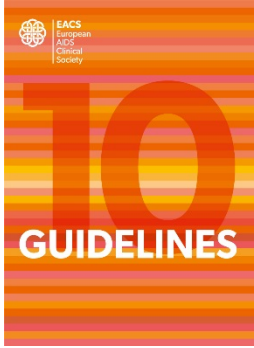

Each part of the guidelines is

Managed by panels of

- Experienced European HIV experts
- External experts

Reviewed by

- Community representatives, Wave and cross-panel experts

Governed by

A 3-person leadership group
- Panel Chair, Co-chair and Young Scientist

The guidelines content is managed by

The EACS Medical Secretariat; guideline coordination chair and assistant working closely with the EACS Secretariat

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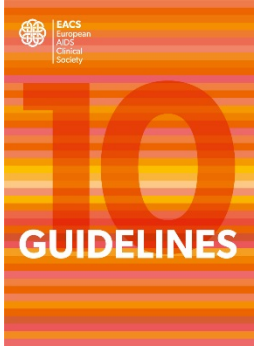
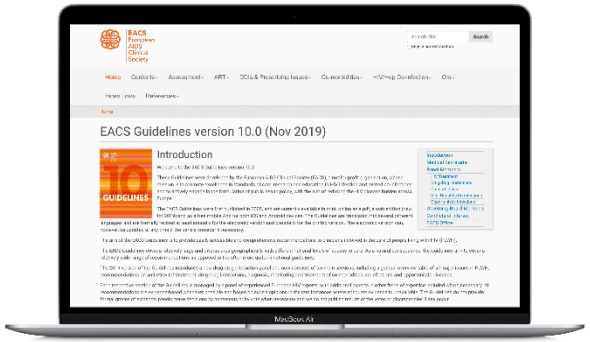
The working for the Guidelines

- Leadership TC’s regularly and two F2F/year
- Panel TC’s and F2F
- Submission and discussions of new content by Mail
- Grade versus non Grade



EACS Guidelines Availabilities



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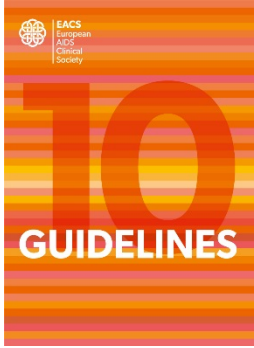

Acknowledgements

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The EACS Medical Secretariat is responsible for the coordination and update of the EACS Guidelines based on the recommendations from the five EACS panels.

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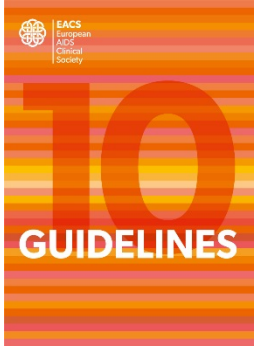

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We hope you will enjoy the 2019 EACS Guidelines!

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ART of PLWH

Jose Arribas for the HIV Treatment EACS guidelines panel

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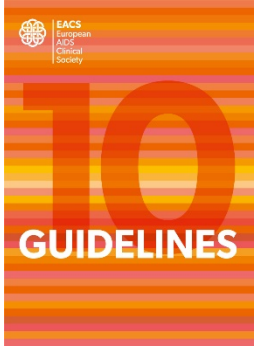

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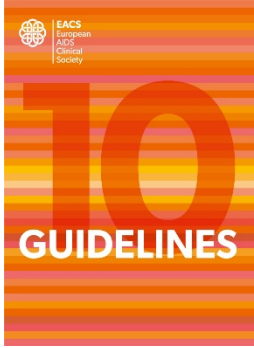

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Opportunistic Infections and Drug-Drug Interactions panels. WAVE - Women Against Viruses in Europe
Guidelines Chair Manuel Battegay & Guidelines Coordinator: Lene Ryom

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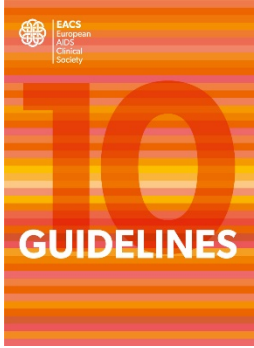
Initial Combination Regimen for ART-naïve Adult PLWH

Before selecting an ART regimen, it is critical to review:

- If a woman **wishes to conceive**: Antiretroviral drugs not recommended in women who wish to conceive
- If a woman is **pregnant**: Antiretroviral regimen for ART-naïve pregnant women
- If the person has an **opportunistic infection**: Initiation of ART regimen in persons with opportunistic infections
- If the person has **TB**: Antiretroviral regimens in TB/HIV co-infection
- If the person has potential **treatment limiting comorbidities**: Comorbidity section, dose adjustment for renal and liver impairment
- If the person is treated with **other medications**: Drug-drug interactions
- If the person has **Swallowing Difficulties:** Administration of ARVs in PLWH with swallowing difficulties

Initial Combination Regimen for ART-naïve Adult PLWH



Uniform layout for naïve adult, pregnancy and TB

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)

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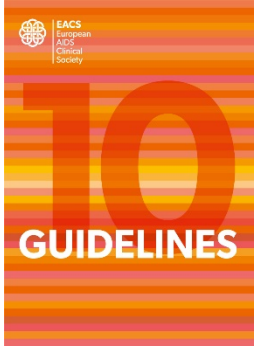
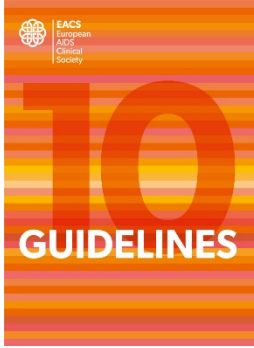
Initial Combination Regimen for ART-naïve Adult PLWH



Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)

Initial Combination Regimen for ART-naïve Adult PLWH



Out of the recommended regimens in PLWH starting ART, we favour the use of an unboosted INSTI with a high genetic barrier (DTG or BIC) as preferred third agent. Tailoring antiretroviral regimens for each individual is essential as other classes of third agents (e.g. PI/b) might be indicated in the presence of resistance

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B HBsA	C: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		F: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)

New recommendation favouring unboosted INSTI with high genetic barrier as third agent

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Initial Combination Regimen for ART-naïve Adult PLWH

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
DTG + 3TC	HBsAg negative HIV-VL < 500,000 copies/mL CD4 count > 200 cells/µL	
2 NRTIs + NNRTI		
TAF/FTC or TDF/FTC or TDF/3TC + DOR TDF/3TC/DOR		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) V (DOR: HIV-2)
TAF/FTC or TDF/FTC or TDF/3TC + RPV TAF/FTC/RPV TDF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on proton pump inhibitor With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (RPV: HIV-2)
2 NRTIs + PI/r or PI/c		
TAF/FTC or TDF/FTC or TDF/3TC + DRV/c or DRV/r TAF/FTC/DRV/c	With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VII (DRV/r: cardiovascular risk)

NEW

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Initial Combination Regimen for ART-naïve Adult PLWH

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk)
TAF/FTC or TDF/FTC or TDF/3TC + DTG		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III Weight increase
TAF/FTC/BIC		
TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
DTG + 3TC	HBsAg negative HIV-VL < 500,000 copies/mL CD4 count > 20	
2 NRTIs + NNRTI		
TAF/FTC or TDF/FTC or TDF/3TC + DOR TDF/3TC/DOR		II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) V (DOR: HIV-2)
TAF/FTC or TDF/FTC or TDF/3TC + RPV TAF/FTC/RPV TDF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on proton pump inhibitor With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (RPV: HIV-2)
2 NRTIs + PI/r or PI/c		
TAF/FTC or TDF/FTC or TDF/3TC + DRV/c or DRV/r TAF/FTC/DRV/c	With food	II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VII (DRV/r: cardiovascular risk)

NEW

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Switch strategies for virologically suppressed persons

Dual therapies

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

DTG + RPV
3TC + DTG
3TC + DRV/b
3TC + ATV/b

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.

Dual therapy options supported only by small trials:

DRV/b+ RPV

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) absence of chronic HBV co-infection

Strategies not recommended

a. Monotherapy with a PI/b
b. Monotherapy with DTG
c. Dual or triple NRTIs combinations
d. Specific two-drug combination, i.e. 1 NRTI + 1 NNRTI or 1 NRTI + 1 unboosted PI, 1 NRTI + RAL, MVC + RAL, PI/b + MVC, ATV/b + RAL
e. Intermittent therapy, sequential or prolonged treatment interruptions

Antiretroviral regimen for ART-naïve pregnant women

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	Initiate after 8 weeks of pregnancy HLA-B*57:01 negative HBsAg negative	
TDF/FTC or TDF/3TC + DTG	Initiate after 8 weeks of pregnancy	
TDF/FTC or TDF/3TC + RAL 400 mg bid		III (Tenofovir salts) IV (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/FTC or TDF/3TC + DRV/r 600 mg/100 mg bid	With food	III (Tenofovir salts) V (DRV dosing) VI (COBI boosting)

Whole section has been updated with treatment guidance regarding different scenarios

Table 1. Antiretroviral drugs not recommended in women who wish to conceive
Table 2. Antiretroviral drugs not recommended in women who become pregnant while on ART
Table 3. Antiretroviral regimen for ART-naïve pregnant women
Labour

