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

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Presenter Disclosure Information

In compliance with the Conflict of Interest Policies, the European AIDS Clinical Society (EACS) requires the following disclosure from the presenters:

Manuel Battegay

• 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
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-naive PLWH initiating treatment
- 2 NRTI + DOR included in recommended regimens
- When indicated, TDF/FTC has been added as a backbone
- Dual therapy with DTG + 3TC has been upgraded to recommended regimen
- Primary HIV infection, page 14
- High genetic barrier INSTI or PIbs 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/r + RPV has been included as dual therapy option supported by small trials
- Monotherapy with PIbs 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 TBI/HIV co-infection, page 20
- New tables have been included (ART in TBI/HIV co-infection and DIDs)
- Post-exposure prophylaxis (PEP), page 22
- TAF/TDC, RAL od and BIC have been included as possible drugs to include in a PEP regimen
- Pre-exposure prophylaxis (PEP), page 23
- TAF/TDC has been included as alternative in MSM and transgender women

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

- 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: cases 45, 47, 48

Co-morbidity section

- All tables have been updated with the addition of BRC and DOR and older ARVs (including older PIs, d4T and d4T) have been removed from all sections apart from that on lipostatigraphy: pages 67, 69, 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/creati-nine ratio for glomerular disease and protein/creatinine ratio for screen- ing and diagnosing AKI-related nephropathy, pages 64-65
- There are updated targets for lipids and a change in threshold for ART modification from 20% 10-year risk of CVD to 15% 10-year risk of CVD, page 64 and 60
- Blood pressure targets have been updated, page 54-55
- The clinical 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 60
- There is a minor update for the screening guidance for HCC in non- cirrhotic PLWH with HBS, pages 5, 18, 77 and 90
- In the sexual health section, there is a statement about HIV, including how this information affects options for conception for PLWH and their partners and screening for HBV: pages, 50
- 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 86

Opportunistic Infections section

- The chapter on when to start ART in the presence of opportunistic infec- tions has been added, page 104
- A table on clinical presentation and management of immune Reconstit- uction inflammatory syndrome (IRIS) has been added, page 104
- Treatment of the following has been updated: CMV, HSV, VZV, intrathymicases, cryptococcosis, pages 108-111
- Treatment details of initial and recurrent genitourinary/cutaneous HSTV has been removed from the OIs section. A cross reference to the Sexua- l 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 110, as well as a table detailing cases for all TB drugs, major side effects and caution when using with ART, page 117

For more detailed summary changes made from v6.1 to v10.0, please see EACS Guidelines App

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EACS, 2019
# Video links

<table>
<thead>
<tr>
<th>EACS Guidelines</th>
<th>Video lectures</th>
<th>Link to video lecture</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary HIV Infection</strong></td>
<td>When to Start ART Part 1</td>
<td><a href="https://vimeo.com/197164442/326941a0d37">https://vimeo.com/197164442/326941a0d37</a></td>
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<tr>
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<td>When to Start ART Part 2</td>
<td><a href="https://vimeo.com/197167653/3800a0e2c64">https://vimeo.com/197167653/3800a0e2c64</a></td>
</tr>
<tr>
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<td>What ART to Start Part 1</td>
<td><a href="https://vimeo.com/197374541/32232a9d037">https://vimeo.com/197374541/32232a9d037</a></td>
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<tr>
<td><strong>Switch Strategies for Virologically Suppressed Persons</strong></td>
<td>How to Change ART</td>
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<td><strong>Virological Failure</strong></td>
<td>Adherence and Prevention of HIV Drug Resistance</td>
<td><a href="https://vimeo.com/197813237/c07e272b0d5">https://vimeo.com/197813237/c07e272b0d5</a></td>
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<td>PrEP Part 1</td>
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<td>PrEP Part 2</td>
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<tr>
<td><strong>Adverse Effects of ARV’s and Drug Classes</strong></td>
<td>Adverse Effects and Monitoring</td>
<td><a href="https://vimeo.com/197275138/3ed9f90e55">https://vimeo.com/197275138/3ed9f90e55</a></td>
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<td><strong>Cancer Screening Methods</strong></td>
<td>Clinical Management of Cancer and HIV Part 1</td>
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<td>CNS and HIV Part 1</td>
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<td><strong>Diagnosis and Treatment of TB in PLWH</strong></td>
<td>Tuberculosis and HIV Co-infection Part 1</td>
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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

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

Reviewed by
- Community representatives, Wave and cross-panel experts

The guidelines content is managed by
The EACS Medical Secretariat; guideline coordination chair and assistant working closely with the EACS Secretariat
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

- Constant Expansion of Guidelines
- Since 2015 as a free App for IOS and Android systems
- **NEW: Webversion!**
  by the Sanford Guide
- Online on the EACS website
- In print as a booklet
Acknowledgements

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Joelle Verluyten and team, Svilen Konov

We hope you will enjoy the 2019 EACS Guidelines!
ART of PLWH

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## Acknowledgements

### HIV Treatment

<table>
<thead>
<tr>
<th>Chair: José Arribas</th>
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<tr>
<td>Vice-Chair: Jean-Michel Molina</td>
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<td>Hamburg, Germany</td>
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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
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**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Main requirements</th>
<th>Additional guidance (footnotes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended regimens</strong></td>
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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/r) might be indicated in the presence of resistance.

