CLINICAL GUIDELINES PROGRAM
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

Selecting an Initial ART Regimen

Updates, Authorship, and Related Guidelines

Date of current publication	March 10, 2025
Highlights of changes, additions, and updates in the March 10, 2025 edition	• In the Available Antiretroviral Medications section: – Table 1: ABC/3TC/DTG removed and listed in Table 3 as an other regimen (not preferred or alternative); TAF 25 mg/FTC or TDF 300 mg/FTC and RAL HD removed and listed as an alternative regimen. – Tables 2 and 3: Regimens containing ABC/3TC (Epzicom) removed. • In the Special Considerations for Comorbid Conditions section: Text and references added on the association between ABC use and increased cardiovascular risk and avoiding ABC in an initial regimen.
Intended users	Clinicians in New York State who are initiating ART in nonpregnant, ART-naive adults with HIV
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Author and writing group conflict of interest disclosures	Antonio E. Urbina, MD: Scientific advisor: Gilead Sciences, Janssen, Merck, ViiV Healthcare
Date of original publication	April 27, 2017
Committee	Medical Care Criteria Committee
Developer and funder	New York State Department of Health AIDS Institute (NYSDOH AI)
Development process	See Supplement: Guideline Development and Recommendation Ratings
Related NYSDOH AI guidelines	• Diagnosis and Management of HIV-2 in Adults • PrEP to Prevent HIV and Promote Sexual Health • Rapid ART Initiation • Second-Line ART After Treatment Failure or for Regimen Simplification • Use of Injectable CAB/RPV LA as Replacement ART in Virally Suppressed Adults

Abbreviations Used in This Guideline

Drug Names:

- 3TC: lamivudine
- ABC: abacavir
- ATV: atazanavir
- BIC: bictegravir
- CAB: cabotegravir
- COBI: cobicistat
- DOR: doravirine
- DRV: darunavir
- DTG: dolutegravir
- EFV: efavirenz
- EVG: elvitegravir
- FTC: emtricitabine
- IDV: indinavir
- LPV: lopinavir
- RAL: raltegravir
- RAL HD: RAL high-dose
- RPV: rilpivirine
- RTV: ritonavir
- TAF: tenofovir alafenamide
- TDF: tenofovir disoproxil fumarate
- ZDV: zidovudine

Other:

- ART: antiretroviral therapy
- ARV: antiretroviral
- CDC: Centers for Disease Control and Prevention
- CrCl: creatinine clearance
- FDA: U.S. Food and Drug Administration
- FDC: fixed-dose combination
- DHHS: U.S. Department of Health and Human Services
- HBV: hepatitis B virus
- HCV: hepatitis C virus
- INSTI: integrase strand transfer inhibitor
- MTR: multi-tablet regimen
- NRTI: nucleoside/nucleotide reverse transcriptase inhibitor
- NNRTI: non-nucleoside reverse transcriptase inhibitor
- PI: protease inhibitor
- PPI: proton pump inhibitor
- PrEP: pre-exposure prophylaxis
- STR: single-tablet regimen
- TB: tuberculosis

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Purpose of This Guideline

This guideline was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) for primary care providers and other practitioners who are initiating therapy in nonpregnant, ART-naive adults with HIV. The guideline aims to achieve the following goals:

- Provide a clear and concise roadmap for clinicians to follow in choosing from among several equally efficacious ART regimens based on individual patient characteristics and preferences.
- Provide a list of ART regimens to avoid.
- Provide dosing considerations for individuals with renal or hepatic impairment and important drug-drug and food interactions.
- Encourage clinicians to seek the assistance of an experienced HIV care provider when treating patients with extensive comorbidities.
- Integrate current evidence-based clinical recommendations into the healthcare-related implementation strategies of the New York State Ending the Epidemic initiative.

The NYSDOH AI is publishing this guideline at a critical time: 1) prompt initiation of ART is now recommended for all individuals diagnosed with HIV; 2) identifying and linking individuals with HIV to care and treatment that achieves optimal virologic suppression are crucial to the success of the New York State Ending the Epidemic initiative; and 3) the ability of primary care providers and other clinicians in New York State to properly select initial ART is key to the successful treatment of individuals with HIV.