Antiretroviral regimen for ART-naïve pregnant women

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG ABC/3TC/DTG	Initiate after 8 weeks of pregnancy HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, may delay starting ART) II (DTG: neural tube defects risk during periconception)
TDF/FTC or TDF/3TC + DTG	Initiate after 8 weeks of pregnancy	III (Tenofovir salts) II (DTG: neural tube defects risk during periconception)
TDF/FTC or TDF/3TC + RAL 400 mg bid		III (Tenofovir salts) IV (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/FTC or TDF/3TC + DRV/r 600 mg/100 mg bid	With food	III (Tenofovir salts) V (DRV dosing) VI (COBI boosting)

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Antiretroviral regimens in TB/HIV co-infection

Regimen	Main require…	Additional guidance (footnotes)
Recommended regimens with rifampicin		
2 NRTIs + NNRTI		
TDF/FTC or TDF/3TC + EFV TDF/FTC/EFV	At bed time or 2 hours before dinner	
ABC/3TC +EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bed time or 2 hours before dinner	
Alternative regimens with rifampicin		
2 NRTIs + INSTI		
TDF/FTC or TDF/3TC + DTG bid		I (tenofovir salts) IV (DTG: dosing)
TDF/FTC or TDF/3TC + RAL bid		I (tenofovir salts) V (RAL: dosing)
ABC/3TC + RAL bid	HBsAg negative HLA-B*57:01 negative	III (ABC: HLA-B*57:01) V (RAL: dosing)

New tables have been included (ART in TB/HIV co-infection and DDIs)

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Antiretroviral regimens in TB/HIV co-infection

Regimen	Main requirements	Additional guidance (footnotes)
Recommended regimens with rifampicin		
2 NRTIs + NNRTI		
TDF/FTC or TDF/3TC + EFV TDF/FTC/EFV	At bed time or 2 hours before dinner	I (tenofovir salts) II (EFV: suicidality. HIV2 or HIV-1 group 0)
ABC/3TC +EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bed time or 2 hours before dinner	III (ABC: HLA-B*57:01) II (EFV: suicidality. HIV-2 or HIV-1 group 0)
Alternative regimens with rifampicin		
2 NRTIs + INSTI		
TDF/FTC or TDF/3TC + DTG bid		I (tenofovir salts) IV (DTG: dosing)
TDF/FTC or TDF/3TC + RAL bid		I (tenofovir salts) V (RAL: dosing)
ABC/3TC + RAL bid	HBsAg negative HLA-B*57:01 negative	III (ABC: HLA-B*57:01) V (RAL: dosing)

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Drug-drug interactions & other prescribing issues in PLWH

Catia Marzolini
for the EACS Drug-Drug interactions Guidelines panel

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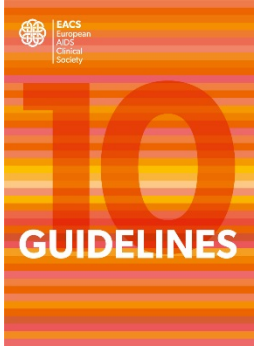
Employee: Never



Part III

Drug-drug interactions and other prescribing issues in PLWH

- Drug-drug interactions between **ARVs** and **non-ARVs**
- Drug-drug interactions between **Antidepressants** and ARVs
- Drug-drug interactions between **Antihypertensives** and ARVs
- Drug-drug interactions between **Analgesics** and ARVs
- Drug-drug interactions between **Anticoagulants/antiplatelets agents** and ARVs
- Drug-drug interactions between **Bronchodilatators (for COPD)** and ARVs
- Drug-drug interactions between **Contraceptives** and ARVs
- Drug-drug interactions between **Corticosteroids** and ARVs
- Drug-drug interactions between **Antimalarial drugs** and ARVs
- Drug-drug interactions between **Pulmonary Antihypertensives** and ARVs
- Drug-drug interactions between **Immunosuppressants (for SOT)** and ARVs
- Drug-drug interactions between **DAAs** 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** **NEW**
- **Prescribing in elderly** PLWH
- **Selected top 10 drug classes to avoid in elderly PLWH** **NEW**
- **Dosage recommendations for hormone therapy when used for gender transitioning** **NEW**

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Major updates to DDIs tables

+ **BICTEGRAVIR** : metabolism by CYP3A4 and UGT1A1
no inhibitory or inducing effects on CYPs or UGTs
inhibition of OCT2, MATE1

➔ **bictegravir does mostly not impact comedications**
exception: **metformin**

➔ **strong inhibitors CYP3A4: no clinically relevant increase in bictegravir exposure**

➔ **strong dual inhibitors CYP3A4 + UGT1A1: contraindicated**

➔ **strong inducers: contraindicated as substantial reduction in bictegravir levels**

➔ **divalent cations: similarly to other INSTIs, bictegravir 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	MVC	BIC	DTG	EVG/c	RAL
Cardiovascular drugs	atorvastatin	↑822%	↑	↑290%	↑	↑490%	↓2%	↓43%	↓37%	↓	↑4% D10%	↔	↔	↔	↑	↔
	fluvastatin	↑	↑	↑	↑	↔	↔	↑	↑	↔	↔	↔	↔	↔	↑	↔
	pravastatin	↑	↑	↑	↑81%	↔	↔	↓44%	↓	↔	↔	↔	↔	↔	↑	↔
	rosuvastatin	↑242%	↑213%	↑93%	↑48%	↑108%	↔	↔	↔	↔	↔	↔	↔	↔	↑38%	↔
	simvastatin	↑	↑	↑	↑	↑	↔	↓68%	↓	↓	↔	↔	↔	↔	↑	↔
	amlodipine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	diltiazem	↑a	↑a	↑	↑	↑a	E	↓69%	↓E	↓	E	E	E	↔	↑	↔
	metoprolol	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
	verapamil	↑a	↑a	↑	↑	↑a	E	↓	↓E	↓	E	E	E	↔	↑	↔
	warfarin	↑	↑ or ↓	↑	↓	↓	↔	↑ or ↓	↑	↑ or ↓	↔	↔	↔	↔	↓	↔
CNS drugs	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↑?	↔
	carbamazepine	↑D	↑D	↑D	↑	↑D b	D	↓27% D36%	D	↓D	D	D	D	D49%	↑ D	D b
	citalopram	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔c	↔	↔	↔	↑	↔
	diazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	lamotrigine	↔	↓32%d	↔	↓	↓50%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↓1%
	midazolam (oral)	↑	↑	↑	↑	↑	↓18%	↓	↓	↓	↔	↑18%	↑15%	↔	↑	↓8%
	mirtazapine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↑↓?	↔
	phenytoin	D	↓D	D	↓D	↓D b	D	↓D	D	D	D	D	D	D	D	D b
	pimozide	↑	↑	↑	↑	↑	↔	↑	↓	↓	↔c	↔	↔	↔	↑	↔
	sertraline	↑	↓	↑	↓49%	↓	↔	↓39%	↓	↓	↔	↔	↔	↔	↓7%	↔
	triazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
Anti-infectives	clarithromycin	↑Ea	↑Ea	↑E	↑	↑a	↑	↓39%	↓39% E42%	↓31% E26%	E c	E	E	↔	↑E	↔
	fluconazole	↑?	↔	↑?	↔	↔	↑	↔	E86%	E100%	E	↔	↔	↔	↑?	↔
	itraconazole	↑E	↑E	↑E	↑E	↑E	↑	↓39%	↓E	↓61%	E	E	E	↔	↑E	↔
	rifabutin	↑D	↑	↑D	↑E50%	↑	D50%	↓38%	↓17% D37%	↑17%	D42%	e	D38%	↔	↑D	E19%
	rifampicin	D	D72%	D	D57%	D75%	D82%	D26%	D	D58%	D80%	D	D75%	D54%g	D	D40%b
	voriconazole	↑↓ E	↑↓ D	↑E	↓	↑↓ E	↑	↓E	↑14% E36%	↓E	E	E	E61%	↔	↑E	↔
	antacids	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	D	D	D	D h
	PPIs	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	E
	H2 blockers	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	E

Major updates to DDIs tables

+ **DORAVIRINE**: metabolism by CYP3A4
no inhibitory or inducing effects on CYPs, UGTs or drug transporters

➔ **doravirine does not impact comedications**

➔ **strong inhibitors: no clinically relevant increase in doravirine exposure**

➔ **strong inducers: contraindicated as substantial reduction in doravirine levels**

➔ **moderate inducers: DDI can be managed by increasing doravirine dose to 100 mg BID**