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<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid</td>
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</tr>
</tbody>
</table>

New recommendation favouring unboosted INSTI with high genetic barrier as third agent.
# Initial Combination Regimen for ART-naïve Adult PLWH

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Main requirements</th>
<th>Additional guidance (footnotes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2 NRTIs + INSTI (PREFERRED)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC + DTG</td>
<td>HLA-B*57:01 negative</td>
<td>I (ABC: HLA-B*57:01, cardiovascular risk)</td>
</tr>
<tr>
<td>ABC/3TC/DTG</td>
<td>HBsAg negative</td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC + DTG</td>
<td>(TDF: prodrug types. Renal and bone toxicity. TAF dosing)</td>
<td>II Weight increase</td>
</tr>
<tr>
<td>TAF/FTC/BIC</td>
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</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC</td>
<td>(TDF: prodrug types. Renal and bone toxicity. TAF dosing)</td>
<td>III (RAL: dosing)</td>
</tr>
<tr>
<td>+ RAL qd or bid</td>
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</tr>
<tr>
<td><strong>1 NRTI + INSTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG + 3TC</td>
<td>HBsAg negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV- VL &lt; 500,000 copies/mL</td>
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</tr>
<tr>
<td></td>
<td>CD4 count &gt; 200 cells/μL</td>
<td></td>
</tr>
<tr>
<td><strong>2 NRTIs + NNRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC + DOR</td>
<td>(TDF: prodrug types. Renal and bone toxicity. TAF dosing)</td>
<td>II (DOR: HIV-2)</td>
</tr>
<tr>
<td>TDF/3TC/DOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC + RPV</td>
<td>(TDF: prodrug types. Renal and bone toxicity. TAF dosing)</td>
<td>III (RPV: HIV-2)</td>
</tr>
<tr>
<td>TAF/FTC/RPV</td>
<td>CD4 count &gt; 200 cells/μL</td>
<td></td>
</tr>
<tr>
<td>TDF/FTC/RPV</td>
<td>HIV- VL &lt; 100,000 copies/mL</td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC + DRV/c or DRV/r</td>
<td>With food</td>
<td></td>
</tr>
<tr>
<td>TAF/FTC/DRV/c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/3TC or TDF/3TC + DRV/r or DRV/c</td>
<td>(TDF: prodrug types. Renal and bone toxicity. TAF dosing)</td>
<td>II (DRV/r: cardiovascular risk)</td>
</tr>
</tbody>
</table>
# Initial Combination Regimen for ART-naïve Adult PLWH

<table>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>2 NRTIs + INSTI (PREFERRED)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC + DTG</td>
<td>HLA-B*57:01 negative HBsAg negative</td>
<td>I (ABC: HLA-B*57:01, cardiovascular risk)</td>
</tr>
<tr>
<td>ABC/3TC/DTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + DTG</td>
<td></td>
<td>II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) III (TAF dosing)</td>
</tr>
<tr>
<td>TAF/FTC/BIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + RAL qd or bid</td>
<td></td>
<td>IV (RAL: dosing)</td>
</tr>
<tr>
<td><strong>1 NRTI + INSTI</strong></td>
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<td></td>
</tr>
<tr>
<td>DTG + 3TC</td>
<td>HBsAg negative HIV-VL &lt; 500,000 copies/mL CD4 count &gt; 200</td>
<td></td>
</tr>
<tr>
<td><strong>2 NRTIs + NNRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + DOR</td>
<td>CD4 count &gt; 200 cells/µL HIV-VL &lt; 100,000 copies/mL Not on proton pump inhibitor</td>
<td>II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) V (DOR: HIV-2)</td>
</tr>
<tr>
<td>TDF/3TC/DOR</td>
<td>With food</td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + RPV</td>
<td>HIV-VL &lt; 100,000 copies/mL</td>
<td>II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (RPV: HIV-2)</td>
</tr>
<tr>
<td>TAF/FTC/RPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF/FTC/RPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2 NRTIs + PI/ir or PI/c</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF/FTC or TDF/FTC or TDF/3TC + DRV/c or DRV/ir</td>
<td>With food</td>
<td>II (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VII (DRV/ir: cardiovascular risk)</td>
</tr>
<tr>
<td>TAF/FTC/DRV/c</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NEW
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

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 un-boosted 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

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

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

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

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Main requirements</th>
<th>Additional guidance (footnotes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended regimens with rifampicin</strong>&lt;br&gt;2 NRTIs + NNRTI&lt;br&gt;TDF/FTC or TDF/3TC + EFV&lt;br&gt;TDF/FTC/EFV</td>
<td>At bed time or 2 hours before dinner</td>
<td>I (tenofovir salts)&lt;br&gt;II (EFV: suicidality, HIV-2 or HIV-1 group 0)</td>
</tr>
<tr>
<td>ABC/3TC +EFV</td>
<td>HLA-B*57:01 negative&lt;br&gt;HBsAg negative&lt;br&gt;HIV-VL &lt; 100,000 copies/mL&lt;br&gt;At bed time or 2 hours before dinner</td>
<td>III (ABC: HLA-B*57:01)&lt;br&gt;II (EFV: suicidality, HIV-2 or HIV-1 group 0)</td>
</tr>
</tbody>
</table>

| **Alternative regimens with rifampicin**<br>2 NRTIs + INSTI<br>TDF/FTC or TDF/3TC + DTG bid | | I (tenofovir salts)<br>IV (DTG: dosing) |
| TDF/FTC or TDF/3TC + RAL bid | | I (tenofovir salts)<br>V (RAL: dosing) |
| ABC/3TC + RAL bid | HBsAg negative<br>HLA-B*57:01 negative | III (ABC: HLA-B*57:01)<br>V (RAL: dosing) |
Drug-drug interactions & other prescribing issues in PLWH