Introduction: The NYSDOH AI Medical Care Criteria Committee recommendations for prescribing ART regimens for treatment-naive, nonpregnant adults (age ≥18 years) with HIV-1 and without acquired resistance are based on a comprehensive review of available clinical trial data. (For guidelines specific to the treatment of adolescents with HIV, please

consult the DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV). In formulating its recommendations for New York State, this committee balanced the strength of published evidence regarding efficacy of treatment regimens with factors that influence adherence, including pill burden, tolerability, and dosing schedule. Preferred regimens are supported by evidence and have favorable adherence profiles, with lower pill burdens, fewer adverse effects, and dosing schedules that may be easier for individuals to manage. The ranking of regimens in this manner is designed to inform discussion and decision-making with patients.

How to use this guideline: Tables presenting preferred and alternative regimens appear first (see guideline section Available ART Regimens). To help guide the choice among regimens of similar efficacy, each table includes comments that address selected pertinent issues regarding each regimen, such as limitations based on a patient's kidney function and drug-drug interactions.

Other sections of the guideline include a review of relevant issues, patient considerations, essential laboratory assessments, and the rationale for the recommendations. Reference to the expanded information is crucial for addressing factors that may be of particular importance when individualizing a patient's treatment, such as loss of bone mineral density with a regimen that includes TDF and the conflicting data on cardiac risk with ABC (see guideline section Specific Factors to Consider and Discuss With Patients). In addition, a review of psychosocial factors and individual patient preferences may help in the selection of an initial ART regimen. Importantly, a patient-centered approach that incorporates both clinical and nonclinical issues should be prioritized.

Scope: This guideline addresses initial treatment of HIV-1 infection with ART **in nonpregnant adults**.

- For information regarding ART in individuals who are or who may become pregnant, see DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
- For recommendations regarding the treatment of HIV-2 infection, see the NYSDOH AI guideline Diagnosis and Management of HIV-2 in Adults.
- For recommendations regarding second-line ART regiments, see the NYSDOH AI guideline Second-Line ART After Treatment Failure or for Regimen Simplification.

Note on "experienced" and "expert" HIV care providers: Throughout this guideline, when reference is made to "experienced HIV care provider" or "expert HIV care provider," those terms are referring to the following 2017 NYSDOH AI definitions:

- Experienced HIV care provider: Practitioners who have been accorded HIV Experienced Provider status by the American Academy of HIV Medicine or have met the HIV Medicine Association's definition of an experienced provider are eligible for designation as an HIV Experienced Provider in New York State. Nurse practitioners and licensed midwives who provide clinical care to individuals with HIV in collaboration with a physician may be considered HIV Experienced Providers as long as all other practice agreements are met (8 NYCRR 79-5:1; 10 NYCRR 85.36; 8 NYCRR 139-6900). Physician assistants who provide clinical care to individuals with HIV under the supervision of an HIV Specialist physician may also be considered HIV Experienced Providers (10 NYCRR 94.2)
- Expert HIV care provider: A provider with extensive experience in the management of complex patients with HIV.

Available Antiretroviral Medications

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

☑ RECOMMENDATIONS

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 regimen options and engage in shared decision-making to optimize the likelihood of adherence. (A3)
  - Assess for comorbidities and chronic coadministered medications that may affect the choice of regimen for a patient's initial ART. (A3)

☑ RECOMMENDATIONS

  - Choose a preferred ART regimen unless one of the alternative regimens is a better choice based on individual patient factors. (A1)
  - Recommend an STR 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 [a] and discuss the use of contraception. (A3)
- 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 HBV status are known. (A1)
  - Genotypic resistance testing results have confirmed that a patient does not have a relevant 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; HBV or HCV coinfection; or active opportunistic infections. (B3)
  - The NYSDOH Clinical Education Initiative provides access to HIV specialists through their toll-free line: 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)

Note:

a. In choosing an initial ART regimen for a patient who is pregnant or planning a pregnancy, refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.

Available ART Regimens

An initial ART regimen should be selected based on patient preferences and clinical characteristics, and a preferred regimen should be used whenever possible. Each of the preferred, alternative, and other initial ART regimens for nonpregnant adults is expected to produce full viral suppression; however, the regimens differ in tolerability, possible toxicities, convenience, and the potential for drug-drug interactions, all of which can affect overall adherence and, therefore, suppression rates.

