HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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SELECTING AN INITIAL ART REGIMEN

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JANUARY 2019 UPDATE

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

Dolutegravir (DTG) Safety Statement, May 2018

On May 18, 2018, the FDA and the DHHS Antiretroviral Guidelines Panels issued statements in response to preliminary results from a study that reported increased risk of neural tube defects in babies born to mothers taking DTG-based ARV drug regimens at the time of conception.

Until more data become available, **DTG-containing regimens should be avoided in any HIV-exposed individual who is pregnant in the first trimester or could become pregnant and is not using effective contraception**. If there are no alternatives to DTG for individuals of child-bearing potential, then clinicians should strongly advise the use of effective contraception and should obtain a pregnancy test before initiating treatment.

For more information, see: *DHHS Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*

ALL RECOMMENDATIONS P.1

- Clinicians should involve their patients when deciding which ART regimen is most likely to result in adherence. (A3)
- Clinicians should perform the following when initiating ART: 1) Assessment for comorbidities and chronic co-administered medications that may affect the choice of regimen for initial therapy (A3); 2) Genotypic resistance testing should be performed at diagnosis, or at the initial visit if not done previously, for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes.

Continued on P.2 ➔

CONTRAINDICATED ART Regimens Based on Routine Baseline [a] Laboratory Parameters

Lab Parameter	Contraindicated ART Regimens
Viral load ≥100,000 copies/mL	• ABC/3TC and COBI/ATV (Epzicom and Evotaz) • ABC/3TC and EFV (Epzicom and Sustiva) • ABC/3TC and RTV and ATV (Epzicom and Norvir and Reyataz) • 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/COBI/DRV (Symtuza) • TAF/FTC/COBI/EVG (Genvoya) [b] • TAF/FTC/RPV (Odefsey) • TDF/FTC (Truvada)

Additional abbreviation: CrCl, creatinine clearance.
Notes:
a. For renal adjustment of fixed-dose combinations and single-tablet regimens while on therapy, see *Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment* in full guideline.
b. Unless CrCl <15 mL/min and on chronic hemodialysis.

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

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

- For individuals who have delayed initiation of ART *and* have engaged in high-risk behaviors associated with acquisition of HIV superinfection, genotypic resistance testing should be repeated before choosing the ART regimen. (B3)
- Clinicians should consult with a care provider experienced in ART management when: 1) Baseline resistance indicates the need for treatment with a regimen other than the listed preferred or alternative regimens (A3); 2) Selecting a regimen for individuals with extensive comorbidities and/or comedications, impaired renal function, HBV or HCV coinfection, or active opportunistic infections (B3).
- Clinicians should ask individuals about their reproductive plans and discuss the use of contraception. (A3) Refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential.
- For ART-naive patients, clinicians should select an initial ART regimen that is preferred; see Preferred Initial ART Regimens for Nonpregnant Adults. (A1)
  - A single-tablet regimen or regimen with once-daily dosing is preferred unless contraindicated by resistance, drug-drug interactions, intolerance, allergy, or access. (A2)
  - In general, a preferred regimen should be selected, although there may be times when an alternative regimen may be a better choice for an individual patient (see Alternative Initial ART Regimens for Nonpregnant Adults).
- Clinicians should not prescribe two-drug regimens as initial therapy. (A2)
- Clinicians or clinic staff should follow up, by telephone or other methods, 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); see the NYSDOH AI guideline *Virologic and Immunologic Monitoring* for more 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 ≥50 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.
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.
Available as Multi-Tablet Regimen with Once-Daily Dosing	
TAF 25 mg/FTC ***and*** **DTG** (A1) [Descovy *and* Tivicay]	• Initiate **only** in patients with CrCl ≥30 mL/min. • Documented DTG resistance after initiation in treatment-naive patients is rare. • Contains 25 mg of TAF, unboosted. • 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 ***and*** **RAL HD** (A2) [Descovy *and* Isentress HD]	• Initiate **only** in patients with CrCl ≥30 mL/min. • To date, no clinical trials have been conducted with TAF and RAL; data are based on bioequivalence pharmacokinetic studies. • Contains 25 mg of TAF, unboosted. • Administer as TAF/FTC once daily and RAL HD 1200 mg once daily, dosed as two 600 mg HD tablets. • Magnesium- or aluminum-containing antacids are contraindicated; co-administration of calcium-containing antacids is not recommended with RAL HD.

