FACT SHEET

HIV TREATMENT AND CARE

WHAT'S NEW IN HIV TREATMENT

NOVEMBER 2015

World Health Organization

WHO recommends initiation of ART for all people living with HIV at any CD4 cell count

Fixed dose combinations (FDCs) containing TDF/XTC/EFV remain the preferred first line regimen for adults, adolescents and older children

For the first time, DTG and EFV400 have been included as alternative first line regimens for adults and adolescents.

DRV/r is an alternative option as part of second-line regimens, along with LPV/r and ATV/r.

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.** DTG is associated with fewer drug interactions, higher virological efficacy, lower treatment discontinuation rates and a higher genetic resistance barrier when compared with other ARVs. EFV 400 mg has comparable efficacy compared to EFV 600 mg, is associated with lower toxicity, and has the potential to reduce costs and pill size. These two options are not recommended as preferred options due to limited use outside of clinical trials and the unknown safety and efficacy of DTG and EFV 400mg/day during pregnancy and for people living with HIV and tuberculosis (TB) using rifampicin. Single generic formulations and FDCs containing these options are expected to be available in 2017.

- **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).

Table 1.

WHAT TO USE IN FIRST-LINE THERAPY IN ADULTS	ARV REGIMEN[1,2]
Preferred Option	TDF+XTC[3]+EFV_{600}
Alternative Options	AZT+3TC+EFV_{600} AZT+3TC+NVP TDF+XTC[3]+NVP TDF+XTC[3]+DTG[4] NEW TDF+XTC3+EFV_{400}[4] NEW

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.

Photo: WHO/Christopher Black

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).

Table 2.

WHAT TO USE IN SECOND-LINE THERAPY IN ADULTS	ARV REGIMEN
Preferred Option	2 NRTI[1]+ATV/r or LPV/r[2]
Alternative Options	2 NRTI[1]+DRV/r[2,3] NEW LPV/r[2]+RAL NEW

1 The following sequence of 2nd line NRTI bacbone 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.

Ongoing research and reseach 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 monotherapy 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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