IAS-USA HIV Treatment Guidelines: 2020 Update

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Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2020 Recommendations of the International Antiviral Society–USA Panel

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IMPORTANCE Data on the use of antiretroviral drugs, including new drugs and formulations, for the treatment and prevention of HIV infection continue to guide optimal practices.

OBJECTIVE To evaluate new data and incorporate them into current recommendations for initiating HIV therapy, monitoring individuals starting on therapy, changing regimens, preventing HIV infection for those at risk, and special considerations for older people with HIV.

EVIDENCE REVIEW New evidence was collected since the previous International Antiviral (formerly AIDS) Society–USA recommendations in 2018, including data published or presented at peer-reviewed scientific conferences through August 22, 2020. A volunteer panel of 15 experts in HIV research and patient care considered these data and updated previous recommendations.

FINDINGS From 5316 citations about antiretroviral drugs identified, 549 were included to form the evidence basis for these recommendations. Antiretroviral therapy is recommended as soon as possible for all individuals with HIV who have detectable viremia. Most patients can start with a 3-drug regimen or now a 2-drug regimen, which includes an integrase strand transfer inhibitor. Effective options are available for patients who may be pregnant, those who have specific clinical conditions, such as kidney, liver, or cardiovascular disease, those who have opportunistic diseases, or those who have health care access issues. Recommended for the first time, a long-acting antiretroviral regimen injected once every 4 weeks for treatment or every 8 weeks pending approval by regulatory bodies and availability. For individuals at risk for HIV, preexposure prophylaxis with an oral regimen is recommended or, pending approval by regulatory bodies and availability, with a long-acting injection given every 8 weeks. Monitoring before and during therapy for effectiveness and safety is recommended. Switching therapy for virological failure is relatively rare at this time, and the recommendations for switching therapies for convenience and for other reasons are included. With the survival benefits provided by therapy, recommendations are made for older individuals with HIV. The current coronavirus disease 2019 pandemic poses particular challenges for HIV research, care, and efforts to end the HIV epidemic.

CONCLUSION AND RELEVANCE Advances in HIV prevention and management with antiretroviral drugs continue to improve clinical care and outcomes among individuals at risk for and with HIV.

Supplemental content

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Evidence Rating

Table 1. Strength of Recommendation and Quality of Evidence Rating Scale[a]

Evidence rating	Definition
Strength of recommendation	
A	Strong panel support
B	Moderate panel support
C	Limited or weak panel support
Quality of evidence	
Ia	Evidence from ≥1 RCTs published in the peer-reviewed literature
Ib	Evidence from ≥1 RCTs presented in abstract form at peer-reviewed scientific meetings
IIa	Evidence from cohort or case-control studies published in the peer-reviewed literature
IIb	Evidence from cohort or case-control studies presented in abstract form at peer-reviewed scientific meetings
III	Based on the panel's analysis of the available evidence

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When to Initiate ART?

As soon as possible after HIV diagnosis, including immediately after diagnosis if the patient is ready to commit to treatment (AIa)

Immediate ART recommended for individuals with acute HIV (AIIa)

Within 2 weeks for most opportunistic infections (AIa); exceptions:

- Cryptococcal meningitis: 4-6 weeks after starting antifungal therapy (BIa)
- TB with CD4 $\geq$50 cells/mm^3: 2-8 weeks after starting TB therapy (AIa)

Immediately after new diagnosis of cancer (BIIa)

"Implementation of immediate ART alone may not improve long-term care retention or durable viral suppression...robust, culturally sensitive care engagement strategies are required, including attention to essential needs such as housing and food."