Catia Marzolini
for the EACS Drug-Drug interactions Guidelines panel
Disclosure Information

Research Support: Gilead
Educational support: Gilead, MSD
Speaker’s Bureau: Never
Board Member/Advisory Panel: Not in past 12 months
Stock/Shareholder: Never
Consultant: Never
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
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
Major updates to DDIs tables

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

- **doravirine** does not impact comediations
- **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

<table>
<thead>
<tr>
<th>Non-ARV drugs</th>
<th>ATVc</th>
<th>ATVp</th>
<th>DRVc</th>
<th>DRVp</th>
<th>LPV</th>
<th>DRV</th>
<th>DOR</th>
<th>ETV</th>
<th>ETV</th>
<th>RPV</th>
<th>RPV</th>
<th>INC</th>
<th>INC</th>
<th>INC</th>
<th>INC</th>
<th>INC</th>
<th>INC</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>atazanavir</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>25%</td>
<td>25%</td>
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<td>efavirenz</td>
<td>0%</td>
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<tr>
<td>indinavir</td>
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<tr>
<td>nevirapine</td>
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<tr>
<td>ritonavir</td>
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</table>

**Note:** DOR = DORAVIRINE, ATP = ATAZANAVIR/PROTEASE, DRV = DORAVIRINE/PROTEASE, LPV = LITAVIRINE/PROTEASE, ETV = EFFAVIRENZ, RPV = RITONAVIR/PROTEASE.
Major updates to DDIs tables

boosted ARVs alter clopidogrel efficacy ➔ avoid
alternative: prasugrel

EACS tables are linked to DDIs websites and have been revised to include all updates made to the websites in the past year
## Prescribing Documents for Elderly PLWH

### Selected Top 10 Drug Classes To Avoid in Elderly PLWH

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Problems/alternatives</th>
</tr>
</thead>
</table>
| **First generation antihistamines** e.g., demastine, 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 |
Dosage recommendations for hormone therapy used for gender transitioning

<table>
<thead>
<tr>
<th>Dosage Recommendations</th>
<th>Estrogens</th>
<th>Orals</th>
<th>Gel (preferred for &gt;45 yo and/or smokers)</th>
<th>Patch (preferred for &gt;40 yo and/or smokers)</th>
<th>Conjugated Estrogens</th>
<th>Ethinylestradiol</th>
<th>Androgen Blockers</th>
</tr>
</thead>
<tbody>
<tr>
<td>a ARVs with no predicted effect:</td>
<td>Estradiol oral</td>
<td>No predicted effect a</td>
<td>2 mg/day</td>
<td>4 mg/day</td>
<td>8 mg/day</td>
<td>Estradiol</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td>b ARVs inhibiting estrogen metabolism:</td>
<td>Estradiol gel</td>
<td>No predicted effect a</td>
<td>0.75 mg bid</td>
<td>0.75 mg tid</td>
<td>1.5 mg tid</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td>c ARVs inducing estrogen metabolism:</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
<td>25 µg/day</td>
<td>37.5-75 µg/day</td>
<td>100 µg/day</td>
<td>Estradiol gel</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td>d ARVs inhibiting androgen metabolism:</td>
<td>Estradiol oral</td>
<td>No predicted effect a</td>
<td>1 mg/day</td>
<td>2 mg/day</td>
<td>4 mg/day</td>
<td>Estradiol</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td>e ARVs inducing androgen metabolism:</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
<td>25 mg/day</td>
<td>50 mg/day</td>
<td>100 mg/day</td>
<td>Estradiol</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Conjugated estrogen</td>
<td>No predicted effect a</td>
<td>0.05 mg/day</td>
<td>0.1 mg/day</td>
<td>0.2 mg/day</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Ethinylestradiol</td>
<td>No predicted effect a</td>
<td>No interaction expected. No dose adjustment required.</td>
<td>No interaction expected. No dose adjustment required.</td>
<td>No interaction expected. No dose adjustment required.</td>
<td>Estradiol</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Spironolactone</td>
<td>No predicted effect a</td>
<td>50 mg/day</td>
<td>150 mg/day</td>
<td>400 mg/day</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Finasteride</td>
<td>No predicted effect a</td>
<td>1 mg/day</td>
<td>2 mg/day</td>
<td>5 mg/day</td>
<td>Estradiol oral</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Cyproterone acetate</td>
<td>No predicted effect a</td>
<td>50 mg/day</td>
<td>150 mg/day</td>
<td>150 mg/day</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Goserelin</td>
<td>No predicted effect a</td>
<td>3.6 mg/day</td>
<td>3.6 mg/day</td>
<td>3.6 mg/day</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
<tr>
<td></td>
<td>Leuprolin acetate</td>
<td>No predicted effect a</td>
<td>3.75 mg/day</td>
<td>3.75 mg/day</td>
<td>3.75 mg/day</td>
<td>Estradiol patch</td>
<td>No predicted effect a</td>
</tr>
</tbody>
</table>
Acknowledgements

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Guidelines Chair: Manuel Battegay  Basel, Switzerland
Guidelines Coordinator: Lene Ryom  Copenhagen, Denmark

Drug-drug Interactions

Chair: Catia Marzolini  Basel, Switzerland
Vice-Chair: Giovanni Guaraldi  Modena, Italy
Sara Gibbons  Liverpool, United Kingdom
François Livio  Lausanne, Switzerland