Additional abbreviation: CrCl, creatinine clearance.
- **ART regimens for individuals of childbearing potential:** Refer to the DHHS guideline: *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health 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 8: ARV Dose Adjustments for Renal and Hepatic Impairment* in the full guideline.

KEY POINTS

- INSTI-based regimens are generally the best choice for most individuals because of tolerability and durability.
- Neither mental health nor substance use disorders are contraindications to initiating therapy. In some special cases, delay of initiation (for as short a time as possible) may be appropriate while addressing adherence issues and/or possible interactions (see the NYSDOH AI guideline *When to Initiate ART*).
- 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 PIs 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 (>750,000 copies/mL).
- When initiating therapy at the time of diagnosis ("rapid start") it is not necessary to have the results of baseline laboratory tests immediately available. Labs 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 documentation of negative HLA-B*5701 test results.

Select Drug-Drug Interactions to Discuss before Initiating ART in Treatment-Naive Patients

Drugs	ARV(s): Comments
H_2-blockers	**ATV**: In treatment-naive patients on boosted ATV, H_2-blockers should be taken simultaneously with ATV or, if simultaneous dosing is not possible, separated from ATV by 10 hours; prescribe no more than 20 mg of famotidine or equivalent for 1 dose and no more than 40 mg twice daily of famotidine or equivalent for daily dose. **RPV**: Use with caution; administer 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]	**DTG; BIC**: 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; co-administration of calcium-containing antacids is not recommended. **EVG**: Separate dosing by 2 hours, either before or after dose of EVG.
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 co-administered 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]	**EFV; COBI/ATV; COBI/DRV; RTV and DRV**: Use alternative or additional (e.g., barrier) contraceptive methods or choose alternative ART regimen. **ATV; RTV and ATV**: 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; PPI, proton-pump inhibitor.
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.

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

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

Regimen (rating)	Comments
Available as a Single-Tablet Formulation	
TAF 10 mg/FTC/COBI/DRV (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/COBI/EVG (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 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* viral load <100,000 copies/mL. · When a "rapid-start" or "test-and-treat" initiation of ART occurs before a patient's viral load and CD4 count are available, avoid use of RPV. · 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 PPIs. · 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 co-administered 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 co-administered 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 co-administered with drugs that are strong CYP3A enzyme inducers.
TDF/FTC *and* DTG (B1) [Truvada *and* Tivicay]	· Initiate ***only*** in patients with CrCl ≥50 mL/min. · Documented DTG resistance after initiation in treatment-naive patients is rare. · 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.
TDF/FTC *and* RAL HD (B1) [Truvada *and* Isentress HD]	· Iniate ***only*** in patients with CrCl ≥50 mL/min. · Consider bone mineral density. · Administer as TDF/FTC once daily and RAL HD 1200 mg once daily, dosed as two 600 mg HD tablets. · Magnesium- or aluminum-containing antacids are contraindicated; co-administration of calcium-containing antacids is not recommended with RAL HD.
Available as Multi-Tablet Regimen with Twice-Daily Dosing	
TAF 25 mg/FTC *and* RAL (B3) [Descovy *and* Isentress]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Administer as ABC/3TC 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; PPI, proton-pump inhibitor.
· **ART regimens for individuals of childbearing potential:** Refer to the DHHS guideline: *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health 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 8: ARV Dose Adjustments for Renal and Hepatic Impairment* in the full guideline.