DDI between ARVs and non-ARVs

	Non-ARV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC	DTG	EVG/c	RAL
Cardiovascular drugs	atorvastatin	↑822%	↑	↑290%	↑	↑490%	↓2%	↓43%	↓37%	↓	↑4% D10%	↔	↔	↔	↑	↔
	fluvastatin	↑	↑	↑	↑	↔	↔	↑	↑	↔	↔	↔	↔	↔	↑	↔
	pravastatin	↑	↑	↑	↑81%	↔	↔	↓44%	↓	↔	↔	↔	↔	↔	↑	↔
	rosuvastatin	↑242%	↑213%	↑93%	↑48%	↑108%	↔	↔	↔	↔	↔	↔	↔	↔	↑38%	↔
	simvastatin	↑	↑	↑	↑	↑	↔	↓68%	↓	↓	↔	↔	↔	↔	↑	↔
	amlodipine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	diltiazem	↑a	↑a	↑	↑	↑a	E	↓69%	↓E	↓	E	E	E	↔	↑	↔
	metoprolol	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
	verapamil	↑a	↑a	↑	↑	↑a	E	↓	↓E	↓	E	E	E	↔	↑	↔
	warfarin	↑	↑ or ↓	↑	↓	↓	↔	↑ or ↓	↑	↑ or ↓	↔	↔	↔	↔	↓	↔
CNS drugs	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↑?	↔
	carbamaze-pine	↑D	↑D	↑D	↑	↑D b	D	↓27% D36%	D	↓D	D	D	D	D49%	↑ D	D b
	citalopram	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔c	↔	↔	↔	↑	↔
	diazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	lamotrigine	↔	↓32%d	↔	↓	↓50%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↓1%
	midazolam (oral)	↑	↑	↑	↑	↑	↓18%	↓	↓	↓	↔	↑18%	↑15%	↔	↑	↓8%
	mirtazapine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↑↓?	↔
	phenytoin	D	↓D	D	↓D	↓D b	D	↓D	D	D	D	D	D	D	D	D b
	pimozide	↑	↑	↑	↑	↑	↔	↑	↓	↓	↔c	↔	↔	↔	↑	↔
	sertraline	↑	↓	↑	↓49%	↓	↔	↓39%	↓	↓	↔	↔	↔	↔	↓7%	↔
	triazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
Anti-infectives	clarithromy-cin	↑Ea	↑Ea	↑E	↑	↑a	↑	↓39%	↓39% E42%	↓31% E26%	E c	E	E	↔	↑E	↔
	fluconazole	↑?	↔	↑?	↔	↔	↑	↔	E86%	E100%	E	↔	↔	↔	↑?	↔
	itraconazole	↑E	↑E	↑E	↑E	↑E	↑	↓39%	↓E	↓61%	E	E	E	↔	↑E	↔
	rifabutin	↑D	↑	↑D	↑E50%	↑	D50%	↓38%	↓17% D37%	↑17%	D42%	e	D38%	↔	↑D	E19%
	rifampicin	D	D72%	D	D57%	D75%	D82%	D26%	D	D58%	D80%	D	D75%	D54%g	D	D40%b
	voriconazole	↑↓ E	↑↓ D	↑E	↓	↑↓ E	↑	↓E	↑14% E36%	↓E	E	E	E61%	↔	↑E	↔
	antacids	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	D	D	D	D h
	PPIs	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	E
	H2 blockers	D	D	↔	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	↔	E

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Major updates to DDIs tables

boosted ARVs alter clopidogrel efficacy ➔ avoid

alternative: prasugrel

www.hiv-druginteractions.org,
Marsousi N et al. Clin Pharmacokinet 2018;
Itkonen MK et al. Clin Pharmacol Ther 2018

DDIs with anticoagulants

Anticoagulants & Antiplatelets		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC	DTG	EVG/c	RAL
Anticoagulants	acenocoumarol	↔	↓	↔	↓	↓	↔	↑or↓	↑	↓	↔	↔	↔	↔	↓	↔
	apixaban	↑a	↑a	↑a	↑a	↑a	↔	↓	↓	↓	↔	↔	↔	↔	↑a	↔
	argatroban	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	dabigatran	↑	↑	↑	↑	↑?	↔	↔	↑	↔	↑?	↔	↔	↔	↑	↔
	dalteparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	edoxaban	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔
	enoxaparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	fondaparinux	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	heparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	phenprocoumon	↑	↑or↓b	↑	↑or↓	↑or↓	↔	↓	↑or↓	↓	↔	↔	↔	↔	↑or↓	↔
	rivaroxaban	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔
	warfarin	↑	↑or↓b	↑	↓	↓	↔	↑or↓	↑	↑or↓	↔	↔	↔	↔	↓	↔
Antiplatelet agents	aspirin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	clopidogrel	↓c	↓c	↓c	↓c	↓c	↔	↓c	↓c	↑d E	↔	↔	↔	↔	↓c	↔
	dipyridamole	↑	↓f	↔	↓	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔
	prasugrel	↓g	↓g	↓g	↓g	↓g	↔	↔	↔	↔	↔	↔	↔	↔	↓g	↔
	ticagrelor	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↔

EACS tables are linked to DDIs websites and have been revised to include all updates made to the websites in the past year

HIV Drug Interactions

www.hiv-druginteractions.org

HEP Drug Interactions

www.hep-druginteractions.org

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Selected Top 10 Drug Classes To Avoid in Elderly PLWH

Drug class	Problems/alternatives
First generation antihistamines e.g., clemastine, diphenhydramine, doxylamine, hydroxyzine	Strong anticholinergic properties, risk of impaired cognition, delirium, falls, peripheral anticholinergic adverse reactions (dry mouth, constipation, blurred vision, urinary retention). Alternatives: cetirizine, desloratadine, loratadine
Tricyclic antidepressants e.g., amitryptiline, clomipramine, doxepin, imipramine, trimipramine	Strong anticholinergic properties, risk of impaired cognition, delirium, falls, peripheral anticholinergic adverse reactions (dry mouth, constipation, blurred vision, urinary retention). Alternatives: citalopram, escitalopram, mirtazapine, venlafaxine
Benzodiazepines Long and short acting benzodiazepines e.g., clonazepam, diazepam, midazolam Non-benzodiazepines hypnotics e.g., zolpidem, zopiclone	Elderly are more sensitive to their effect, risk of falls, fractures, delirium, cognitive impairment, drug dependency. Use with caution, at the lowest dose and for a short duration. Alternatives: non-pharmacological treatment of sleep disturbance/sleep hygiene.
Atypical antipsychotics e.g., clozapine, olanzapine, quetiapine	Anticholinergic adverse reactions, increased risk of stroke and mortality (all antipsychotics). Alternatives: aripiprazole, ziprasidone
Urological spasmolytic agents e.g., oxybutynin, solifenacin, tolterodine	Strong anticholinergic properties, risk of impaired cognition, delirium, falls, peripheral anticholinergic adverse reactions (dry mouth, constipation, blurred vision, urinary retention). Alternatives: non-pharmacological treatment (pelvic floor exercises).
Stimulant laxatives e.g., senna, bisacodyl	Long-term use may cause bowel dysfunction. Alternatives: fibres, hydration, osmotic laxatives
NSAIDs e.g., diclofenac, indomethacin, ketorolac, naproxen	Avoid regular, long-term use of NSAIDs due to risk of gastrointestinal bleeding, renal failure, worsening of heart failure. Alternatives: paracetamol, weak opioids
Digoxin Dosage > 0.125 mg/day	Avoid doses higher than 0.125 mg/day due to risk of toxicity. Alternatives for atrial fibrillation: beta-blockers
Long acting sulfonylureas e.g., glyburide, chlorpropamide	Can cause severe prolonged hypoglycemia. Alternatives: metformin or other antidiabetic classes
Cold medications Most of these products contain antihistamines (e.g., diphenhy-	First generation antihistamines can cause central and peripheral anticholinergic adverse reactions as described above. Oral decongestants can increase blood pressure

Dosage recommendations for hormone therapy used for gender transitioning

a ARVs with no predicted effect:
DOR, RPV, MVC, BIC, DTG, RAL, NRTI

b ARVs inhibiting estrogen metabolism:
ATV, ATV/c, DRV/c, DRV/c

c ARVs inducing estrogen metabolism:
ATV/r, DRV/r, LPV/r, EFV, ETV, NVP

d ARVs inhibiting androgen metabolism:
ATV, ATV/c, ATV/r, DRV/c, DRV/r, EVG/c, LPV/r

e ARVs inducing androgen metabolism:
EFV, ETV, NVP

		HIV Drugs	Starting Dose	Average Dose	Maximum Dose
Estrogens	Estradiol oral	No predicted effect a	2 mg/day	4 mg/day	8 mg/day
		Inhibits metabolism b	1 mg/day	2 mg/day	4 mg/day
		Induces metabolism c	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.		
	Estradiol gel (preferred for >40 y and/or smokers)	No predicted effect a	0.75 mg bid	0.75 mg tid	1.5 mg tid
		Inhibits metabolism b	0.5 mg bid	0.5 mg tid	1 mg tid
		Induces metabolism c	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.		
	Estradiol patch (preferred for >40 y and/or smokers)	No predicted effect a	25 µg/day	50-100 µg/day	150 µg/day
		Inhibits metabolism b	25 µg/day*	37.5-75 µg/day	100 µg/day
		Induces metabolism c	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.		
	Conjugated estrogen†	No predicted effect a	1.25-2.5 mg/day	5 mg/day	10 mg/day
		Inhibits metabolism b	0.625-1.25 mg/day	2.5 mg/day	5 mg/day
		Induces metabolism c	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.		
	Ethinylestradiol	No predicted effect a	No interaction expected, but not recommended due to thrombotic risks		
		Inhibits metabolism b	Not recommended		
		Induces metabolism c	Not recommended		
Androgen Blockers ‡	Spironolactone	No predicted effect a	50 mg/day	150 mg/day	400 mg/day
		Inhibits metabolism d	No interaction expected. No dose adjustment required.		
		Induces metabolism e	No interaction expected. No dose adjustment required.		
	Finasteride	No predicted effect a	2.5 mg/day	2.5 mg/day	5 mg/day
		Inhibits metabolism d	Finasteride has a large safety margin. No dose adjustment required.		
		Induces metabolism e	Increase finasteride dosage as needed based on clinical effects and monitored hormone levels.		
	Cyproterone acetate	No predicted effect a	50 mg/day	150 mg/day	150 mg/day
		No predicted effect a	25 mg/day	75 mg/day	75 mg/day
		Induces metabolism e	Increase cyproterone dosage as needed based on clinical effects and monitored hormone levels.		
	Goserelin	No predicted effect a	3.6 mg/month	3.6 mg/month	3.6 mg/month
		Inhibits metabolism d	No interaction expected. No dose adjustment required.		
		Induces metabolism e	No interaction expected. No dose adjustment required.		
	Leuprorelin acetate	No predicted effect a	3.75 mg/month	3.75 mg/month	3.75 mg/month
		Inhibits metabolism d	No interaction expected. No dose adjustment required.		