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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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- NIH
- Wellcome Trust
- Health Research Board (Ireland)
- 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
Co-morbidities Guidelines V10

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 lipatrophy, 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
# Hypertension

## Hypertension: Diagnosis, Grading and Management

<table>
<thead>
<tr>
<th>Other risk factors, asymptomatic organ damage or disease</th>
<th>Blood pressure (mmHg)</th>
<th>Blood pressure (mmHg)</th>
<th>Blood pressure (mmHg)</th>
<th>Blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High normal SBP 130-139 or DBP 85-89</td>
<td>Grade 1 hypertension</td>
<td>Grade 2 hypertension</td>
<td>Grade 3 hypertension</td>
<td></td>
</tr>
<tr>
<td>SBP 140-159 or DBP 90-99</td>
<td>SBP 160-179 or DBP 100-109</td>
<td>SBP ≥ 180 or DBP ≥ 110</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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\(^{(i)}\)
- • 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\(^{(i)}\)
- • 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\(^{(i)}\)
- • Immediate BP drugs targeting < 130/80\(^{(ii)}\)

### Organ damage, CKD stage 3 or diabetes

- • Lifestyle changes\(^{(i)}\)
- • Consider blood pressure drugs targeting < 130/80\(^{(i)}\)
- • Lifestyle changes\(^{(i)}\)
- • BP drugs targeting < 130/80\(^{(i)}\)
- • Lifestyle changes\(^{(i)}\)
- • Immediate BP drugs targeting < 130/80\(^{(i)}\)

### Symptomatic CVD, CKD stage ≥ 4 or diabetes with organ damage/risk factors

- • Lifestyle changes\(^{(i)}\)
- • Consider blood pressure drugs targeting < 130/80\(^{(i)}\)
- • Lifestyle changes\(^{(i)}\)
- • BP drugs targeting < 130/80\(^{(i)}\)
- • Lifestyle changes\(^{(i)}\)
- • Immediate BP drugs targeting < 130/80\(^{(i)}\)

---

**BP** blood pressure

**DBP** diastolic blood pressure

**SBP** systolic blood pressure

Repeated blood pressure measurements should be used for stratification

\(^{(i)}\) Recommended lifestyle interventions, see page 53

\(^{(ii)}\) Age 18-65: 120-129

Age 65+: Target 130-139

Table adapted from [6] and 2018 ESC/ESH guidelines for the management of arterial hypertension [7]
# Hypertension

## Hypertension: Diagnosis, Grading and Management

<table>
<thead>
<tr>
<th>Other risk factors, asymptomatic organ damage or disease</th>
<th>Blood pressure (mmHg)</th>
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<td>Grade 3 hypertension</td>
<td></td>
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<tr>
<td></td>
<td>SBP 140-159 or DBP 90-99</td>
<td>SBP 160-179 or DBP 100-109</td>
<td>SBP ≥ 180 or DBP ≥ 110</td>
<td></td>
</tr>
</tbody>
</table>

### No other risk factors

- • Lifestyle changes(i)
- • No BP drug intervention

### 1-2 risk factors

- • Lifestyle changes(i)
- • No BP drug intervention

### ≥ 3 risk factors

- • Lifestyle changes(i)
- • i.e. no BP drug intervention

### Organ damage, CKD stage 3 or diabetes

- • Lifestyle changes(i)
- • Consider blood pressure drugs targeting < 130/80(i)

### Symptomatic CVD, CKD stage ≥ 4 or diabetes with organ damage/risk factors

- • Lifestyle changes(i)
- • Consider blood pressure drugs targeting < 130/80(i)

### Recommended lifestyle interventions

- • Lifestyle changes(i) for several weeks
- • Then add BP drugs targeting < 130/80(ii)

---

Notes:

(i) Repeated blood pressure measurements should be used for stratification

(ii) Grade 1 hypertension: SBP 140-159 or DBP 90-99

(iii) Grade 2 hypertension: SBP 160-179 or DBP 100-109

(iv) Grade 3 hypertension: SBP ≥ 180 or DBP ≥ 110

(EACS Guidelines 10.0)
Hypertension - management

Choosing drugs\(^{(i)}\) for persons newly diagnosed with hypertension

<table>
<thead>
<tr>
<th>&lt; 55 years</th>
<th>≥ 55 years or black(^{(ii)}) person of any age</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(^{(iii)})</td>
<td>C(^{(ii,iv)})</td>
</tr>
</tbody>
</table>

A + C\(^{(ii)}\) (white person) : A + C or C + D\(^{(i)}\) (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
# Hypertension - management

Choosing drugs\(^{(i)}\) for persons newly diagnosed with hypertension

<table>
<thead>
<tr>
<th>&lt; 55 years</th>
<th>(\geq 55) years or black(^{(ii)}) person of any age</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(^{(iii)})</td>
<td>C(^{(ii, iv)})</td>
</tr>
<tr>
<td>(\downarrow)</td>
<td>(\downarrow)</td>
</tr>
<tr>
<td>A + C(^{(iii)}) (white person)</td>
<td>A + C or C + D(^{(iii)}) (black person)</td>
</tr>
<tr>
<td>(\downarrow)</td>
<td></td>
</tr>
<tr>
<td>A + C + D(^{(iii)})</td>
<td></td>
</tr>
</tbody>
</table>

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

\(A^*\) (white person) : A + C or C + D\(^{(ii)}\) (black person)

\^\(^{(v)}\) Add a-blocker (e.g. doxazosin [slow release]) or \(\beta\)-blocker (e.g. bisoprolol). Refer to specialist.
Cardiovascular Disease prevention

