HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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SELECTING AN INITIAL ART REGIMEN

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JULY 2018 UPDATE

ALL RECOMMENDATIONS P.1

- Clinicians should involve their patients when deciding which ART regimen is most likely to result in patient adherence (A3).
- Clinicians should perform the following when initiating ART: 1) Assessment for comorbidities that may affect the choice of regimen for initial therapy (A3); 2) Genotypic resistance testing for the protease and reverse transcriptase genes at diagnosis or at the initial visit if not done previously (A2).
- Baseline testing is not recommended for either integrase resistance or tropism (A3).
- For patients 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:
  - Baseline resistance requires treatment with a regimen other than the listed preferred or alternative regimens (A3).
  - Selecting a regimen for patients with extensive comorbidities (B3), impaired renal function (B3), HBV or HCV co-infections (B3), active opportunistic infections (B3), or very high viral loads (B3).
- Clinicians should: 1) Ask individuals about their reproductive plans and discuss the use of contraception (A3); 2) Refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential.
- A single-tablet regimen or a regimen with once-daily dosing is preferred unless contraindicated by drug-drug interactions, intolerance, allergy, or access (A2).

Continued on P.2 →

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

- For ART-naïve patients, clinicians should select an initial ART regimen that is preferred (see Preferred Initial ART regimens) (A1).
  - Clinicians should select an alternative or other regimen only when a preferred initial regimen cannot be used.
- Two-drug regimens are not recommended as initial therapy (A2).
- Clinicians or clinical 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 initiation to assess response to therapy (A3); see the NYSDOH AI guideline Virologic and Immunologic Monitoring for more information.

Potential Increased Risk of Neural Tube Defects with Dolutegravir (DTG)-based ART Regimens

On May 18, 2018, the FDA and the DHHS Antiretroviral Guidelines Panel issued statements in response to preliminary results from a study that reported increased risk of neural tube defects in babies born to mothers who were taking DTG-based ART at the time of conception. Clinicians should refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential.

Food Requirements for ARVs

- **Can be taken with or without food:** 3TC, ABC, DTG, FTC, RAL, TAF, TDF, TAF/FTC/BIC
- **Must be taken with food:** ATV/COBI; ATV and RTV; DRV/COBI; DRV and RTV; EVG; RPV; TAF/FTC/COBI/EVG; TDF/FTC/COBI/EVG
- **Must be taken on an empty stomach:** EFV

PREFERRED Initial ART Regimens for Non-Pregnant Adults

Alphabetical list; for details see Specific Factors to Consider or drug package inserts

Regimen	Comments
Available as a Single-Tablet Formulation	
ABC/3TC/DTG (Triumeq)	• Initiate **only** in patients confirmed to be negative for HLA-B*5701 • Initiate **only** in patients with CrCl ≥50 mL/min • Consider underlying risk of coronary heart disease • No documented DTG resistance after initiation in treatment-naïve patients to date • See footnote 7
TAF 25 mg/FTC/BIC (Biktarvy)	• Initiate **only** in patients with CrCl ≥30 mL/min • Contains 25 mg of TAF, unboosted
TAF 10 mg/FTC/ COBI/EVG (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
Available as Multi-Tablet Regimen with Once-Daily Dosing	
TAF 25 mg/FTC *and* DTG (Descovy *and* Tivicay)	• Initiate **only** in patients with CrCl ≥30 mL/min • Documented DTG resistance after initiation in treatment-naïve patients is rare • Contains 25 mg of TAF, unboosted • See footnote 7
TAF 25 mg/FTC *and* RAL HD (Descovy *and* Isentress HD)	• Initiate **only** in patients with CrCl ≥30 mL/min • To date, no clinical trials have been conducted with TAF; data are based on bioequivalence pharmacokinetic studies • Contains 25 mg of TAF, unboosted • TAF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets

Notes: 1) In all cases, FTC and 3TC are interchangeable when not being used in fixed-dose combinations; 2) Because of their drug-interaction profiles, COBI and RTV should not be considered interchangeable; 3) TAF 10 mg and TAF 25 mg are not interchangeable; 4) Refer to full guideline Table 9: *ARV Dose Adjustments for Renal and Hepatic Impairment* for adjustment based on renal or hepatic function; 5) When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg; 6) When a "rapid start" or "test and treat" initiation of ART occurs before baseline laboratory test results are available, avoid use of abacavir until a patient's HLA-B*5701 is confirmed negative; 7) Clinicians should refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential: *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the US.*

CONTRAINDICATED ART Regimens Based on Routine Baseline* 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) • RAL and RTV and DRV (Isentress and Norvir and Prezista) • TAF/FTC/RPV (Odefsey) • TDF/FTC/RPV (Complera)
CD4 <200 cells/mm³	• TAF/FTC/RPV (Odefsey) • TDF/FTC/RPV (Complera)
CrCl <70 mL/min	• TDF/FTC and COBI/ATV (Truvada and Evotaz) • TDF/FTC and COBI/DRV (Truvada and Prezcobix) • TDF/FTC/COBI/EVG (Stribild)
CrCl <50 mL/min	• ABC/3TC (Epzicom) • ABC/3TC/DTG (Triumeq) • TDF/FTC/EFV (Atripla) • TDF/FTC/RPV (Complera)
CrCl <30 mL/min	• TAF/FTC (Descovy) • TAF/FTC/BIC (Biktarvy) • TAF/FTC/COBI/EVG (Genvoya) • TAF/FTC/RPV (Odefsey) • TDF/FTC (Truvada)