Preferred backbone: This committee recommends that either formulation of tenofovir (TAF or TDF) can be used as part of the backbone in preferred regimens. A recent meta-analysis of 14 clinical trials [Pilkington, et al. 2020], comparing the efficacy and safety of TAF versus TDF in boosted and unboosted subgroups, found comparable efficacy and safety profiles with the use of unboosted TDF compared with TAF (see Box 1, below). Studies have shown that TDF-related renal toxicity is more common when using TDF in a regimen containing COBI or RTV [Pilkington, et al. 2020; Hill, et al. 2018; Cuzin, et al. 2017; Ryom, et al. 2013; Goicoechea, et al. 2008]. Therefore, this committee does not recommend TDF use with boosted regimens when initiating therapy.

In a study of ART-naive individuals, RAL HD 1,200 mg once daily was noninferior to 400 mg tablets dosed twice daily and is thus preferred [Cahn(b), et al. 2017].

Greater weight gain has also been observed after initiation of TAF or with a switch from TDF to TAF, especially in conjunction with INSTIs [Łomiak, et al. 2021; Surial, et al. 2021; Bourgi(a), et al. 2020; Bourgi(b), et al. 2020; Calmy, et al. 2020; Lake, et al. 2020; Sax, et al. 2020; Venter, et al. 2020; Venter, et al. 2019]. However, the predictors, mechanisms of actions, and clinical significance of these findings are unknown.

Third drug: An INSTI as the third drug is preferred over PIs and NNRTIs based on tolerability and a lower incidence of drug-drug interactions. RPV is not appropriate for patients with a viral load >100,000 copies/mL *or* CD4 count ≤200 cells/mm^3 and is contraindicated with PPIs. TAF/FTC/RPV is included as an alternative regimen.

EFV-containing regimens, although efficacious, are less well tolerated than the preferred or alternative regimens.

LPV/RTV-containing regimens are no longer included among the options for initial treatment because of pill burden and reduced tolerability in comparison with other boosted PIs.

Single-Tablet Regimens Versus Multi-Tablet Regimens

The advantages of STRs compared with MTRs include simplicity, convenience, and lower risk of selective nonadherence [Gardner, et al. 2008]. A recent meta-analysis demonstrated that STRs had better adherence rates when compared with MTRs of any frequency (once daily or twice daily) and had higher 48-week viral suppression rates with comparable adverse effects [Clay, et al. 2015].

In another retrospective study, INSTI-based regimens generally had greater rates of suppression and a lower probability of viral rebound after suppression in comparison to NNRTI-based regimens, regardless of whether an STR or MTR was used, but STR INSTI-based therapy was more durable [Mills(b), et al. 2016]. In the same study, STR NNRTI-based therapy led to greater rates of suppression than MTR NNRTI-based therapy [Mills(b), et al. 2016].

Box 1: Important Clinical Considerations With Either TDF/FTC or TAF/FTC as Initial ART [a]

☑ **If the patient is at risk for chronic kidney disease (e.g., age >40 years, with hypertension, diabetes, or preexisting mild kidney disease):** The greater possibility of kidney disease among individuals who have risk factors is an essential component of the risk-benefit discussion and shared decision-making regarding initiation of tenofovir-containing regimens.

- Higher rates of renal dysfunction have been reported in individuals taking TDF in conjunction with RTV- and COBI-containing regimens [Pilkington, et al. 2020; Hill, et al. 2018; Cuzin, et al. 2017; Ryom, et al. 2013; Goicoechea, et al. 2008].
- For people at low risk for kidney disease, TDF, when not combined with a regimen that contains a pharmacokinetic booster (RTV or COBI), appears to have similar renal safety to TAF [Pilkington, et al. 2020; Hill, et al. 2018].
- TAF has fewer adverse effects on renal function and is associated with lower rates of proteinuria than TDF [Mills(a), et al. 2016; Pozniak, et al. 2016; Sax, et al. 2015].
- TDF/FTC should be initiated only in individuals with CrCl ≥50 mL/min.
- TAF/FTC should be initiated only in individuals with CrCl ≥30 mL/min.

☑ **If the patient has osteopenia, osteomalacia, or osteoporosis:**

- The risk of bone loss in individuals with preexisting risk factors or documented osteopenia, osteomalacia, or osteoporosis is an important component of the risk-benefit discussion and shared decision-making regarding initiation of TDF/FTC or TAF/FTC.
- TDF is associated with osteomalacia and decreases in bone mineral density [McComsey, et al. 2011; Stellbrink, et al. 2010; Perrot, et al. 2009].
- TAF/FTC is preferred for people with osteoporosis.