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10 GUIDELINES

Acknowledgements

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Guidelines Coordinator: Lene Ryom **Copenhagen, Denmark**

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Part IV Prevention and Management of Co-morbidities in PLWH

Prof. Patrick Mallon
for the EACS Co-morbidities Guidelines panel

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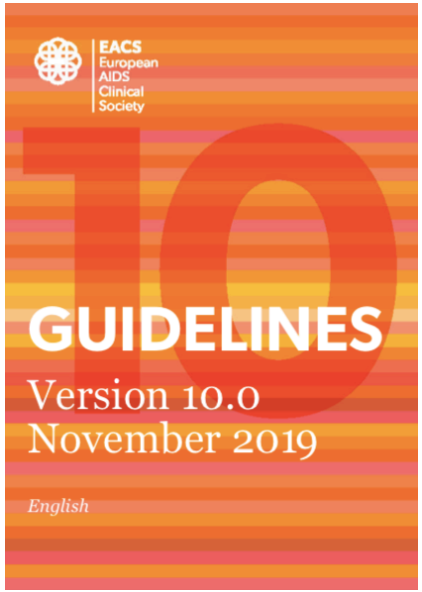
Enterprise Ireland

Co-morbidities Guidelines V10

- 44 pages in length
- 42 sections (12 online)
- 12 groups of conditions



- Bone diseases
- Cardiovascular diseases
- Diabetes mellitus
- Frailty
- Immunosuppression & Transplantation
- Liver disease & Cirrhosis
- Mental health
- Metabolic diseases (inc. Obesity)
- Neurocognitive function
- Renal disease
- Sexual and Reproductive Health
- Travel & Vaccination

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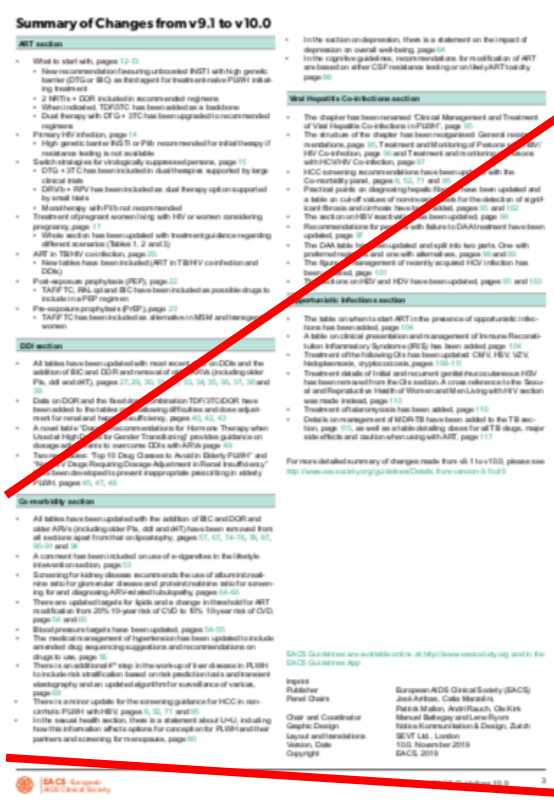
Co-morbidities Guidelines V10


Summary of Changes from v9.1 to v10.0

ART section

- What to start with, pages 12-13
  - New recommendation favouring unboosted INSTI with high genetic barrier (DTG or BIC) as third agent for treatment-naive PLWH initiating treatment
  - 2 NRTIs + DOR included in recommended regimens
  - When indicated, TDF/3TC has been added as a backbone
  - Dual therapy with DTG + 3TC has been upgraded to recommended regimens
- Primary HIV infection, page 14
  - High genetic barrier INSTI or PIb recommended for initial therapy if resistance testing is not available
- Switch strategies for virologically suppressed persons, page 15
  - DTG + 3TC has been included in dual therapies supported by large clinical trials
  - DRVb + RPV has been included as dual therapy option supported by small trials
  - Monotherapy with PIb not recommended
- Treatment of pregnant women living with HIV or women considering pregnancy, page 17
  - Whole section has been updated with treatment guidance regarding different scenarios (Tables 1, 2 and 3)
- ART in TB/HIV co-infection, page 25
  - New tables have been included (ART in TB/HIV co-infection and DDIs)
- Post-exposure prophylaxis (PEP), page 22
  - TAF/FTC, RAL-qd and BIC have been included as possible drugs to include in a PEP regimen
- Pre-exposure prophylaxis (PrEP), page 23
  - TAF/FTC has been included as alternative in MSM and transgender women

DDI section

- All tables have been updated with most recent information on DDIs and the addition of BIC and DOR and removal of older ARVs (including older PIs, ddI and d4T), pages 27, 28, 30, 31, 32, 33, 34, 35, 36, 37, 38 and 39
- Data on DOR and the fixed-dose combination TDF/3TC/DOR have been added to the tables and the following difficulties and dose adjustment for renal and hepatic insufficiency, pages 40, 42, 43
- A novel table "Drug Interactions for Hormone Therapy when Used at High Doses for Gender Transitioning" provides guidance on dosage adjustments to overcome DDIs with ARVs page 49
- Two new tables "Top 10 Drug Classes to Avoid in Elderly PLWH" and "Top 10 Drugs Requiring Dosage Adjustment in Renal Insufficiency" have been developed to prevent inappropriate prescribing in elderly PLWH, pages 45, 47, 48

Co-morbidity section

- All tables have been updated with the addition of BIC and DOR and older ARVs (including older PIs, ddI and d4T) have been removed from all sections apart from that on lipoatrophy, pages 57, 67, 74-76, 78, 87, 90-91 and 94
- A comment has been included on use of e-cigarettes in the lifestyle intervention section, page 53
- Screening for kidney disease recommends the use of albumin/creatinine ratio for glomerular disease and protein/creatinine ratio for screening for and diagnosing ARV-related tubulopathy, pages 64-66
- There are updated targets for lipids and a change in threshold for ART modification from 20% 10-year risk of CVD to 10% 10-year risk of CVD, page 54 and 60
- Blood pressure targets have been updated, pages 54-55
- The medical management of hypertension has been updated to include amended drug sequencing suggestions and recommendations on drugs to use, page 56
- There is an additional 4th step in the work-up of liver disease in PLWH to include risk stratification based on risk prediction tools and transient elastography and an updated algorithm for surveillance of varices, page 69
- There is a minor update for the screening guidance for HCC in non-cirrhotic PLWH with HBV, pages 8, 52, 71 and 95
- In the sexual health section, there is a statement about U=U, including how this information affects options for conception for PLWH and their partners and screening for menopause, page 80
- In the section on depression, there is a statement on the impact of depression on overall well-being, page 84
- In the cognitive guidelines, recommendations for modification of ART are based on either CSF resistance testing or on likely ART toxicity, page 88

Viral Hepatitis Co-infections section

- The chapter has been renamed 'Clinical Management and Treatment of Viral Hepatitis Co-infections in PLWH', page 95
- The structure of the chapter has been reorganised. General recommendations, page 95, Treatment and Monitoring of Persons with HBV/HIV Co-infection, page 96 and Treatment and monitoring of persons with HCV/HIV Co-infection, page 97
- HCC screening recommendations have been updated with the Co-morbidity panel, pages 8, 52, 71 and 95
- Practical points on diagnosing hepatic fibrosis have been updated and a table on cut-off values of noninvasive methods for the detection of significant fibrosis and cirrhosis have been added, pages 98 and 102
- The section on HBV exacerbations has been updated, page 96
- Recommendations for persons with failure to DAA treatment have been updated, page 97
- The DAA table has been updated and split into two parts. One with preferred regimens and one with alternatives, pages 98 and 99
- The flowchart on management of recently acquired HCV infection has been updated, page 100
- The sections on HDV and HDV have been updated, pages 95 and 103

Opportunistic infections section

- The table on when to start ART in the presence of opportunistic infections has been added, page 104
- A table on clinical presentation and management of Immune Reconstitution Inflammatory Syndrome (IRIS) has been added page 104
- Treatment of the following OIs has been updated: CMV, HSV, VZV, histoplasmosis, cryptococcosis, pages 108-110
- Treatment details of Initial and recurrent genital mucocutaneous HSV has been removed from the OIs section. A cross-reference to the Sexual and Reproductive Health of Women and Men Living with HIV section was made instead, page 110
- Treatment of talaromycosis has been added, page 110
- Details on management of MDR-TB have been added to the TB section, page 111, as well as a table detailing doses for all TB drugs, major side effects and caution when using with ART, page 117

For more detailed summary of changes made from v9.1 to v10.0, please see http://www.eacsociety.org/guidelines/Details_from-version-9.1to10

EACS Guidelines are available online at http://www.eacsociety.org and in the EACS Guidelines App

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Hypertension

Hypertension: Diagnosis, Grading and Management

Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)
	High normal SBP 130-139 or DBP 85-89	Grade 1 hypertension SBP 140-159 or DBP 90-99	Grade 2 hypertension SBP 160-179 or DBP 100-109	Grade 3 hypertension SBP ≥ 180 or DBP ≥ 110
No other risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several months • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
1-2 risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
≥ 3 risk factors	• Lifestyle changes[i] • i.e. no BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
Organ damage, CKD stage 3 or diabetes	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]
Symptomatic CVD, CKD stage ≥ 4 or diabetes with organ damage/risk factors	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • BP drugs targeting < 130/80[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 130/80[ii]

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- Lifestyle changes[i] for several weeks
- Then add BP drugs targeting < 130/80[ii]

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Hypertension - management

Choosing drugs[i] for persons newly diagnosed with hypertension

< 55 years	≥ 55 years or black[ii] person of any age
A[iii]	C[iii,iv]
↓	↓
A + C*[iii] (white person) :	A + C or C + D[ii] (black person)
↓	
A + C + D[iii]	
↓	
A + C + D[iii] + Spirolactone (12.5 to 50 mg)	

[v] Add a-blocker (e.g. doxazosin [slow release]) or β-blocker (e.g. bisoprolol). Refer to specialist.

