HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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SELECTING AN INITIAL ART REGIMEN

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE AUGUST 2022 UPDATE

Note: The recommendations in this guideline pertain to initial ART regimens for adults with HIV who are *not pregnant*.

Dolutegravir (DTG) Safety Statement, August 2022

The recommendation regarding discussion of the small risk of teratogenicity with DTG in the first trimester and the need for birth control while using DTG was removed. DTG has been shown to be safe throughout pregnancy.

For more information, see *Use of Dolutegravir in Individuals of Childbearing Capacity* at hivguidelines.org

ALL RECOMMENDATIONS P.1

Regimen Selection

- When selecting an initial ART regimen for treatment naive-patients, clinicians should:
  - Perform genotypic HIV resistance testing results for protease (A2), reverse transcriptase (A2), and integrase (B2) genotypic resistance if the testing has not already been performed or results are not otherwise available.
  - Inform patients of the options and engage in shared decision-making to optimize the likelihood of adherence. (A3)
  - Assess for comorbidities and chronic co-administered medications that may affect the choice of regimen for a patient's initial ART. (A3)
  - Choose a preferred ART regimen unless one of the alternative regimens is a better choice based on individual patient factors. (A1)

Continued on P.2 ➔

ALL RECOMMENDATIONS *(continued from P.1)* P.2

Regimen Selection, cont.

  - Recommend a single-tablet regimen or a regimen with once-daily dosing unless those regimens are contraindicated by HIV resistance, drug-drug interactions, intolerance, allergy, or access. (A2)
  - Ask patients about their reproductive plans and discuss the use of contraception. (A3)
    - Refer to the DHHS guideline in choosing an initial ART regimen for a patient who is pregnant or planning a pregnancy: *Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.*
  - With the exception of DTG/3TC, clinicians should not prescribe 2-drug regimens as initial ART. (A3) Clinicians should prescribe DTG/3TC only after:
    - HIV resistance and hepatitis B virus status are known. (A1)
    - Genotypic resistance testing results have confirmed that a patient does not have a major reverse transcriptase mutation, including the M184V/I resistance mutation. DTG/3TC is contraindicated in patients with these resistance-associated mutations. (A1)

Expert Consultation

- Clinicians should consult with an experienced HIV care provider when selecting an initial ART regimen for a patient who has:
  - Baseline genotypic testing results indicating the need for an ART regimen other than the available preferred or alternative regimens. (A3)
  - Extensive comorbidities, including metabolic complications and obesity; comedications; impaired renal function; hepatitis B virus or hepatitis C virus coinfection; or active opportunistic infections. (B3)
    - The NYSDOH Clinical Education Initiative (CEI) provides access to HIV specialists through their toll-free CEI Line: 1-866-637-2342.

Follow-up

- Clinicians or clinical support staff should follow up by telephone or other methods, preferably within 2 weeks after treatment initiation, to assess tolerance and adherence; adherence should be reinforced at regular intervals. (A3)
- Clinicians should obtain a viral load test within 4 weeks after ART initiation to assess initial response to therapy. (A3)

KEY POINTS

Special Considerations

- Neither mental health nor substance use disorders are contraindications to initiating ART. In some special cases, delay of initiation (for as short a time as possible) may be appropriate while addressing adherence issues and possible interactions (see the NYSDOH AI guideline *When to Initiate ART, With Protocol for Rapid Initiation*).
- Both COBI and DTG can cause decreased tubular excretion of creatinine and may cause a slight increase in measured creatinine.
- ABC has been associated with a higher risk of myocardial infarction in some studies, although not in others. No clear causal link has been established.
- Boosted protease inhibitors and COBI-boosted EVG are associated with a higher incidence of hyperlipidemia than unboosted integrase strand transfer inhibitors.
- Consultation with an experienced HIV care provider is advised when a patient's baseline viral load is very high (HIV RNA level >750,000 copies/mL).

ART-Initiation Laboratory Testing

- When initiating ART at the time of diagnosis ("rapid start"), it is not necessary to have the results of baseline laboratory tests immediately available. Laboratory tests should be ordered at the time of initiation of ART, and any necessary adjustments to therapy should be made as soon as the results are available (such as for renal function or evidence of resistance).
- ABC-containing regimens should not be used for rapid start without a documented negative HLA-B*5701 test result.

DRUG NAME ABBREVIATION KEY: 3TC: lamivudine; **ABC**: abacavir; **ATV**: atazanavir; **BIC**: bictegravir; **COBI**: cobicistat; **DOR**: doravirine; **DRV**: darunavir; **DTG**: dolutegravir; **EFV**: efavirenz; **EVG**: elvitegravir; **FTC**: emtricitabine; **RAL**: raltegravir; **RPV**: rilpivirine; **RTV**: ritonavir; **TAF**: tenofovir alafenamide; **TDF**: tenofovir disoproxil fumarate

➔ Use this code with your phone's QR code reader to go directly to a mobile-friendly version of the guideline.

This ¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Selecting an Initial ART Regimen*. The full guideline is available at www.hivguidelines.org.

Selected Drug-Drug Interactions to Discuss Before Initiating ART in Treatment-Naive Patients

Drug Class	ARV(s): Comments
H_2-blockers	**ATV**: In treatment-naive patients on boosted ATV, H_2-blockers should be taken simultaneously with ATV/RTV with food. If simultaneous dosing with food is not possible, ATV/RTV should be taken at least 10 hours *after* the H_2-blocker. H_2-blocker doses should not exceed the equivalents of 40 mg famotidine twice daily for ART-naive patients, or 20 mg famotidine twice daily for ART-experienced patients. **RPV**: Use with caution; administer H_2-blockers at least 12 hours before or at least 4 hours after RPV.
Inhaled steroids Statins	**COBI; RTV**: Alternatives or dose adjustments may be needed. Consult the package inserts for drug-drug interactions between specific statins and ARVs.
Polyvalent cations [a]	**BIC; DTG**: Take 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. **RAL**: Magnesium- or aluminum-containing antacids are contraindicated; calcium-containing antacids are acceptable. **RAL HD**: Magnesium- or aluminum-containing antacids are contraindicated; coadministration of calcium-containing antacids is not recommended. **EVG**: Separate dosing by 2 hours, either before or after dose of EVG.
Proton pump inhibitors (PPIs)	**ATV**: Contraindicated with ATV in treatment-experienced patients; in treatment-naive patients, use no more than equivalent of 20 mg of omeprazole with ATV, separated by 12 hours **RPV**: Contraindicated.
Metformin	**DTG**: Metformin levels are significantly raised when coadministered with DTG. If used concomitantly, total daily dose of metformin should not exceed 1,000 mg without clinical evaluation of efficacy and adverse events.
Ethinyl estradiol and norethindrone [b]	**ATV/COBI; DRV/COBI; DRV/RTV; EFV**: Use alternative or additional (e.g., barrier) contraceptive methods or choose alternative ART regimen. **ATV; ATV/RTV**: Use with caution; see manufacturer's package insert for specific dosing information.
Factor Xa inhibitors	**COBI; RTV**: - Apixaban: Reduce dose by 50% if patient is on 5 mg twice daily; avoid use if the indicated dose is 2.5 mg twice daily (based on age, weight, creatinine level). - Dabigatran: No adjustment needed if CrCl ≥50 mL/min; avoid if CrCl <50 mL/min. - Rivaroxaban: Avoid use.
Platelet inhibitors	**COBI; RTV**: - Clopidogrel: Avoid use. - Prasugrel: No adjustment needed. - Ticagrelor: Avoid use.

Additional abbreviations: CrCl, creatinine clearance.

Notes: a) Aluminum, calcium, magnesium, or iron in some antacids or vitamin preparations. b) For emergency contraception, other oral combinations, and patch, ring, or injectable formulations, please refer to package insert for specific ARV for dosing instructions and safety information.

PREFERRED Initial ART Regimens for Nonpregnant Adults *(listed alphabetically)*

Regimen (rating)	Comments
Available as a Single-Tablet Formulation	
ABC/3TC/DTG (A1) [Triumeq]	· Initiate ***only*** in patients confirmed to be negative for HLA-B*5701, including when a "rapid-start" or "test-and-treat" initiation of ART occurs before baseline laboratory test results are available. · Initiate ***only*** in patients with CrCl ≥30 mL/min · Consider underlying risk of coronary heart disease. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.
DTG/3TC (A1) [Dovato]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Do not use in patients with HBV coinfection · Do not initiate before HIV resistance tests results are available. · Do not initiate in patients with NRTI resistance, including the M184V/I mutation. · Do not initiate in patients with baseline HIV RNA levels >500,000 copies/mL until additional study data are available. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.
TAF 25 mg/FTC/BIC (A1) [Biktarvy]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after BIC; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. · Documented DTG resistance after initiation in treatment-naive patients is rare.
Available as Multi-Tablet Regimen with Once-Daily Dosing	
TAF 25 mg/FTC or TDF 300 mg/FTC *and* DTG (A1) [Descovy or Truvada *and* Tivicay]	· For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted. · For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min. · For TDF/FTC, consider bone mineral density. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. · Documented DTG resistance after initiation in treatment-naive patients is rare.
TAF 25 mg/FTC or TDF 300 mg/FTC *and* RAL HD (A2) [Descovy or Truvada *and* Isentress HD]	· For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted. · For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min. · For TDF/FTC, consider bone mineral density. · Administer as TAF/FTC or TDF/FTC once daily and RAL HD 1200 mg once daily, dosed as two 600 mg HD tablets. · To date, no clinical trials have been conducted with TAF and RAL; data are based on bioequivalence pharmacokinetic studies. · Magnesium- or aluminum-containing antacids are contraindicated; coadministration of calcium-containing antacids is not recommended with RAL HD.

