

2009 Recommendations for Antiretroviral Therapy in Adults and Adolescents

Summary of WHO Rapid Advice

Guiding principles

1. Do no harm

When introducing changes preserve access for the sickest and most in need

2. Ensure access and equity

All clinically eligible people should be able to enter treatment services (including ART) with fair and equitable distribution of treatment services

3. Promote quality and efficiency

Ensure delivery of the highest standards of care within a public health approach so as to achieve the greatest health impact with the optimal use of available human and financial resources

4. Be sustainable

Understand the long-term consequences of change with the vision of providing continued, life-long access to ART for those in need

When to start

- ▶ Start antiretroviral treatment in all patients with HIV who have CD4 count ≤ 350 cells/mm³ irrespective of clinical symptoms
(Strong recommendation, moderate quality of evidence)
- ▶ CD4 testing is required to identify if patients with HIV and WHO clinical stage 1 or 2 disease need to start antiretroviral treatment
(Strong recommendation, low quality of evidence)
- ▶ Start antiretroviral treatment in all patients with HIV and WHO clinical stage 3 or 4 irrespective of CD4 count
(Strong recommendation, low quality of evidence)

The panel placed high value on avoiding death, disease progression and likely HIV transmission over and above cost and feasibility

What to start

- ▶ Start one of the following regimens in ART-naïve individuals eligible for treatment
 - ▶ AZT + 3TC + EFV
 - ▶ AZT + 3TC + NVP
 - ▶ TDF + 3TC or FTC + EFV
 - ▶ TDF + 3TC or FTC + NVP

(Strong recommendation, moderate quality of evidence)

The panel placed high value on avoiding d4T toxicity, the need to select regimens that are suitable for use in most patient groups and the benefits of using fixed dose combinations

Current evidence suggests that these regimens are comparable in terms of efficacy

ART for HIV/tuberculosis co-infection

- ▶ Start ART in all HIV-infected individuals with active tuberculosis (TB) irrespective of CD4 cell count
(Strong recommendation, low quality of evidence)
- ▶ Start TB treatment first, followed by ART as soon as possible after starting TB treatment
(Strong recommendation, moderate quality of evidence)
- ▶ Use efavirenz (EFV) as the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI) in patients starting ART while on TB treatment
(Strong recommendation, high quality of evidence)

The panel placed high value on reduction of early mortality from HIV/TB co-infection and reduction of TB transmission when ART is initiated earlier and improved management of TB

ART for HIV/HBV co-infection

- ▶ Start ART in all HIV/HBV co-infected individuals who require treatment for their HBV infection, irrespective of CD4 cell count or WHO clinical stage

(Strong recommendation, low quality of evidence)

- ▶ Start TDF and 3TC or FTC containing antiretroviral regimens in all HIV/HBV co-infected individuals needing treatment

(Strong recommendation, moderate quality of evidence)

The panel placed high value on promoting HBV diagnosis and more effective treatment of HIV/HBV co-infection

ART for pregnant women

- ▶ Start ART in all pregnant women with HIV and CD4 count ≤ 350 cells/mm³, irrespective of clinical symptoms
(Strong recommendation, moderate quality of evidence)
- ▶ CD4 testing is required to identify if pregnant women with HIV and WHO clinical stage I or 2 disease need to start antiretroviral treatment or prophylaxis.
(Strong recommendation, low quality of evidence)
- ▶ Start ART in all pregnant women with HIV and WHO clinical stage 3 or 4, irrespective of CD4 count
(Strong recommendation, low quality of evidence)
- ▶ Start one the following regimens in ART-naïve pregnant women eligible for treatment:
 - ▶ AZT + 3TC + EFV
 - ▶ AZT + 3TC + NVP
 - ▶ TDF + 3TC/FTC+ EFV
 - ▶ TDF + 3TC/FTC + NVP**(Strong recommendation, moderate quality of evidence)**
- ▶ Do not start EFV during the first-trimester of pregnancy
(Strong recommendation, low quality of evidence)

The ART and PMCT panels placed high value on ensuring treatment is started early for pregnant women to avoid mother-to-child transmission and improve maternal and child-health outcomes, over and above concerns for the cost or feasibility

When to Switch ART

- ▶ Where available use viral load (VL) to confirm treatment failure
(Strong recommendation, low quality of evidence)
- ▶ Where routinely available use VL every 6 months to detect viral replication
(Conditional recommendation, low quality of evidence)
- ▶ A persistent viral load above 5,000 copies/ml confirms treatment failure
(Conditional recommendation, low quality of evidence)
- ▶ Where VL is not available, use immunological criteria to confirm clinical failure
(Strong recommendation, moderate quality of evidence)

The panel were concerned by the limitations of clinical/immunological monitoring for diagnosing treatment failure, and placed high value on avoiding premature switching to expensive second line ART, supporting adherence and the need to optimize the use of virological monitoring and ensure adherence

Second-line ART

- ▶ A boosted protease inhibitor (PI/r) plus two nucleoside analogues (NRTIs) are recommended for second-line ART
(Strong recommendation, moderate quality of evidence)
- ▶ r-ATV/r and LPV/r are the preferred boosted PI's for second-line ART.
(Strong recommendation, moderate quality of evidence)
- ▶ Simplification of second NRTI options is recommended
 - ▶ If d4T or AZT has been used in first-line use TDF+3TC or FTC as the NRTI backbone in second-line
 - ▶ If TDF has been used in first-line use AZT + 3TC as the NRTI backbone in second-line**(Strong recommendation, moderate quality of evidence)**

The panel placed high value on using simpler second-line regimens and the availability of heat-stable, fixed-dose combinations

Third-line regimens

- ▶ National programs should develop policies for third-line therapy that consider funding, sustainability and the provision of equitable access to ART.

(Conditional recommendation, low quality of evidence)

- ▶ Third line regimens should include new drugs likely to have anti HIV activity such as integrase inhibitors and second generation NNRTIs and PIs.

(Conditional recommendation, low quality of evidence)

- ▶ Patients on a failing second-line regimen with no new ARV options, should continue with a tolerated regimen.

(Conditional recommendation, very low quality of evidence)

The panel was concerned by the reports of high mortality for patients failing second-line therapy, but placed high value on balancing the need to develop policies for third-line therapy while maintaining increased access to first-line therapy. It was recognised that most countries have financial constraints that might limit the adoption of third-line regimens