A = ACE inhibitor
C = Dihydropyridine Calcium Channel Blocker
D = Thiazide-type diuretic

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10 GUIDELINES

Hypertension - management

Choosing drugs[(i)] for persons newly diagnosed with hypertension

< 55 years	≥ 55 years or black[(ii)] person of any age
A[(iii)]	C[(iii,iv)]
↓	↓
A + C*[(iii)] (white person) :	A + C or C + D[(ii)] (black person)
↓	
A + C + D[(iii)]	

A + C*[(iii)] (white person) : A + C or C + D[(ii)] (black person)

[(v)] Add a-blocker (e.g. doxazosin [slow release]) or β-blocker (e.g. bisoprolol). Refer to specialist.

A = ACE inhibitor
C = Dihydropyridine Calcium Channel Blocker
D = Thiazide-type diuretic

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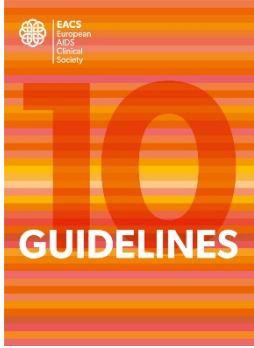
Cardiovascular Disease prevention



Assess CVD risk in next 10 years[i]

↓

Advise on diet and lifestyle in all persons

Consider ART modification if 10-year CVD risk ≥ 10%[ii]

↓

Smoking (see page 53) → Identify key modifiable risk factors[iii]

Blood pressure

↓

Drug treatment if: SBP ≥ 140 or DBP ≥ 90 mmHg (especially if 10-year CVD risk ≥ 10%)

↓

Target[v]

SBP < 130 mmHg

DBP < 80 mmHg

↓

Treatment (see page 55-57)

Coagulation

↓

Drug treatment if: established CVD only

↓

Target - N/A

↓

Consider treating with acetylsalicylic acid 75-150 mg[vii]

Glucose

↓

Confirm DM and treat with diet and drugs

↓

Target

HbA1C 6.5-7.0%

↓

Treatment (see page 59)

Lipids

↓

Drug treatment[iv] if: established CVD or type 2 diabetes or 10-year CVD risk ≥ 10%

↓

Target*

	2ry prevention or very high risk	1ry Prevention
LDL**	< 1.4 (55)	< 2.0 (80)
Non LDL	< 2.2 (85)	< 3.0 (115)

↓

Treatment (see page 60)

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Cardiovascular Disease prevention

Assess CVD risk in next 10 years[i]

Advise on diet and lifestyle in all persons

Consider ART modification if 10-year CVD risk ≥ 10%[ii]

Smoking (see page 53) → Identify key modifiable risk factors[iii]

Blood pressure

Drug treatment if: SBP ≥ 140 or DBP ≥ 90 mmHg (especially if 10-year CVD risk ≥ 10%)

Target[v]

SBP < 130 mmHg

DBP < 80 mmHg

Treatment (see page 55-57)

Coagulation

Drug treatment if: established CVD only

Target - N/A

Consider treating with acetylsalicylic acid 75-150 mg[vii]

Glucose

Confirm DM and treat with diet and drugs

Target

HbA1C 6.5-7.0%

Treatment (see page 59)

Lipids

Drug treatment[iv] if: established CVD or type 2 diabetes or 10-year CVD risk ≥ 10%

Target*

	2ry prevention or very high risk	1ry Prevention
LDL**	< 1.4 (55)	< 2.0 (80)
Non LDL	< 2.2 (85)	< 3.0 (115)

Treatment (see page 60)

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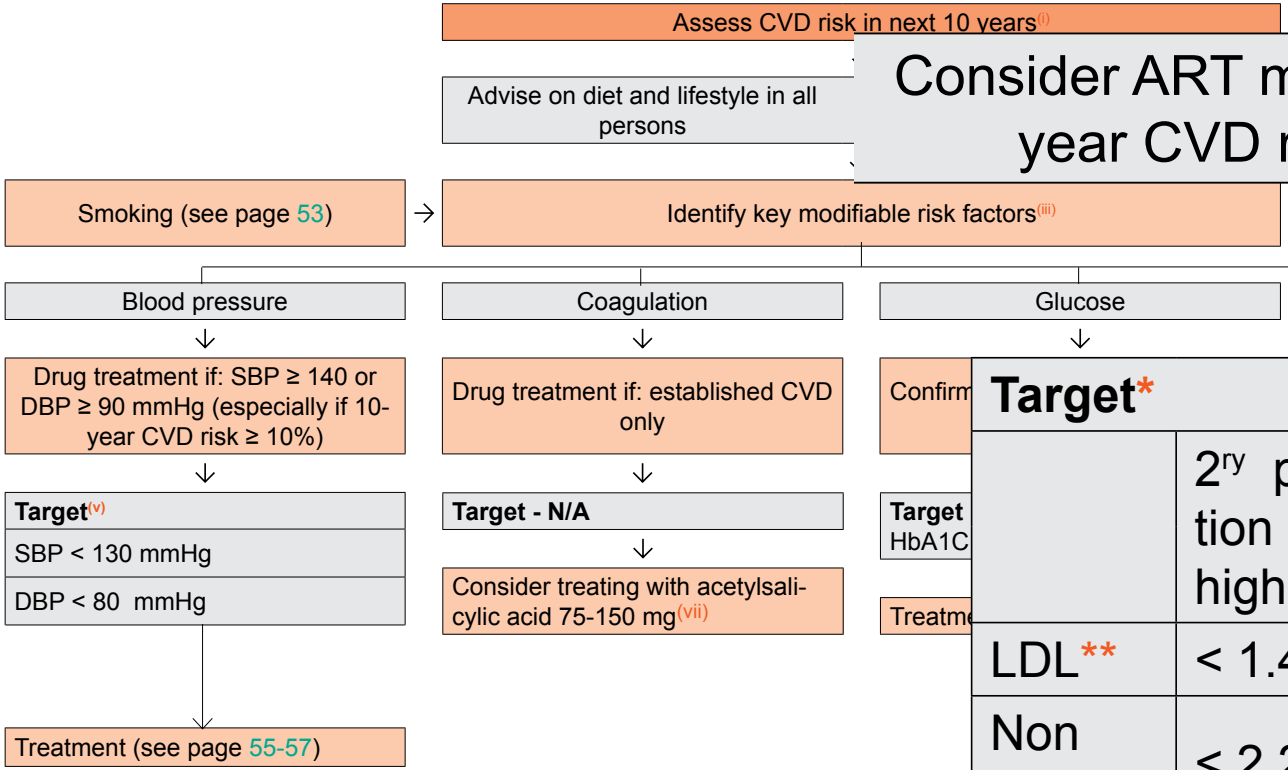
Cardiovascular Disease prevention



Target*		
	2ry prevention or very high risk	1ry Prevention
LDL**	< 1.4 (55)	< 2.0 (80)
Non LDL	< 2.2 (85)	< 3.0 (115)

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Kidney Disease

Kidney Disease: Definition, Diagnosis and Management

Diagnosis of kidney disease

		eGFR[i]			
		> 60 mL/min	**> 60 mL/min, but accelerated decline of eGFR***	**> 30 - ≤ 60 mL/min**	**≤ 30 mL/min**
Proteinuria (mg/mmol)[ii]	UA/C[iii] < 3	Regular follow-up			• Check risk factors for CKD and nephrotoxic medicines including ART[iv] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • Urgent referral to nephrologist
	UA/C[iii] 3-30	• Check risk factors for CKD[x] and nephrotoxic medicines including ART[iv, x] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • If haematuria present with any level of proteinuria refer to nephrologist • Refer to nephrologist if new CKD or progressive decline in eGFR			
	UA/C[iii] > 30				

Kidney Disease

Kidney Disease: Definition, Diagnosis and Management

Proteinuria (mg/mmol)[ii]		> 60 mL/min, but accelerated decline of eGFR*	> 30 - ≤ 60 mL/ min	≤ 30 mL/min
	UA/C[iii] < 3			
	UA/C[iii] 3-30	up ctors for CKD[x] and nephrotoxic luding ART[iv, x] r adjust drug dosages where ultrasound present with any level of proteinu- phrologist rologist if new CKD or progressive FR		• Check risk factors for CKD and nephrotoxic medicines including ART[iv] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • Urgent referral to nephrologist
	UA/C[iii] > 30			

Kidney Disease

Indications and Tests for Proximal Renal Tubulopathy (PRT)