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Recommended Initial ART Regimens

Recommended for most individuals with HIV:

- Bictegravir/TAF/FTC (AIa)
- Dolutegravir plus TAF/FTC, TDF/FTC, or TDF/3TC (all AIa)
- Dolutegravir/3TC (AIa)*

  *Not recommended for rapid start (because genotype result should be available) or in setting of chronic HBV, active OI treatment, HIV RNA >500,000 copies/mL, perhaps CD4 count <200 cells/mm^3

With rifamycin-based TB treatment:

- Dolutegravir 50 mg BID or raltegravir 800 mg BID or efavirenz 600 mg QD plus 2 NRTI's (AIa); TAF with rifampin may be ok but data limited

Recommended during pregnancy:

- Atazanavir + rtv (AIIa), darunavir + rtv (AIIa), dolutegravir (AIb), efavirenz (BIa), raltegravir (AIIa), or rilpivirine (BIIa), plus TDF/FTC or TDF/3TC
- Dolutegravir plus TAF/FTC (AIb)

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Language on TAF vs TDF

- TAF and TDF have similar virologic efficacy
- TAF: fewer adverse effects, such as proximal renal tubular toxicity and reductions in bone mineral density; however, differences most pronounced when TDF used with booster
- TDF reduces plasma lipid levels and TAF associated with more weight gain; however, clinical significance unknown
- Cost of TDF-containing regimens is likely to decrease as generic formulations become available

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Language on Weight Gain with ART

- Initiation of ART often leads to weight gain; can lead to obesity among individuals with HIV who start treatment with a normal or greater baseline weight
- Risk factors for excess weight gain: low pre-treatment CD4, high viral load, Black race, female sex, DTG and BIC more than EFV, TAF more than TDF (TDF may inhibit weight gain)
- *Clinical consequences and mechanisms unknown and data insufficient to change recommendations for initial ART; PWH should be counseled about potential for weight gain*

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Switching or Simplifying ART

General recommendations:

- Review ART history, tolerability, co-medications, food requirements, cost, and results from prior resistance tests before any switch (AIa)
- Recheck HIV RNA level 1 month after any switch (BIII)

Switching when HIV RNA level suppressed:

- With HBV co-infection: include TAF or TDF; if contraindicated, include other HBV suppressive therapy (AIIa)
- Avoid switch from boosted PI to NNRTI or raltegravir-based ART if NRTI resistance mutations present (AIa)
- Switch to 2-drug oral maintenance appropriate to manage toxic effects, intolerance, adherence, or patient preference, provided both drugs are fully active
  - Options: dolutegravir/rilpivirine (AIa), dolutegravir/lamivudine (AIa), or long-acting IM cabotegravir + rilpivirine q4 weeks (AIa) or 8 weeks (BIb)

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Switching ART After Virologic Failure

Resistance testing recommended while taking failing ART regimen (AIa) or within 4 weeks of stopping (AIIa)
Virologic failure, defined as HIV RNA level above 200 copies/mL, should be confirmed and if resistance identified, ART should be changed based on new and past resistance assay results (BIIa)
Dolutegravir plus 2 NRTI's (at least one active) recommended after failure of an NNRTI plus 2 NRTI's (AIa)
Bictegravir/FTC/TAF or dolutegravir plus FTC/TAF or ABC/3TC may be effective in patients with an isolated M184V/I NRTI mutation (AIa)
In setting of multiclass resistance (3-class), next regimen should use agents from new classes if available, such as fostemsavir (AIb) or ibalizumab (BII), with ≥1 additional active drug in an optimized regimen

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Switching in the Setting of Comorbidities

- Cardiovascular (CV) disease:
  If moderate to high risk for a CV event or if already experienced a CV event, switch off abacavir or PI (except atazanavir) recommended (AIIa)

- TAF or INSTI-associated weight gain:
  "It is unknown whether ART-induced weight gain translates into significant metabolic and cardiovascular adverse outcomes, or whether the INSTI-induced and TAF–induced weight gain is reversible after switching regimens."

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Baseline Laboratory Testing

- If new HIV diagnosis and CD4 count <100 cells/mm^3:
  Check serum cryptococcal antigen even if no symptoms (AIIa); positive result may facilitate preemptive treatment of disseminated cryptococcal disease before the development of cryptococcal meningitis
- Baseline genotype resistance testing:
  Baseline RT and PR genotype recommended (AIIa); given the low prevalence of transmitted INSTI resistance, INSTI genotype not recommended unless there is suspicion that HIV was transmitted from a partner with INSTI failure (BIII)

Low-Level Viremia

- Patients with intermittent or persistent low-level viremia between 50 copies/mL and 200 copies/mL should be assessed for treatment adherence, tolerability, and toxicity; however, changing ART regimens is not recommended unless ART toxicity or intolerability are identified (BIII)

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