Assess CVD risk in next 10 years

↓

Advise on diet and lifestyle in all persons

Consider ART modification if 10-year CVD risk ≥ 10%

Smoking (see page 53)

↓

Identify key modifiable risk factors

Blood pressure

↓

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

Target

SBP < 130 mmHg

DBP < 80 mmHg

Treatment (see page 55-57)

↓

Drug treatment if: established CVD only

Target - N/A

Consider treating with acetylsalicylic acid 75-150 mg

Coagulation

↓

Drug treatment if: established CVD only

Target - N/A

Consider treating with acetylsalicylic acid 75-150 mg

Glucose

↓

Confirm DM and treat with diet and drugs

Lipids

↓

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

HbA1C 6.5-7.0%

Treatment (see page 59)

Target

LDL ** < 1.4 (55) < 2.0 (80)

Non LDL < 2.2 (85) < 3.0 (115)

Treatment (see page 60)

*Fasting or non-fasting samples may be used

**≥ 50% reduction from baseline
Cardiovascular Disease prevention

Assess CVD risk in next 10 years

Consider ART modification if 10-year CVD risk ≥ 10% (ii)

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

Blood pressure → Coagulation → Glucose → Lipids

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

Drug treatment if: established CVD only

Confirm DM and treat with diet and drugs

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

Target (v)

SBP < 130 mmHg

DBP < 80 mmHg

Treatment (see page 55-57)

Target - N/A → Consider treating with acetylsalicylic acid 75-150 mg (vi)

Target

HbA1C 6.5-7.0%

Treatment (see page 59)

Target*

2\textsuperscript{\textdegree} prevention or very high risk

1\textsuperscript{\textdegree} Prevention

LDL** < 1.4 (55) < 2.0 (80)

Non LDL < 2.2 (85) < 3.0 (115)

Treatment (see page 60)
Cardiovascular Disease prevention

Assess CVD risk in next 10 years

Consider ART modification if 10-year CVD risk ≥ 10%\(^{(ii)}\)

Blood pressure

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

Target\(^{(iv)}\)

SBP < 130 mmHg

DBP < 80 mmHg

Treatment (see page 55-57)

Identify key modifiable risk factors\(^{(iii)}\)

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

Non

LDL

< 2.2 (85)

< 3.0 (115)

\(1^{\text{ry}}\) Prevention

LDL**

< 1.4 (55)

< 2.0 (80)

\(2^{\text{ry}}\) prevention or very high risk

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

Target

HbA1C 6.5-7.0%

**Fasting or non-fasting samples may be used**

\(1^{\text{ry}}\) Prevention

Coagulation

Treatment (see page 58-59)

Smoking (see page 53)

Advise on diet and lifestyle in all persons

Lipids

\(\varphi\)
## Kidney Disease: Definition, Diagnosis and Management

### Diagnosis of kidney disease

<table>
<thead>
<tr>
<th>Proteinuria (mg/mmol)</th>
<th>eGFR (L/min)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>UA/C &lt; 3</td>
<td>&gt; 60</td>
<td>Regular follow-up</td>
</tr>
<tr>
<td>UA/C 3-30</td>
<td>&gt; 60, but accelerated decline of eGFR*</td>
<td></td>
</tr>
<tr>
<td>UA/C &gt; 30</td>
<td>&gt; 30 - ≤ 60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 30</td>
<td></td>
</tr>
</tbody>
</table>

- **UA/C** largely detects glomerular disease and can be used for screening.
- **UP/C:** < 15, 15-50, > 50 mg/mmol
- **Urinalysis:** Use urine dipstick to screen for haematuria. To screen for CKD, refer to nephrologist.
- **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**

*Since proteinuria is a symptom of glomerular dysfunction, its presence warrants further investigation to determine the cause and appropriate management.*
# Kidney Disease

## Kidney Disease: Definition, Diagnosis and Management

<table>
<thead>
<tr>
<th>Proteinuria (mg/mmol)</th>
<th>UA/C&lt;sub&gt;(iii)&lt;/sub&gt; &lt; 3</th>
<th>UA/C&lt;sub&gt;(iii)&lt;/sub&gt; 3-30</th>
<th>UA/C&lt;sub&gt;(iii)&lt;/sub&gt; &gt; 30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 60 mL/min, but</td>
<td>≥ 30 - ≤ 60 mL/min</td>
<td>≤ 30 mL/min</td>
</tr>
<tr>
<td></td>
<td>accelerated decline of</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>eGFR&lt;sup&gt;+&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Check risk factors for</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CKD and nephrotoxic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>medicines including ART&lt;sup&gt;(iv)&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discontinue or adjust</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>drug dosages where</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>appropriate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discontinue or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>adjust drug dosages</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>where appropriate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perform renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ultrasound</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urgent referral to</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>nephrologist</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*UA/C largely detects glomerular disease and can be used for screening for HIV-associated renal disease and in diabetics but is not appropriate without impairing actual glomerular filtration: consider new set point after 2-3 weeks apart.

**UA/C (mmol/L); may also be expressed as mg/mg. Conversion factor for mg to min/1.73m² calculated as urine protein albumin (or protein) (mg/L) / urine creatinine.

For eGFR: Use CKD-EPI formula based on serum creatinine, gender, age and ethnicity because eGFR quantification is validated ≥ 60 mL/min.

Different models have been developed for calculating a 5-years CKD risk score while using different nephrotoxic ARVs integrating HIV-independent factors for CKD<sup>(x)</sup> and nephrotoxic medicines including ART<sup>(iv, x)</sup>.