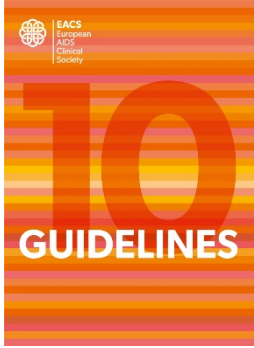
Indications for proximal renal tubulopathy tests	Proximal renal tubulopathy tests[iv], including	Replace TDF by non-tenofovir drug or TAF* alternative drug if:
• Progressive decline in eGFR[i] & eGFR ≤ 90 mL/min & no other cause and/or • Confirmed hypophosphataemia[ii] and/or • Confirmed increase in UP/C[iii] • Renal insufficiency even if stable (eGFR ≤ 60 mL/min) • Tubular proteinuria[v]	• Blood phosphate and urinary phosphate excretion[vi] • Blood glucose and glucosuria • Serum bicarbonate and urinary pH[vii] • Blood uric acid level and urinary uric acid excretion[viii] • Serum potassium and urinary potassium excretion	• Confirmed proximal renal tubulopathy with no other cause

Kidney Disease

Indications and Tests for Proximal Renal Tubulopathy (PRT)

Indications for proximal renal tubulopathy tests	Proximal renal tubulopathy tests[iv], including	Replace TDF by non-tenofovir drug or TAF* alternative drug if:
• Progressive decline in eGFR[i] & eGFR ≤ 90 mL/min & no other cause and/or • Confirmed hypophosphataemia[ii] and/or • Confirmed increase in UP/C[iii] • Renal insufficiency even if stable (eGFR ≤ 60 mL/min) • Tubular proteinuria[v]		med proximal renal tubulo- with no other cause

What about HIV and Ageing?



- Current guidelines cover a range of age-related conditions
- Comprehensive guidance on screening, prevention and management
- No agreed ‘old age’ cut-off
- Sections include age-specific guidance

New section – Frailty and Ageing

Feature	Frailty Phenotype	Frailty Index
Clinical definition	Based on presence of signs, symptoms (pre-disability syndrome)	Based on presence of diseases, disabilities (accumulation of deficits)
How to assess	Assessed by five specific features [22]: 1. self-reported weight loss (a) 2. self-reported exhaustion (b) 3. low levels of physical activity as measured by Minnesota Leisure physical activity questionnaire (c) 4. measured 4 m walk speed time (d) 5. measured grip strength (e)	A frailty index is calculated based on the number of health deficits out of > 30 assessed health deficits [23] Health variables, including signs and symptoms of disease, laboratory measures, and self-reported data Data routinely collected in medical records can be included if they characterise age-related, acquired health deficits which cover a range of physiologic systems
How to interpret	Categorical variables Total score of 5 items: 0 deficits = fit 1-2 deficits = pre-frail 3 + deficits = frail	Continuous variables Index ranges from 0 to 1: > 0.25 = fit 0.25 - 0.4 = frail > 0.4 = most frail
How to address frailty [24]	Promote Comprehensive Geriatric Assessment (CGA), aimed at personalising interventions according to benefits/priorities for a given person through a multidisciplinary diagnostic and treatment process, that identifies medical, psychosocial, and functional limitations aimed at maximising overall health with ageing and the improvement of quality of life	
Recommendations [25], [26]	In PLWH who are frail: 1. Sustain and recover physical function impairment and sarcopenia prescribing physical activity with a resistance training component 2. Address polypharmacy by reducing or deprescribing any inappropriate/superfluous medications, see Prescribing in Elderly PLWH 3. Screen for, and address modifiable causes of fatigue 4. For PLWH exhibiting unintentional weight loss, screen for reversible causes and consider food fortification and protein/caloric supplementation 5. Prescribe vitamin D for individuals deficient in vitamin D, see page 62	

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1. self-reported weight loss (a)
2. self-reported exhaustion (b)
3. low levels of physical activity as measured by Minnesota Leisure physical activity questionnaire (c)
4. measured 4 m walk speed time (d)
5. measured grip strength (e)

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Promote Comprehensive Geriatric Assessment (CGA), aimed at personalising interventions according to benefits/priorities for a given person through a multidisciplinary diagnostic and treatment process, that identifies medical, psychosocial, and functional limitations aimed at maximising overall health with ageing and the improvement of quality of life

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What about obesity?

Obesity

Definition:
Body mass index (BMI) > 30 kg/m²
Also body fat > 25% (men) or > 33% (women) for persons with low muscle mass
Waist circumference is an indicator of abdominal fat and a useful predictor of cardiometabolic diseases. Cut-off points indicating higher cardiometabolic risks are > 88 cm for women and > 102 cm for men.Naturally, different ethnicities have different body builds and proportions. Asians have a naturally slimmer, petite frame and therefore the waist circumference cut off for Japanese, Chinese and South Asian people is lower than for Caucasians.
Visceral adipose tissue (VAT) area ≥ 130 cm² is a validated threshold for increased cardiometabolic risk
Consequences:
Not only cosmetic concern
Worse outcomes with surgery and actute infections (e.g. pneumonia, influenza)
Increased risk of diabetes mellitus, hypertension, cardiovascular disease, some cancers, obstructive sleep apnea, colelithiasis, erectile dysfunction, non-alcoholic fatty liver disease, ostheoarthritis and depression
Contributing factors:
Older age
Sedentary lifestyle
Intake of excess or poor quality calories (e.g. saturated fats, processed sugars)
Excess alcohol consumption
Some medications (e.g. psychotropic drugs, steroids, antidiabetci drugs)
Endocrine disorders (e.g. GH deficiency, hypothyroidism, Cushing's syndrome, hypogonadism)
Assessment:
Weight, waist circumference and BMI, see page 53
Fasting lipids and glucose, see pages 54, 58 and 60
Dyslipidaemia management, see page 60
Assess NAFLD, see page 72
Prevention of cardiovascular disease, see page 54
Aim:
An objective of 5% weight loss from initial weight may have a beneficial impact on obesity-related comorbidities
Management:
Structured exercise
Dietary intervention
No data on ART switch
Treat underlying or associated conditions
There are several drugs approved to treat obesity (e.g. orlistat, phentermine/topiramate, lorcaserin, nalterxone/bupropion, liraglutide) but they should be prescribed by an endocrinologist or obesity expert. All of them may have adverse effects and drug-drug interactions with ART.
Bariatric surgery may 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 theraputic drug monitoring and drug dose adjustment post-bariatric surgery
Surgery can be considered for localised lipomas and dorsocervical fat accumulation for cosmetic purposes only

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10 GUIDELINES

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Worse outcomes with surgery and actute infections (e.g. pneumonia, influenza)
Increased risk of diabetes mellitus, hypertension, cardiovascular disease, some cancers, obstructive sleep apnea, colelithiasis, erectile dysfunction, non-alco-

- Rapidly evolving field
- Will continue to update
- No ART-specific recommendations

Prevention of cardiovascular disease, see page 34
Aim:
An objective of 5% weight loss from initial weight may have a beneficial impact on obesity-related comorbidities
Management:
Structured exercise
Dietary intervention
No data on ART switch
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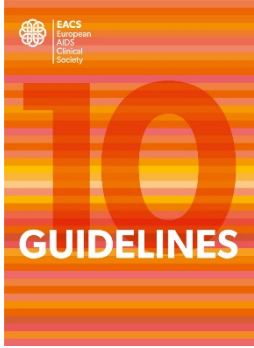
What about obesity?

Obesity

	Skin	Digestive	Liver	CV	Musculo-skeletal	Genito-urinary	Nervous	Body fat	Metabolic	Other
NRTIs										
TAF[iii]									**Weight increase**	
INSTI										
RAL		Nausea			Myopathy, Rhabdomy-olysis		Sleep disturbance, Headache			Systemic hypersensitivity syndrome[viii] **Weight increase**
DTG	Rash	Nausea				↓ eGFR[iv]	**Sleep disturbance, Headache**			Systemic hypersensitivity syndrome (< 1%) **Weight increase**
EVG/c		**Nausea,** Diarrhoea				↓ **eGFR**[iv]	Sleep disturbance, Headache			**Weight increase**
BIC						↓ eGFR[iv]	Sleep disturbance, Headache			**Weight increase**

Acknowledgements



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Young Scientist: Aoife Cotter	**Dublin, Ireland**
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Georg Behrens	Hanover, Germany
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Juliet Compston	Cambridge, UK
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Leonardo Fabbri	Modena, Italy
Christoph Fux	Aarau, Switzerland
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Guidelines Chair: **Manuel Battegay**
Guidelines Coordinator: **Lene Ryom**

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

Charles Béguelin for the Viral Hepatitis Co-infections EACS guidelines panel

Disclosures

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Speaker’s Bureau: Never
Board Member/Advisory Panel: Not in the past 12 months
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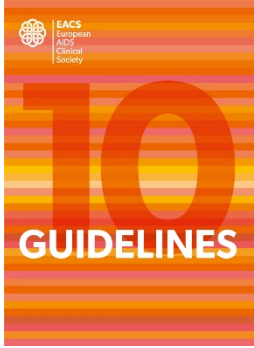
Consultant: Never
Employee: Never

Summary of Changes

- New chapter **name**:
  - «Clinical management and treatment of **Viral Hepatitis** Co-infections in PLWH»

- New chapter **structure**:
  - General recomendations
  - Treatment and monitoring of persons with **HBV**/HIV Co-infection
  - Treatment and monitoring of persons with **HCV**/HIV Co-infection
  - **Hepatitis D and E** in PLWH



General recomendation

- **Diagnosing hepatic fibrosis**:

The combination of **liver stiffness** measurement and **blood tests** or repeated assessments may improve accuracy.

