To support simplification of HIV treatment, WHO recommends a limited formulary of preferred treatment options. As well as giving priority to antiretroviral drugs (ARVs) with superior efficacy and tolerability, WHO prioritizes choices based on:

- convenience,
- availability as fixed dose combinations (FDCs),
- compatibility with treatment of common co-morbidities, and
- potential to use across all populations.

**First-line regimens**

- **In 2015 WHO maintains the 2013 recommendation of TDF + 3TC (or FTC) + EFV at standard doses (600 mg/day) as the preferred first-line regimen for treatment initiation in antiretroviral therapy (ART)-naïve adults and adolescents.** This approach has clinical, operational and programmatic benefits when compared with other NNRTI- and PI-based options.

- **Dolutegravir (DTG) and EFV at lower dose (400 mg/day) are included as new alternative options in first-line regimens,** along with LPV/r and ATV/r.

- **AZT and NVP are maintained as alternative drug options** as DTG and EFV 400mg/day are not likely to be available until beyond 2016 (see Table 1).

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**Table 1.**

<table>
<thead>
<tr>
<th>WHAT TO USE IN FIRST-LINE THERAPY IN ADULTS</th>
<th>ARV REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred Option</td>
<td>TDF+XTC(^3)+EFV(^600)</td>
</tr>
<tr>
<td>Alternative Options</td>
<td>AZT+3TC+EFV(^600)</td>
</tr>
<tr>
<td></td>
<td>AZT+3TC+NVP</td>
</tr>
<tr>
<td></td>
<td>TDF+XTC(^3)+NVP</td>
</tr>
<tr>
<td></td>
<td>TDF+XTC(^3)+DTG(^4)</td>
</tr>
<tr>
<td></td>
<td>TDF+XTC(^3)+EFV(^600)</td>
</tr>
</tbody>
</table>

1 FDCs are the preferred approach
2 Countries should discontinue d4T use in first-line regimens due to well-recognized metabolic toxicities.
3 XTC=3TC or FTC
4 Safety data for pregnant women and people living with HIV and active TB pending.
**Second-line regimens**

- WHO guidelines place value on the use of **simple second-line regimens** that should include the combination of **2 NRTIs + a heat stable boosted protease inhibitor**. In 2015, WHO maintains **LPV/r and ATV/r** heat stable co-formulations as the preferred PI options for second line therapy, and recommends **DRV/r as an alternative option**.

- A systematic review and network meta-analysis found equivalence between **DRV/r, ATV/r and LPV/r** containing regimens in patients failing on NNRTI containing regimens. Once daily **DRV/r (800/100 mg OD)** is comparable to twice daily **DRV/r (600/100 mg BD)** in second-line regimens and the use of one NRTI sparing regimen (RAL + LPV/r) is equivalent to standard **2 NRTI + ATV/r or LPV/r** regimens. The use of **DRV/r** as a boosted PI option and NRTI-sparing regimens such as **RAL + LPV/r** will, in the short term, increase the cost of second-line ART and these options have not demonstrated better performance when compared with current standard of care (i.e. **2 NRTI + ATV/r or LPV/r**). Heat-stable co-formulations of **DRV/r** are expected to be available in 2017 and the price is anticipated to fall through generic competition. For these reasons, these options are recommended as alternative choices for second-line ART (see Table 2).

**Ongoing research and research gaps**

- Ongoing studies comparing drugs and ARV classes will provide more data on appropriate second-line regimens, including NRTI-sparing and NRTI-limiting approaches.

- Several trials are in progress examining induction and maintenance strategies using PI/r mono-therapy or in combination with 3TC as maintenance therapy. The potential of rifabutin as part of FDCs for TB treatment needs to be explored.

- Simplified sequencing strategies for PI options in second- and third-line ART.

- The role of **DRV/r** in second- and third-line regimens, including optimal dosing in adults and children, co-formulations with other boosting agents and integrase inhibitors, and sequencing strategies.

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**Table 2.**

<table>
<thead>
<tr>
<th>WHAT TO USE IN SECOND-LINE THERAPY IN ADULTS</th>
<th>ARV REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred Option</td>
<td><strong>2 NRTI + ATV/r or LPV/r</strong></td>
</tr>
<tr>
<td>Alternative Options</td>
<td><strong>2 NRTI + DRV/r</strong>, <strong>LPV/r + RAL</strong></td>
</tr>
</tbody>
</table>

1 The following sequence of 2nd line NRTI backbone options is recommended:

- If failure with TDF+XTC in 1st line, use AZT+3TC
- If failure with AZT+3TC in 1st line, use TDF+XTC
- Use of NRTI backbones as FDCs is recommended as the preferred approach.

2 Heat stable FDCs of boosted PIs are the preferred approach.

3 DRV/r as FDC tablet (400/50mg) expected to be available in 2017.