· **Additional abbreviations:** CrCl, creatinine clearance; HBV, hepatitis B virus; NRTI, nucleoside reverse transcriptase inhibitor.
· **ART Regimens for individuals of childbearing potential:** Refer to the DHHS guideline: *Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States*.
· **Substitutions:** 1) In all cases, FTC and 3TC are interchangeable. 2) TAF 10 mg and TAF 25 mg are not interchangeable.
· **Dose adjustments:** Refer to *Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment* in the full guideline.

CONTRAINDICATED ART Regimens Based on Routine Baseline Laboratory Parameters

Lab Parameter	Contraindicated ART Regimens
HIV RNA level ≥100,000 copies/mL	· ABC/3TC and ATV/COBI (Epzicom and Evotaz) · ABC/3TC and EFV (Epzicom and Sustiva) · ABC/3TC and ATV and RTV (Epzicom and Reyataz and Norvir) · TAF/FTC/RPV (Odefsey) · TDF/FTC/RPV (Complera)
CD4 <200 cells/mm^3	· TAF/FTC/RPV (Odefsey) · TDF/FTC/RPV (Complera)
CrCl <50 mL/min	· ABC/3TC (Epzicom) · ABC/3TC/DTG (Triumeq) · TDF/3TC/DOR (Delstrigo) · TDF/FTC/EFV (Atripla) · TDF/FTC/RPV (Complera)
CrCl <30 mL/min	· TAF/FTC (Descovy) · TAF/FTC/BIC (Biktarvy) · TAF/FTC/DRV/COBI (Symtuza) · TAF/FTC/EVG/COBI (Genvoya) [a] · TAF/FTC/RPV (Odefsey) · TDF/FTC (Truvada) · DTG/3TC (Dovato)

· **Additional abbreviations:** CrCl, creatinine clearance
· **Dose adjustments:** Refer to *Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment* in the full guideline.
· **Note:** a) Unless CrCl <15 mL/min and on chronic hemodialysis.

ALTERNATIVE Initial ART Regimens for Nonpregnant Adults *(listed alphabetically)*

Regimen (rating)	Comments
Available as a Single-Tablet Formulation	
TAF 10 mg/FTC/DRV/COBI (B2) [Symtuza]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg TAF, boosted.
TAF 10 mg/FTC/EVG/COBI (B1) [Genvoya]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg of TAF, boosted with COBI. · Separate dosing of cation-containing (Ca++, AL, Mg) antacids by 2 hours, either before or after dose of EVG.
TAF 25 mg/FTC/RPV (B3) [Odefsey]	· Initiate ***only*** in patients confirmed to have a CD4 cell count ≥200 cells/mm^3 and HIV RNA level <100,000 copies/mL. Avoid use of RPV in a rapid start or test-and-treat regimen if a patient's viral load and CD4 count results are not available. · Initiate ***only*** in patients with CrCl ≥30 mL/min. · Use with caution in patients with depression or a history of suicidality. · To date, no clinical trials have been conducted; data are based on bioequivalence pharmacokinetic studies of TAF compared with TDF. · Contraindicated with proton pump inhibitors. · Use H_2-blockers with caution and separate dosing by 12 hours. · Must take with food. · Contains 25 mg of TAF, unboosted.
TDF/3TC/DOR (B1) [Delstrigo]	· Initiate ***only*** in patients with CrCl ≥50 mL/min. · Contraindicated when coadministered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers. · Consider bone mineral density.
Available as Multi-Tablet Regimen with Once-Daily Dosing	
ABC/3TC *and* DOR (B2) [Epzicom *and* Pifeltro]	· Initiate ***only*** in patients confirmed to be negative for HLA-B*5701. · When a "rapid-start" or "test-and-treat" initiation of ART occurs before baseline laboratory test results are available, avoid use of ABC until a patient's HLA-B*5701 test is confirmed negative. · Consider underlying risk of coronary heart disease. · Contraindicated when coadministered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers.
TAF 25 mg/FTC *and* DOR (B2) [Descovy *and* Pifeltro]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Contraindicated when coadministered with drugs that are strong CYP3A enzyme inducers.
Available as Multi-Tablet Regimen with Twice-Daily Dosing	
TAF 25 mg/FTC or TDF 300 mg/FTC *and* RAL (B3) [Descovy or Truvada *and* Isentress]	· For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min. · For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min. · For TFD/FTC, consider bone mineral density. · Administer as TAF/FTC or TDF/FTC once daily and RAL 400 mg twice daily. · Magnesium- or aluminum-containing antacids are contraindicated; calcium-containing antacids are acceptable with RAL.

· **Additional abbreviations:** CrCl, creatinine clearance.
· **ART Regimens for individuals of childbearing potential:** Refer to the DHHS guideline: *Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States*.
· **Substitutions:** 1) In all cases, FTC and 3TC are interchangeable. 2) TAF 10 mg and TAF 25 mg are not interchangeable. 3) COBI and RTV should not be considered interchangeable because of their drug-interaction profiles.
· **Dose adjustments:** Refer to *Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment* in the full guideline.