☑ **If the patient has concerns about weight gain, hyperlipidemia, or metabolic disorders:**

- Greater weight gain has been observed with initiation of TAF than TDF and with a switch from TDF to TAF, especially in conjunction with INSTIs [Łomiak, et al. 2021; Surial, et al. 2021; Bourgi(a), et al. 2020; Bourgi(b), et al. 2020; Calmy, et al. 2020; Lake, et al. 2020; Sax, et al. 2020; Venter, et al. 2020; Venter, et al. 2019].
- TDF is associated with lower lipid levels than TAF [Souza, et al. 2013].

☑ **If the patient is an adolescent or youth:** There is limited data on bone safety in adolescents taking TAF/FTC. However, given the more favorable bone biomarkers of TAF versus TDF, TAF may have an advantage in adolescents who have not achieved bone maturation. Because this advantage is theoretical and not currently supported with clinical data, a clear recommendation cannot be made at this time.

Box 1: Important Clinical Considerations With Either TDF/FTC or TAF/FTC as Initial ART [a]

☑ If the patient is pregnant or attempting to conceive:

- Information about the potential benefits and risks of taking tenofovir-containing regimens during pregnancy is an essential component of shared decision-making regarding risk reduction.
- Due to the greater experience with TDF in this population, TDF/FTC is the preferred dual NRTI backbone for use as HIV treatment during pregnancy [b].
- Prospectively report information regarding the use of ART medications during pregnancy to the Antiretroviral Pregnancy Registry.

☑ If the patient has active chronic HBV:

- TDF, TAF, and FTC are active against HBV. TDF and TAF are considered equally effective against HBV [c].
- Discontinuation of TDF/FTC or TAF/FTC in patients with chronic HBV requires close monitoring for rebound HBV viremia.

Abbreviations: 3TC, lamivudine; ART, antiretroviral therapy; COBI, cobicistat; CrCl, creatinine clearance; DHHS, U.S. Department of Health and Human Services; FDA, U.S. Food and Drug Administration; FTC, emtricitabine; HBV, hepatitis B virus; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

Notes:

a. Consider safety, cost, and access when choosing between use of TDF/FTC or TAF/FTC.
b. Refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
c. TDF and TAF are approved by the FDA as treatment for HBV. FTC is also active against HBV but is not FDA-approved for HBV treatment. TDF or TAF in combination with FTC or 3TC, which is FDA-approved for HBV treatment and is molecularly similar to FTC, is commonly used in patients with HIV/HBV coinfection as part of an antiretroviral regimen to treat both infections.

Other studies have demonstrated better efficacy and adherence, lower cost to patients, and fewer hospital admissions associated with STRs than with MTRs [Griffith, et al. 2019; Mills(b), et al. 2016; Armstrong, et al. 2015; Maggiolo, et al. 2015; Hanna, et al. 2014; Nachega, et al. 2014; Sweet, et al. 2014; Cohen(a), et al. 2013; Colombo, et al. 2013; Raboud, et al. 2011; Bangalore, et al. 2007].

There are 2 STRs listed below as preferred regimens. These regimens may contain 1 or more components that are not appropriate for an individual patient, do not allow for adjustment of individual components for renal function, have significant drug-drug interactions, are poorly tolerated, or may be more expensive than the individual components prescribed separately, particularly if available as generic formulations. With full adherence, any of the preferred or alternative regimens should lead to full suppression. This includes MTRs, which can be used when an STR is not possible or not tolerated. Cost and access may also be determinative factors.

For patients with impaired baseline renal function, separating the drugs into individual components and adjusting each may be appropriate (see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment).

Table 1 includes initial ART regimens **preferred** by this committee; Table 2 lists **alternative** initial regimens. Table 3 lists other available ART regimens that this committee considers neither preferred nor alternative. Within each table, regimens are listed alphabetically. For specific details on choosing a regimen, see the discussions in other sections of this guideline and/or the package inserts for the drugs listed below.