Cut-off Values of Non-invasive Tests for the Detection of Significant Fibrosis and Cirrhosis

HIV/Hepatitis C co-infection (according to EASL recommendations on Treatment of Hepatitis C 2018 [1])

Test	Stage of fibrosis	Cut off (kPa)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Fibroscan	F3*	10	72	80	62	89
	F4*	13	72-77	85-90	42-56	95-98
APRI	F4	2	48	94	n.a.	n.a.
		1	77	75	n.a.	n.a.
Fib-4	F4	3.25	55	92	n.a.	n.a.
		1.45	90	58	n.a.	n.a.

These cut-offs were derived from different studies and the optimal values might vary between populations and must be interpreted together with the individual clinical assessment

*The distinction between F3 and F4 is often imprecise and must be interpreted in the individual clinical context

HIV/Hepatitis B co-infection [2], [3], [4]

Test	Stage of fibrosis	Cut off (kPa)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Fibroscan	F3	7.6	85	87	77	92
	F4	9.4	92	94	79	98
APRI	F4	2	35	89	26	92
		1	65	75	22	95

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HBV/HIV Co-infection

- **HCC screening**

In HBV-positive non-cirrhotic, HCC screening should follow current HCC EASL guidelines (http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/easl-clinical-practice-guidelines-on-hepatocellular carcinoma). Risk factors for HCC in this population include family history of HCC, ethnicity (Asians, Africans), HDV and **age >45 years**.

Wandeler et al. J. Hepatol. 2019

HBV/HIV Co-infection

- **HBV reactivation**

HBs-Ag negative, anti-HBc positive persons undergoing immunosuppression:

– **Severe immunosuppressive therapy** (chemotherapy for lymphoma/leukaemia or stem-cell or solid-organ transplantation)
➢ **TDF/TAF** therapy to prevent HBV reactivation.

– **B-cell-depleting agents** (rituximab, ofatumumab, natalizumab, alemtuzumab, ibritumomab)
➢ **TDF/TAF** should be part of the ART. If contraindicated, second line options include 3TC and FTC (cave reactivation due to resistance)

– **Other immunosuppressive therapy** (e.g. TNF alpha inhibitor)
➢ **careful monitoring** with HBV DNA and HBsAg is required for HBV reactivation. If this is not possible, addition of TDF/TAF is recommended

Caution with ART simplification strategy without TDF/TAF or NRTI free regimens

HCV/HIV Co-infection

- **DAA table has been split in two parts:**

Preferred 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[ii]		Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/LDV +/- RBV	8-12 weeks without RBV[iii]	12 weeks with RBV[iii]	
2	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV
3	GLE/PIB	8 weeks[iv]	12 weeks[iv]	Not recommended
	SOF/VEL +/- RBV	12 weeks[v]	12 weeks with RBV[vi] or 24 weeks without RBV	
	SOF/VEL/VOX	-	12 weeks	Not recommended
5 & 6	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/LDV +/- RBV	12 weeks +/- RBV[viii]	12 weeks with RBV[iii]	
	SOF/VEL	12 weeks		12 weeks with RBV

Treatment options if preferred not available

DAA HCV treatment options (except for persons pre-treated with Protease or NS5A inhibitors) to be used if preferred option is not avaible

HCV GT	Treatment regimen	Treatment duration & RBV usage		
		Non-cirrhotic	Compensated cirrhotic	Decompensated cirrhotics CTP class B/C
1 & 4	OBV/PTV/r + DSV	8[ix]-12 weeks in GT 1b	12 weeks in GT 1b	Not recommended
	OBV/PTV/r + DSV + RBV	12 weeks in GT 1a	24 weeks in GT 1a	Not recommended
	OBV/PTV/r + RBV	12 weeks in GT 4		Not recommended
	SOF + DCV +/- RBV	12 weeks +/- RBV[x]	12 weeks with RBV[iii]	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
3	SOF + DCV +/- RBV	12 weeks +/- RBV[xi] or 24 weeks without RBV	24 weeks with RBV	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
5 & 6	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[xii]	12 weeks with RBV[iii]	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended

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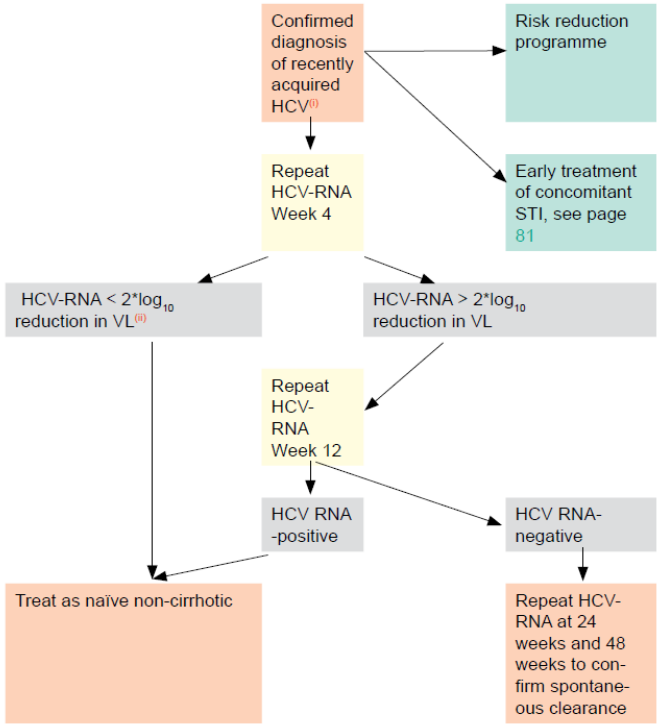
HCV/HIV Co-infection

- Figure on management of **recently acquired HCV infection:**

HCV-RNA <2log reduction at 4 weeks is considered as **early chronic HCV infection**



a) Treat with short duration DAAs
b) Enrol in clinical trial for acute HCV treatment

European AIDS Treatment Network (NEAT) consensus conference statement june 2019 (www.neat-id.org).

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HDV and HEV in PLWH

- Screen for HDV antibodies in all HBsAg postive PLWH
- Use non invasive markers with caution
- Refer early to university centers

Hepatitis D and E in PLWH

Hepatitis Delta Virus (HDV)

1. HDV antibodies should be screened for in all HBsAg positive PLWH
2. In PLWH with positive HDV antibodies, HDV-RNA should be measured in order to assess activity of the disease
3. In PLWH with chronic HDV co-infection and significant liver fibrosis (≥ F2), long-term (at least 12 months) treatment with PEG-IFN might be considered in association with TDF-based ART
4. Non-invasive fibrosis markers (transient elastography and serum markers) should be used with caution in PLWH with chronic HDV infection as there are no well-established thresholds
5. Because of its anti-HBV activity, TDF/TAF should be added to PEG-IFN in order to reduce HBV-DNA load
6. PLWH without response to PEG-IFN treatment should be referred to university centers and if possible enrolled in trials on new drugs active against HDV
7. Treatment efficacy should be monitored with HBV-DNA and HDV-RNA measurements, when available, and with follow-up of biochemical and liver fibrosis estimates
8. Persistent off-treatment HDV-RNA negativity and anti-HBs seroconversion are the ideal goals of antiviral treatment for HDV even if they can only be obtained in a minority of PLWH. Histological remission of liver disease is a less ambitious but more likely achievable goal
9. In PLWH with HDV and ESLD or HCC, liver transplantation from HBsAg negative donors should be strongly considered. Transplant with anti-HBV prophylaxis post-OLTX cures HBV and HDV infection

Hepatitis E Virus (HEV)

10. Screening for HEV infection is warranted in PLWH with symptoms consistent with acute hepatitis, unexplained flares of aminotransferases (even if suspected drug induced liver injury), unexplained elevated liver function tests, neuralgic amyotrophy, Guillain-Barrè, encephalitis or proteinuria
11. Screening should include anti-HEV IgG and IgM and HEV-RNA in blood and if possible in stool
12. Treatment with RBV (600 mg daily) may be considered in cases of severe acute HEV, acute-on-chronic liver failure, extrahepatic HEV related disease or in persons with persisting HEV replication three months after first detection of HEV-RNA. RBV should be given for a duration of 12 weeks followed by HEV-RNA measurements in serum and stool. If HEV-RNA is undetectable in both, RBV can be stopped. In PLWH in whom HEV-RNA is still detectable in serum and/or stool, RBV may be continued for an additional three months. In the setting of chronic HEV infection in immunosuppressed persons, reduction in immunosuppression should be considered

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Acknowledgements

Viral Hepatitis Co-infections	
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Lene Ryom

Co-morbidity panel

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Part VI Opportunistic Infections

Ole Kirk for the Opportunistic Infection EACS guidelines panel

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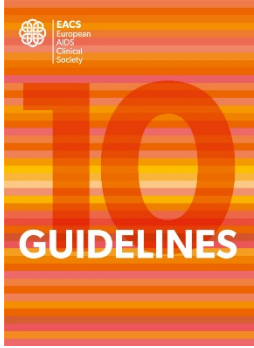

Changes

- Table on when to start ART in PLWH with OIs
- Table on prevention and treatment of IRIS
- Extensive revision of section on treatment of resistant TB
- Table on TB drug doses
- Minor revisions in text for individual OIs

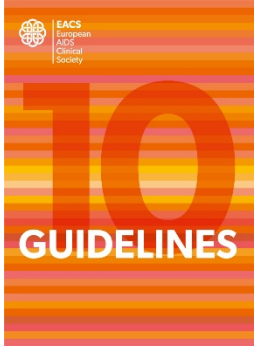

Table on when to start ART in PLWH with OIs

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When to start ART in PLWH with Opportunistic Infections (OIs)

