

# 2022 IAS-USA HIV Treatment and Prevention Guidelines

Brian R. Wood, MD  
Associate Editor, National HIV Curriculum  
Associate Professor of Medicine,  
Division of Allergy and Infectious Diseases  
University of Washington

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# Disclosures

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## Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults

### 2022 Recommendations of the International Antiviral Society-USA Panel

Rajesh T. Gandhi, MD; Roger Bedimo, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Davey M. Smith, MD; Ellen F. Eaton, MD; Clara Lehmann, MD; Sandra A. Springer, MD; Paul E. Sax, MD; Melanie A. Thompson, MD; Constance A. Benson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Michael S. Saag, MD

**IMPORTANCE** Recent advances in treatment and prevention of HIV warrant updated recommendations to guide optimal practice.

**OBJECTIVE** Based on a critical evaluation of new data, to provide clinicians with recommendations on use of antiretroviral drugs for the treatment and prevention of HIV, laboratory monitoring, care of people aging with HIV, substance use disorder and HIV, and new challenges in people with HIV, including COVID-19 and monkeypox virus infection.

**EVIDENCE REVIEW** A panel of volunteer expert physician scientists were appointed to update the 2020 consensus recommendations. Relevant evidence in the literature (PubMed and Embase searches, which initially yielded 7891 unique citations, of which 834 were considered relevant) and studies presented at peer-reviewed scientific conferences between January 2020 and October 2022 were considered.

**FINDINGS** Initiation of antiretroviral therapy (ART) is recommended as soon as possible after diagnosis of HIV. Barriers to care should be addressed, including ensuring access to ART and adherence support. Integrase strand transfer inhibitor-containing regimens remain the mainstay of initial therapy. For people who have achieved viral suppression with a daily oral regimen, long-acting injectable therapy with cabotegravir plus rilpivirine given as infrequently as every 2 months is now an option. Weight gain and metabolic complications have been linked to certain antiretroviral medications; novel strategies to ameliorate these complications are needed. Management of comorbidities throughout the life span is increasingly important, because people with HIV are living longer and confronting the health challenges of aging. In addition, management of substance use disorder in people with HIV requires an evidence-based, integrated approach. Options for preexposure prophylaxis include oral medications (tenofovir disoproxil fumarate or tenofovir alafenamide plus emtricitabine) and, for the first time, a long-acting injectable agent, cabotegravir. Recent global health emergencies, like the SARS-CoV-2 pandemic and monkeypox virus outbreak, continue to have a major effect on people with HIV and the delivery of services. To address these and other challenges, an equity-based approach is essential.

**CONCLUSIONS AND RELEVANCE** Advances in treatment and prevention of HIV continue to improve outcomes, but challenges and opportunities remain.

 Multimedia Supplemental content

# Recommendations for Timing of ART Initiation

- As soon as possible after diagnosis, ideally within 7 days
  - Includes same day as diagnosis or first visit, if no suspicion for an OI (AIII)
- At time of diagnosis of acute HIV (AIIa)
- If diagnosed during pregnancy, begin ART immediately (AIIa)
- Elite controllers: theoretical benefits, so treatment “reasonable”

# Recommendations for ART Timing with an Opportunistic Infection (OI)

- Generally, start ART within 2 weeks of starting OI treatment

OI Scenario	Specific Considerations for ART Initiation Timing
TB without meningitis	Within 2 weeks after starting TB treatment, especially if CD4 <50 (A1a)
TB with meningitis	Within 2 weeks of starting TB treatment and corticosteroids (B1a)
Cryptococcal meningitis	2-4 weeks after starting antifungal treatment (B11b)
Cryptococcal antigenemia	Start ART immediately (B111)
New cancer diagnosis	Start ART immediately, with attention to drug interactions (B11a)

# Recommended Initial Regimens for Most People with HIV

## Initial Regimens (Listed in Alphabetical Order)

Bictegravir/TAF/FTC (A1a)

Dolutegravir + TXF/XTC (A1a) (TXF/XTC = TAF or TDF with FTC or 3TC)

Dolutegravir/3TC (A1a) – only if HIV RNA <500,000 copies/mL and no HBV (should not be used for rapid initiation when genotype, HIV RNA, HBV serology pending)

“Although INSTIs and [TAF] have been implicated in weight gain for some individuals and preliminary data raise concern about metabolic adverse effects with INSTIs, such concerns do not override the potential benefit...(AIII).”

# Recommended Initial Regimens After PrEP Exposure

Acquire HIV while  
receiving oral PrEP  
(TXF/XTC)



Draw blood for genotype; ok  
to start DTG or BIC +  
TXF/XTC prior to result (AIII)

Acquire HIV after  
exposure to cabotegravir



Draw blood for genotype  
(with integrase); start  
boosted PI + TXF/XTC if  
initiate ART prior to result  
(AIII)

# Recommended Regimens During Pregnancy

## Recommended ART Regimens During Pregnancy

Dolutegravir + TAF/FTC (A1a)

Dolutegravir + TDF/XTC is a suitable alternative (A1a)

If dolutegravir not an option, may replace with:

- Raltegravir 400 mg BID (A1a)
- Atazanavir plus ritonavir (B1a)
- Darunavir plus ritonavir (B1a)
- Rilpivirine (B1a)

If already taking a bictegravir or doravirine 3-drug regimen or 2-drug regimen of dolutegravir/rilpivirine or dolutegravir/3TC, ok to continue, but counsel about uncertainties and monitor HIV RNA more frequently. Avoid cobicistat-containing regimens during pregnancy (A1b).