EACS Guidelines 10.0 PART IV Indications and Tests for CVD, CKD and Endocrinology
## Indications and Tests for Proximal Renal Tubulopathy (PRT)

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

---

$i$ For eGFR: use CKD-EPI formula. The abbreviated MDRD (Modification of Diet in Renal Disease) or the Cockcroft-Gault (CG) equation may be used as an alternative, see [https://www.chip.dk/Tools-Standards/Clinical-risk-scores](https://www.chip.dk/Tools-Standards/Clinical-risk-scores).

$ii$ Serum phosphate < 0.8 mmol/L or according to local thresholds; consider renal bone disease, particularly if alkaline phosphatase increased from baseline: measure 25(OH) vitamin D, PTH.

$iii$ UP/C in spot urine, detects total urinary protein, including protein of glomerular or tubular origin. The urine dipstick analysis primarily detects albuminuria as a marker of glomerular disease and is inadequate to detect tubular disease.

$iv$ It is uncertain which tests discriminate best for TDF renal toxicity. Proximal tubulopathy is characterised by: proteinuria, hypophosphataemia, hypokalaemia, hypouricaemia, renal acidosis, glucosuria with normal blood glucose level. Renal insufficiency and polyuria may be associated. Most often, only some of these abnormalities are observed.

$v$ Tests for tubular proteinuria include retinol binding protein, α1- or β2-microglobulinuria, urine cystatin C, aminoaciduria.

$vi$ Quantified as fractional excretion of phosphate (FEPhos): $(\text{PO}_4^{(\text{urine})} / \text{PO}_4^{(\text{serum})} / (\text{Creatinine(urate)} / \text{Creatinine(serum)})$ in a spot urine sample collected in the morning in fasting state. Abnormal > 0.2 (> 0.1 with serum phosphate < 0.8 mmol/L).

$vii$ $S$-bicarbonate < 21 mmol/L and urinary pH > 5.5 suggests renal tubular acidosis.

$viii$ Fractional excretion of uric acid (FEUricAcid): $(\text{UricAcid(urate)} / \text{UricAcid(serum)} / (\text{Creatinine(urate)} / \text{Creatinine(serum)})$ in a spot urine sample collected in the morning in fasting state; abnormal > 0.1*

*Particularly if eGFR > 30 mL/min, as there are limited data on use of TAF with eGFR ≤ 30 mL/min.
## Kidney Disease

### Indications and Tests for Proximal Renal Tubulopathy (PRT)

<table>
<thead>
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<tr>
<td>• Confirmed increase in UP/C(^{(ii)})</td>
<td>• Renal insufficiency even if stable (eGFR ≤ 60 mL/min)</td>
<td></td>
</tr>
<tr>
<td>• Tubular proteinuria(^{(v)})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{*}\) TAF with eGFR ≤ 30 mL/min particularly if eGFR > 30 mL/min, as there are limited data on use of TAF with eGFR ≤ 30 mL/min.

- Serum phosphate < 0.8 mmol/L or according to local thresholds; confirm proximal renal tubulopathy with no other cause.
- Blood glucose and glucosuria
- Blood uric acid level and urinary uric acid excretion
- Serum bicarbonate and urinary pH
- Blood phosphate and urinary phosphate excretion

For eGFR: use CKD-EPI formula. The abbreviated MDRD (Modification of Diet in Renal Disease) or the Cockcroft-Gault (CG) equation may be used as an alternative, see https://www.chip.dk/Tools-Standards/Clinical-risks-

---

\(^{(i)}\) From baseline: measure 25(OH) vitamin D, PTH.

\(^{(ii)}\) Confirmed proximal renal tubulopathy with no other cause.

\(^{(iv)}\) eGFR ≤ 90 mL/min.

\(^{(v)}\) For TDF renal toxicity, confirm proximal renal tubulopathy with no other cause.

\(^{*}\) Replace TDF by non-tenofovir drug or TAF alternative drug.
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

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frailty Phenotype</th>
<th>Frailty Index</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical definition</strong></td>
<td>Based on presence of signs, symptoms (pre-disability syndrome)</td>
<td>Based on presence of diseases, disabilities (accumulation of deficits)</td>
</tr>
<tr>
<td><strong>How to assess</strong></td>
<td>Assessed by five specific features [22]:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1. self-reported weight loss (a)</td>
<td>A frailty index is calculated based on the number of health deficits out of &gt; 30 assessed health deficits [23]</td>
</tr>
<tr>
<td></td>
<td>2. self-reported exhaustion (b)</td>
<td>Health variables, including signs and symptoms of disease, laboratory measures, and self-reported data</td>
</tr>
<tr>
<td></td>
<td>3. low levels of physical activity as measured by Minnesota Leisure physical activity questionnaire (c)</td>
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<td>5. measured grip strength (e)</td>
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</tr>
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<td><strong>How to interpret</strong></td>
<td>Categorical variables</td>
<td>Continuous variables</td>
</tr>
<tr>
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<td>Total score of 5 items:</td>
<td>Index ranges from 0 to 1:</td>
</tr>
<tr>
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<td>0 deficits = fit</td>
<td>&gt; 0.25 = fit</td>
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<tr>
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<td>0.25 - 0.4 = frail</td>
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<tr>
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</tr>
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<td><strong>How to address frailty</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>Recommendations</strong></td>
<td>In PLWH who are frail:</td>
<td></td>
</tr>
<tr>
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<td>1. Sustain and recover physical function impairment and sarcopenia prescribing physical activity with a resistance training component</td>
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<td></td>
<td>5. Prescribe vitamin D for individuals deficient in vitamin D, see page 62</td>
<td></td>
</tr>
</tbody>
</table>
### Frailty and Ageing