	CD4 count	Initiation of ART	Comments
General recommendation	Any	As soon as possible and within 2 weeks after starting treatment for the opportunistic infection	
Tuberculosis	< 50 cells/µL > 50 cells/µL	As soon as possible and within 2 weeks after starting TB treatment Can be delayed up to 8 weeks after starting TB treatment, especially if difficulties with adherence, drug-drug-interactions or toxicity	A threshold of 100 cells/µL may be more appropriate due to variability in CD4 count assessments CD4 thresholds also apply for TB meningitis – with close monitoring due to increased risk of adverse effects For details, see ART in TB/HIV Co-infection section, page 20
Cryptococcal meningitis	Any	Defer initiation of ART for at least 4 weeks (some specialists recommend a delay of 6-10 weeks in severe cryptococcal meningitis)	
CMV end organ disease	Any	A delay of a maximum of 2 weeks might be considered	Especially for persons with chorioretinitis and encephalitis due to risk of IRIS

IRIS - definition and prevention

Definition	
Paradoxical IRIS	**Paradoxical worsening** symptoms during the ART-induced immune-reconstitution period in association with inflammatory signs (by physical exam, imaging or tissue biopsy), after exclusion of the expected course of a treated/untreated OI or drug toxicities [1]
Unmasking IRIS	**New onset** of symptoms during the ART-induced immune-reconstitution period in association with inflammatory signs (by physical exam, imaging or tissue biopsy), after exclusion of the expected course of a treated/untreated OI or drug toxicities [1]
Prevention	
Cryptococcal meningitis:	
paradoxical IRIS	Start therapy with **amphotericin B plus flucytosine** and defer start of cART for at least 4 weeks.
unmasking IRIS	Determine serum cryptococcal antigen in newly diagnosed PLWH with CD4 counts < 100 cells/µL. If cryptococcal antigen is detected, exclude active cryptococcal disease, and in particular examine CSF to rule out cryptococcal meningitis. If meningitis is ruled out, start pre-emptive therapy. For details, see below the specific section on cryptococcal disease
Tuberculosis	
paradoxical IRIS	Simultaneous initiation of ART and prophylactic prednisone in persons with CD4 cell count < 100 cells/µL, who started anti-TB treatment within 30 days prior to ART, may reduce risk of TB-IRIS by 30%. **Prednisone** dose: 40 mg qd for 2 weeks, followed by 20 mg qd for 2 weeks [2]

IRIS – treatment

Treatment	
In general, OI-IRIS resolve within a few weeks with continuation of specific treatment for the OI, without discontinuing ART and without anti-inflammatory treatment In cases where anti-inflammatory treatment is contemplated by the physician, corticosteroids or non-steroidal anti-inflammatory agents can be used. However, little or no data support their use or specific administration schedules in the specific conditions	
TB-IRIS	Start of systemic corticosteroids is recommended (e.g., oral prednisone 1.5 mg/kg/day for 2 weeks, then 0.75 mg/kg/day for 2 weeks) [3]
Life-threatening CNS-IRIS:	
TB-meningitis	Oral **prednisone** (1.5 mg/kg/day for 2 weeks, then tapering) [4]
PML	iv **methylprednisolone** (1 g/day for 3-5 days or iv dexamethasone 0.3 mg/kg/day for 3-5 days), then oral tapering

Individual OIs

PCP/cerebral toxoplasmosis:

- Primary prophylaxis:
  - Stop: if CD4 count >100 cells/µL and HIV-VL undetectable over 3 months
  - Typo in booklet: atovaquone dose should be **1500 mg qd**

- PCP treatment:
  - 'Some experts recommend adding caspofungin or other echinocandins to standard treatment in persons with severe PcP (requiring intensive care unit admission)'

Individual OIs

MAC:

- Primary prophylaxis (CD4 count <50 cells/µL) is not recommended if ART is started

Herpes Simplex:

- Initial and recurrent genital and mucocutaneous HSV -> Section on Sexual and Reproductive Health

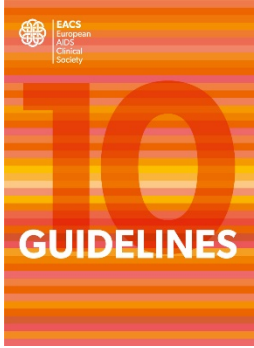
Individual OIs

Talaromycosis

Talaromycosis (*Talaromyces* (former *Penicillium marneffei*))

Treatment [7]			
Consider diagnosis in PLWH who lived in Asia. **Diagnosis:** antigen detection in blood, urine or broncho-alveolar fluid, OR positive microscopy, OR mycological culture of blood, urine, broncho-alveolar fluid, CSF or tissue biopsy or PCR in blood OR other clinical samples. *Aspergillus* galactomanan assays may be helpful to diagnose disseminated infections as cross reactivity occurs.			
	Drug	**Dose**	**Comments**
Severe disseminated talaromycosis	**Induction therapy:** **liposomal amphotericin B**	3 mg/kg qd iv	For 2 weeks or until clinical improvement
	Consolidation therapy: **itraconazole**	200 mg tid po for 3 days, then 200 mg bid po	For at least 10 weeks (followed by secondary prophylaxis)
Moderate talaromycosis	**itraconazole**	200 mg tid po for 3 days, then 200 mg bid po	For 8 weeks (followed by secondary prophylaxis)
Secondary prophylaxis / Maintenance therapy			
Secondary prophylaxis: itraconazole 200 mg qd po **Stop:** if CD4 count > 100 cells/µL and HIV-VL undetectable over 6 months, negative fungal blood cultures or negative PCR/ negative antigen			

MDR-TB – new recommendation



- EACS Guidelines in agreement with new WHO Guidelines:
  - 4 drugs for 6 months,
  - followed by 3 drugs for 12-14 months

- 'Treatment of MDR-/XDR-TB is a specialist area…. Other specialists have different views and practice may vary'

Group A: **Include all three medicines**	• levofloxacin (LFX) or moxifloxacin (MFX) • bedaquiline(BED) • linezolid (LZD)
Group B: **Add one or both medicines**	• clofazimine (CFX) • cycloserine (CS) or terizidone (TRD)
Group C: **Add to complete the regimen and when medicines from Groups A and B cannot be used**	• ethambutol (E) • delamanide (DLM) • pyrazinamide (Z) • amikacin (AMK) (or streptomycin (S) – only if susceptible) • imipenem–cilastatin (IPM-CLN) or meropenem (MPM) with amoxicillin/clavulanic acid (AMX) • ethionamide (ETO) or prothionamide (PTO) • p-aminosalicylic acid (PAS)

TB Drug Doses

- Doses of all TB drugs and common adverse events – e.g.:

Moxifloxacin	400 mg qd	Max 800 mg qd (used in the standardized shorter MDR-TB regimen) Monitor ECG in respect of QT prolongation
Bedaquiline	400 mg qd for 2 weeks 200 mg qd three times weekly for 22 weeks	EFV, ETV: potential reduction of bedaquiline exposure and activity. Not recommended Boosted regimens: increase in bedaquiline exposure. Potential risk of QT interval prolongation, ECG monitoring recommended. Avoid coadministration > 14 days
Linezolid	600 mg qd	Max 1200 mg qd Caution: hematological side effects and neurotoxicity, including optic neuropathy
Clofazimine	100 mg qd	Alternative: 200 mg for 2 months then 100 mg qd Caution: skin toxicity Monitor ECG in respect of QT prolongation

Acknowledgements

Opportunistic Infections

Chair: Ole Kirk	**Copenhagen, Denmark**
Vice-Chair: Paola Cinque	**Milan, Italy**
Young scientist: Daria Podlekareva	**Copenhagen, Denmark**
Juan Ambrosioni	Barcelona, Spain
Nathalie De Castro	Paris, France
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 Manuel Battegay & Guidelines Coordinator Lene Ryom

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Clinical
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Community perspectives

Simon Collins
HIV i-Base and EATG
i-base.info

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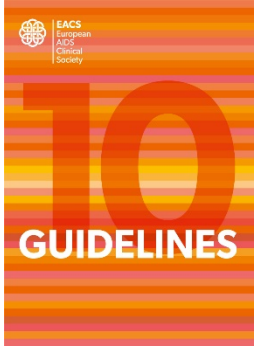
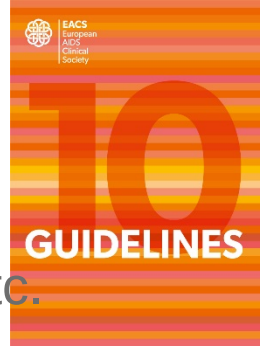


Community perspectives: 2019

- International guidelines, updated annually, to cover standards of care across Europe.
- Translated into key languages.
- Good history of community involvement – including person-centred language.
- HIV+ use guidelines as a reference for minimum care.
- New ARVs and strategies: INSTIs, dual etc.
- Comprehensive focus on long-term health and quality of life in context of HIV and ageing.
- Emerging issues – ie frailty, ageing, transgender health.
- Includes sexual health. menopause and U=U.
- Lifestyle – and modifiable changes (usually needs additional support).



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Guidelines Chair Manuel Battegay & Guidelines Coordinator: Lene Ryom

The collective group of more than 60 doctors, researchers, invited experts and community representatives that have contributed to this update.

The network of community activists who continue to advocate for the health and rights of HIV positive people – often working in challenging and difficult circumstances globally.

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