# Other ART Regimens and Considerations

Regimen	Potential Uses and Cautions
Darunavir/cobicistat/TAF/FTC	Preferred if prior CAB PrEP exposure but INSTI genotype not available
Boosted darunavir + TXF/XTC	Potential use for known or suspected multidrug resistance or INSTI resistance or if high risk of poor adherence
Doravirine/TDF/3TC or doravirine + TXF/XTC	May be useful for persons who do not tolerate INSTIs
Rilpivirine/TAF/FTC	Small pill size, but only use if current HIV RNA <100,000 and CD4 >200 cells/mm <sup>3</sup> (and no PPI and can adhere to meal requirement)
Raltegravir + TXF/XTC	Potential use for HIV-TB coinfection or if pregnancy, pregnancy intention, or high risk of drug interactions

# Switching ART Regimens

- Guidelines emphasize efficacy of bictegravir/TAF/FTC or dolutegravir + TXF/XTC in setting of NRTI resistance (M184V +/- K65R) if viral suppression
- Switching to long-acting, injectable cabotegravir/rilpivirine:
  - Not recommended in setting of viremia outside of research setting
  - Administered by clinic staff, so requires more resources (and visits) than oral ART
  - With on-time injections, still small risk of treatment failure and resistance (1-2%)
  - Collect proviral genotype before switching if don't have pre-ART genotype results

# Virologic Failure

Virologic Failure Scenario	Recommended ART Options
At least one active NRTI	<ul style="list-style-type: none"> <li>• Dolutegravir + TXF/XTC</li> <li>• Bictegravir/TAF/FTC</li> </ul>
No active NRTI	<ul style="list-style-type: none"> <li>• Boosted darunavir + TXF/XTC</li> <li>• Boosted darunavir + dolutegravir +/- additional agents</li> <li>• Alternative: dolutegravir + TXF/XTC (4% risk of emergent dolutegravir resistance)</li> </ul>
Low-level INSTI resistance	<ul style="list-style-type: none"> <li>• Dolutegravir BID + 1 or preferably 2 active drugs from classes not previously used (fostemsavir, lenacapavir, maraviroc if R5-tropic, ibalizumab, enfuvirtide) +/- recycled NRTIs</li> </ul>
High-level INSTI resistance + PI resistance	<ul style="list-style-type: none"> <li>• At least 2 fully active agents + recycled NRTIs</li> </ul>

# Laboratory Monitoring

Lab	At HIV diagnosis/ Start of ART	During ART	At virologic failure
HIV RNA	Yes	Within 6 weeks of starting; once suppressed: every 3 months for 1 year then every 6 months	Yes
CD4	Yes	Every 6 months until >250 cells/mm <sup>3</sup> for 1 year, then stop	Yes
RT genotype	Yes	N/A	Yes
INSTI genotype	If partner known to have failing ART regimen that includes an INSTI, or patient received CAB for PrEP	N/A	If failing ART regimen includes an INSTI
Cryptococcal antigen test	If CD4 <100 cells/mm <sup>3</sup>	N/A	N/A

Source: Gandhi RT, et al. JAMA. 2023;329:63-84.

# Weight Gain and Metabolic Complications

- Weight gain generally occurs within first year following start of any ART
- Greater weight gain associated with INSTI or TAF vs. EFV, PI, TDF
- Can occur with switch to INSTI +/- TAF
- More likely for individuals born female and Black or Hispanic individuals
- Use of EFV or TDF associated with weight suppression
- INSTIs may be associated with incident CVD, DM, hyperglycemia, HTN, MASLD; more data on long-term complications & management needed

# Weight Gain and Metabolic Complications

1) Counsel about possible weight gain and cardiometabolic complications when initiating or switching ART (AIII)

2) Document weight and BMI at baseline and every 6 months (AIIa)

3) Yearly diabetes screen and CVD risk score if receiving INSTI (BIII)

4) Lifestyle changes if gain greater than 5% body weight change (AIII)

5) Until there are data proving benefit, switching ART because of weight gain not recommended (BIIa)

# Summary

- Generally preferred to start ART as soon as possible
- Most PWH should start bictegravir or dolutegravir-based ART
- If at least one NRTI remains active, bictegravir or dolutegravir-based options generally remain effective, especially if the viral load suppressed
- With multiclass drug resistance and no NRTI options, need salvage ARV options to create an effective regimen
- INSTIs, especially dolutegravir and bictegravir, may lead to greater weight gain than other classes, especially if combined with TAF; the mechanisms, predictors, and optimal management require further study

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