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

More tables on the inside →

KEY POINTS

- INSTI-based regimens are generally the best choice for most patients because of tolerability and durability.
- Neither mental health nor substance use disorders are contraindications to initiating therapy, although, in some cases, delay of initiation may be appropriate (see the NYSDOH AI guideline When to Initiate ART).
- When initiating ART at the time of diagnosis (i.e., "rapid start" or "test and treat") avoid regimens containing ABC unless results of HLA-B*5701 testing are known to be negative. Similarly, RPV is not appropriate for patients whose viral load has not been confirmed to be <100,000 copies/mL *and* CD4 count confirmed to be ≥200 cells/mm^3.
- COBI and DTG can both cause decreased tubular excretion of creatinine and will dependably 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 more hyperlipidemia than unboosted INSTIs.
- Consultation with an experienced HIV care provider is advised when a patient's baseline viral load is very high.

ALTERNATIVE Initial ART Regimens for Non-Pregnant Adults

Alphabetical list; for details see Specific Factors to Consider or drug package inserts

Regimen	Comments
Available as a Single-Tablet Formulation	
TAF 25 mg/FTC/RPV (Odefsey)	• Initiate ***only*** in patients confirmed to have a CD4 cell count ≥200 cells/mm^3 and viral load <100,000 copies/mL • Initiate ***only*** in patients with CrCl of ≥30 mL/min • Use with caution in patients with depression or history of suicidality • To date, no clinical trials have been conducted; data are based on bioequivalence pharmacokinetic studies • 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/FTC/COBI/EVG (Stribild)	• Initiate ***only*** in patients with CrCl ≥70 mL/min • Carefully consider drug-drug interactions with COBI • Consider bone mineral density
Available as Multi-Tablet Regimen with Once-Daily Dosing	
TDF/FTC *and* DRV/COBI (Truvada *and* Prezcobix)	• Initiate ***only*** in patients with CrCl ≥70 mL/min • Carefully consider drug-drug interactions with COBI • Consider bone mineral density
TDF/FTC *and* DRV *and* RTV (Truvada *and* Prezista *and* Norvir)	• Initiate ***only*** in patients with CrCl ≥50 mL/min. • Carefully consider drug-drug interactions with RTV • Consider bone mineral density
TDF/FTC *and* DTG (Truvada *and* Tivicay)	• Initiate ***only*** in patients with CrCl ≥50 mL/min • Documented DTG resistance after initiation in treatment-naïve patients is rare • Consider bone mineral density • See footnote 7
TDF/FTC *and* RAL HD (Truvada *and* Isentress HD)	• Iniate ***only*** in patients with CrCl ≥50 mL/min • Consider bone mineral density • TDF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets
Available as Multi-Tablet Regimen with Twice-Daily Dosing	
TAF 25 mg/FTC *and* RAL (Descovy *and* Isentress)	• Initiate ***only*** in patients with CrCl ≥50 mL/min • TDF/FTC once daily and RAL twice daily

Notes: 1) In all cases, FTC and 3TC are interchangeable when not being used in fixed-dose combinations; 2) Because of their drug-interaction profiles, COBI and RTV should not be considered interchangeable; 3) TAF 10 mg and TAF 25 mg are not interchangeable; 4) Refer to full guideline Table 9: *ARV Dose Adjustments for Renal and Hepatic Impairment* for adjustment based on renal or hepatic function; 5) When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg; 6) When a "rapid start" or "test and treat" initiation of ART occurs before baseline laboratory test results are available, avoid use of abacavir until a patient's HLA-B*5701 is confirmed negative; 7) Clinicians should refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential: *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the US.*

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

Drugs	ARV(s): Comments
H_2-blockers	**ATV**: In treatment-naïve patients on boosted ATV, H_2-blockers should be either 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 one 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 [aluminum, calcium, magnesium, or iron in some antacids or vitamin preparations]	**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; 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-naïve 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. The dose of metformin should not exceed 1000 mg
Ethinyl estradiol and norethindrone	**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 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
Factor Xa inhibitors	**COBI; RTV**: - Apixiban: 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) - 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

This pocket guide is a companion to the NYSDOH AI guideline Selecting an Initial ART Regimen. The full guideline includes the following:

- Available ART Regimens, including: Preferred (Table 1), Alternative (Table 2), and Other (Table 3)
- General Principles in Choosing an Initial ART Regimen, including Combinations to Avoid (Table 4)
- General Considerations with Initial ART Regimens
- Specific Factors to Consider and Discuss with Patients, including Select Drug-Drug Interactions (Table 5) and Alternatives to the Tablet Form of ARVs (Table 6)
- Special Considerations for Comorbid Conditions
- Pre-ART Initiation Lab Testing, including Contraindicated Regimens Based on Lab Parameters (Table 7)
- ARV Dose Adjustments for Renal and Hepatic Impairment (Table 8)

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