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frailty Phenotype</th>
<th>Frailty Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical definition</td>
<td>Based on presence of signs, symptoms (pre-disability syndrome)</td>
<td>Based on presence of diseases, disabilities (accumulation of deficits)</td>
</tr>
<tr>
<td>How to assess</td>
<td>Assessed by five specific features [22]:</td>
<td>A frailty index is calculated based on the number of health deficits out of &gt;30 evaluated health deficits:</td>
</tr>
<tr>
<td></td>
<td>1. self-reported weight loss (a)</td>
<td></td>
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<td></td>
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<td></td>
<td>4 deficiencies</td>
<td>&gt; 0.25 = fit</td>
</tr>
<tr>
<td></td>
<td>5 deficiencies</td>
<td></td>
</tr>
<tr>
<td>How to address frailty [24]</td>
<td>Prior to being frail that identifies medical, psychosocial, and functional limitations aimed at maximising overall health with ageing and the improvement of quality of life</td>
<td></td>
</tr>
<tr>
<td>Recommendations [25], [26]</td>
<td>In PLWH who are frail:</td>
<td></td>
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</tr>
</tbody>
</table>

---

**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)
New section – Frailty and Ageing

### Frailty Phenotype

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</thead>
<tbody>
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</tr>
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<td>A frailty index is calculated based on the number of health deficits out of &gt; 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</td>
</tr>
<tr>
<td>How to interpret</td>
<td>Categorical variables Total score of 5 items: 0 deficits = fit 1-2 deficits = pre-frail 3+ deficits = frail</td>
<td>Continuous variables Index ranges from 0 to 1: &gt; 0.25 = fit 0.25 - 0.4 = frail &gt; 0.4 = most frail</td>
</tr>
</tbody>
</table>

### Frailty Index

- **AIDS Clinical Society**
  - Women: BMI ≤ 23 and strength < 17 kg; BMI 23.1–26 and strength < 17.3 kg; BMI 26.1–29 and strength < 18 kg; BMI > 29 and strength < 21 kg
  - Men: BMI ≤ 24 kg and strength < 29 kg; BMI 24.1–26 and strength < 30 kg; BMI 26.1–28 and strength < 30 kg; BMI > 28 and strength < 32 kg

- **European Society for Clinical Investigation**
  - Women: height ≤ 159 cm and speed ≤ 0.6531 m/s; height > 159 cm and speed ≤ 0.762 m/s
  - Men: height ≤ 173 cm and speed ≤ 0.6531 m/s; height > 173 cm and speed ≤ 0.762 m/s

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

**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
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 acute 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, osteoarthritis 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, antidiabetic 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, naltrexone/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 therapeutic drug monitoring and drug dose adjustment post-bariatric surgery
Surgery can be considered for localised lipomas and dorsocervical fat accumulation for cosmetic purposes only
What about obesity?

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**Consequences:**
- Not only cosmetic concern
- Worse outcomes with surgery and acute infections (e.g. pneumonia, influenza)
- Increased risk of diabetes mellitus, hypertension, cardiovascular disease, some cancers, obstructive sleep apnea, cholelithiasis, erectile dysfunction, non-alcoholic fatty liver disease, osteoarthritis, 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, antidiabetic drugs)
- Endocrine disorders (e.g. GH deficiency, hypothyroidism, Cushing's syndrome, hypogonadism)

**Assessment:**
- Weight, waist circumference, 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

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Surgery can be considered for localised lipomas and dorsocervical fat accumulation for cosmetic purposes only.

- **Rapidly evolving field**
- **Will continue to update**
- **No ART-specific recommendations**
### What about obesity?

#### Obesity

<table>
<thead>
<tr>
<th>Skin</th>
<th>Digestive</th>
<th>Liver</th>
<th>CV</th>
<th>Musculo-skeletal</th>
<th>Genito-urinary</th>
<th>Nervous</th>
<th>Body fat</th>
<th>Metabolic</th>
<th>Other</th>
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<tbody>
<tr>
<td><strong>NRTIs</strong></td>
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<tr>
<td>TAF&lt;sup&gt;(ii)&lt;/sup&gt;</td>
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<td><strong>Weight increase</strong></td>
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<td><strong>INSTI</strong></td>
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<tr>
<td>RAL</td>
<td>Nausea</td>
<td>Myopathy, Rhabdomyolysis</td>
<td>Sleep disturbance, Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systemic hypersensitivity syndrome&lt;sup&gt;(viii)&lt;/sup&gt;</td>
<td>Weight increase</td>
</tr>
<tr>
<td>DTG</td>
<td>Rash</td>
<td>Nausea</td>
<td>↓ eGFR&lt;sup&gt;(iv)&lt;/sup&gt;</td>
<td>Sleep disturbance, Headache</td>
<td></td>
<td></td>
<td></td>
<td>Systemic hypersensitivity syndrome (&lt; 1%)</td>
<td>Weight increase</td>
</tr>
<tr>
<td>EVG/c</td>
<td>Nausea, Diarrhoea</td>
<td>↓ eGFR&lt;sup&gt;(iv)&lt;/sup&gt;</td>
<td>Sleep disturbance, Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weight increase</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td></td>
<td>↓ eGFR&lt;sup&gt;(iv)&lt;/sup&gt;</td>
<td>Sleep disturbance, Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weight increase</td>
<td></td>
</tr>
</tbody>
</table>

Notes:

- Hepatitis
- Steatosis
- Cholelithiasis
- Jaundice, ↓ BMD, ↓ eGFR, ↓ plasma lipid profile
- Diarrhoea, Nausea, Vomiting
- Nervous disturbance...
- Headache, Disturbance, Sleep disturbance, Depression, ↑ anxiety, ↑ ideation, Suicidal
disturbance, ↑ sleep
- Anaemia, ↓ vitamin D
- Myopathy, Rhabdomyolysis
- Weight increase
- Myopathy, Rhabdomyolysis
- Hair loss
- Rash
- Diarrhoea
- Nausea
- Anaemia, ↓ vitamin D

Blood tests is often done every 3-6 months during ART. Most laboratory tests are completed within 6 months after therapy commencement.
Acknowledgements

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Vice chair: Alan Winston
Young Scientist: Aoife Cotter

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Hanover, Germany
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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

Research Support: Gilead
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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 recommendations
  - 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.
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:

<table>
<thead>
<tr>
<th>Preferred DAA HCV treatment options (except for persons pre-treated with Protease or NNRTI inhibitors)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV GT</strong></td>
</tr>
<tr>
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<tr>
<td>1 &amp; 4</td>
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<td>5 &amp; 6</td>
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<table>
<thead>
<tr>
<th>Treatment options if preferred not available</th>
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<td><strong>HCV GT</strong></td>
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<tr>
<td>5 &amp; 6</td>
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</tbody>
</table>
HCV/HIV Co-infection

- Figure on management of recently acquired HCV infection:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV-RNA &lt; 2 log reduction at 4 weeks</td>
<td>Considered as early chronic HCV infection</td>
</tr>
</tbody>
</table>
| HCV-RNA < $2^{10}$ reduction in VL | a) Treat with short duration DAAs  
b) Enrol in clinical trial for acute HCV treatment |
| HCV-RNA > $2^{10}$ reduction in VL | Treat as naive non-cirrhotic |
| HCV RNA-negative | Repeat HCV-RNA at 24 weeks and 48 weeks to confirm spontaneous clearance |
| HCV RNA-positive | Repeat HCV-RNA at 4 weeks and early treatment of concomitant STI, see page 81 |

European AIDS Treatment Network (NEAT) consensus conference statement June 2019 (www.neat-id.org)
HDV and HEV in PLWH

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

Viral Hepatitis Co-infections

Chair: Andri Rauch
Vice-Chair: Sanjay Bhagani
Young scientist:
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Juan Berenguer
Christoph Boesecke
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London, United Kingdom
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Lisbon, Portugal
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Lene Ryom
Co-morbidity panel
Part VI Opportunistic Infections

Ole Kirk for the Opportunistic Infection EACS guidelines panel
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Employee: Never
Stock/Shareholder: Never
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

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

<table>
<thead>
<tr>
<th>CD4 count</th>
<th>Initiation of ART</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>As soon as possible and within 2 weeks after starting treatment for the opportunistic infection</td>
<td></td>
</tr>
</tbody>
</table>
| **Tuberculosis** | - < 50 cells/μL: As soon as possible and within 2 weeks after starting TB treatment  
                  | - > 50 cells/μL: 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

<table>
<thead>
<tr>
<th>Paradoxical IRIS</th>
<th>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]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmasking IRIS</td>
<td>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]</td>
</tr>
</tbody>
</table>

### 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, 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

<table>
<thead>
<tr>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>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</td>
<td></td>
</tr>
<tr>
<td>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</td>
<td></td>
</tr>
</tbody>
</table>

| **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] |
|-------------|---------------------------------------------------------------------------------------------------------------------------------

<table>
<thead>
<tr>
<th><strong>Life-threatening CNS-IRIS:</strong></th>
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<tbody>
<tr>
<td><strong>TB-meningitis</strong></td>
<td>Oral prednisone (1.5 mg/kg/day for 2 weeks, then tapering) [4]</td>
</tr>
<tr>
<td><strong>PML</strong></td>
<td>iv methylprednisolone (1 g/day for 3-5 days or iv dexamethasone 0.3 mg/kg/day for 3-5 days), then oral tapering</td>
</tr>
</tbody>
</table>
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* galactomannan assays may be helpful to diagnose disseminated infections as cross reactivity occurs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe disseminated talaromycosis</td>
<td>Induction therapy: liposomal amphotericin B, consolidation therapy: itraconazole</td>
<td>3 mg/kg qd iv For 2 weeks or until clinical improvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200 mg tid po for 3 days, then 200 mg bid po</td>
</tr>
<tr>
<td>Moderate talaromycosis</td>
<td>itraconazole</td>
<td>200 mg tid po for 3 days, then 200 mg bid po</td>
</tr>
</tbody>
</table>

**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

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EACS European AIDS Clinical Society
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.:**

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

## Opportunistic Infections

<table>
<thead>
<tr>
<th>Chair: Ole Kirk</th>
<th>Copenhagen, Denmark</th>
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<tr>
<td>Vice-Chair: Paola Cinque</td>
<td>Milan, Italy</td>
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<td>London, United Kingdom</td>
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<tr>
<td>Alain Volny-Anne</td>
<td>Paris, France</td>
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</tbody>
</table>

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
Disclosure information

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HIV i-Base receives industry support for some projects, including from Gilead, Janssen, MSD and Gilead.
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).
Acknowledgements

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.