Table 1: Preferred Initial ART Regimens for Nonpregnant Adults [a]
(listed alphabetically; for specific details, see guideline section Specific Factors to Consider and Discuss With Patients and drug package inserts)

Regimen	Comments	Rating
Available as a Single-Tablet Formulation		
Lamivudine/dolutegravir [b,c] (3TC/DTG; Dovato)	• Initiate ***only*** in patients with CrCl ≥30 mL/min [d]. • Do not use in patients with HBV coinfection. • Do not initiate before HIV resistance tests results are available. • Do not initiate in patients with relevant NRTI resistance mutations, 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.	A1
Tenofovir alafenamide/ emtricitabine/bictegravir [c] (TAF 25 mg/FTC/BIC; Biktarvy)	• Initiate ***only*** in patients with CrCl ≥30 mL/min [d]. • Contains 25 mg of TAF, unboosted [c]. • 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.	A1
Available as a Multi-Tablet Regimen With Once-Daily Dosing		
Tenofovir alafenamide/emtricitabine or tenofovir disoproxil fumarate/ emtricitabine *and* dolutegravir [b,c] (TAF 25 mg/FTC or TDF 300 mg/FTC *and* DTG; Descovy or Truvada *and* Tivicay)	• For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min [d]. • Contains 25 mg of TAF, unboosted [c]. • For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min [d]. • For TDF/FTC, use with caution in patients with or at risk for osteoporosis. • 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.	A1

Abbreviations: ART, antiretroviral therapy; CrCl, creatinine clearance; DHHS, U.S. Department of Health and Human Services; HBV, hepatitis B virus; NRTI, nucleoside/nucleotide reverse transcriptase inhibitors.

Notes:

a. In choosing ART regimens for individuals of childbearing potential, refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
b. 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 has been removed. DTG has been shown to be safe throughout pregnancy. See the MCCC's statement on Use of Dolutegravir in Individuals of Childbearing Capacity for further discussion [Zash, et al. 2022].
c. Substitutions:
   – In all cases, FTC and 3TC are interchangeable.
   – TAF 10 mg and TAF 25 mg are not interchangeable.
d. For dose adjustments, see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment.

Table 2: Alternative Initial ART Regimens for Nonpregnant Adults [a]
(listed alphabetically; for specific details, see guideline section Specific Factors to Consider and Discuss With Patients and drug package inserts)

Regimen	Comments	Rating
Available as a Single-Tablet Formulation		
Tenofovir alafenamide/emtricitabine/ darunavir/cobicistat [b] (TAF 10 mg/FTC/DRV/COBI; Symtuza)	• Initiate ***only*** in patients with CrCl ≥30 mL/min [c]. • Carefully consider drug-drug interactions with COBI [Eron(a), et al. 2018]. • Contains 10 mg TAF, boosted [c].	B2
Tenofovir alafenamide/emtricitabine/ elvitegravir/cobicistat [b] (TAF 10 mg/FTC/EVG/COBI; Genvoya)	• Initiate ***only*** in patients with CrCl ≥30 mL/min [c]. • Carefully consider drug-drug interactions with COBI. • Contains 10 mg of TAF, boosted with COBI [b]. • Separate dosing of cation-containing (calcium, aluminum, magnesium) antacids by 2 hours, either before or after dose of EVG.	B1
Tenofovir alafenamide/emtricitabine/ rilpivirine [b] (TAF 25 mg/FTC/RPV; Odefsey)	• Initiate ***only*** in patients confirmed to have a CD4 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 [c]. • Use with caution in patients with depression or a history of suicidality. • To date, no clinical trials have been conducted for initial therapy; 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 [b].	B3
Tenofovir disoproxil fumarate/ lamivudine/doravirine [b] (TDF/3TC/DOR; Delstrigo)	• Initiate ***only*** in patients with CrCl ≥50 mL/min [c]. • Contraindicated when coadministered with drugs that are strong CYP3A enzyme inducers. • Use with caution in patients with or at risk for osteoporosis.	B1
Available as a Multi-Tablet Regimen With Once-Daily Dosing		
Tenofovir alafenamide/emtricitabine *and* doravirine [b] (TAF 25 mg/FTC *and* DOR; Descovy *and* Pifeltro)	• Initiate ***only*** in patients with CrCl ≥30 mL/min [c]. • Contraindicated when coadministered with drugs that are strong CYP3A enzyme inducers.	B2
Available as a Multi-Tablet Regimen With Twice-Daily Dosing		
Tenofovir alafenamide/emtricitabine or tenofovir disoproxil fumarate/ emtricitabine *and* raltegravir [b] (TAF 25 mg/FTC or TDF 300 mg/FTC *and* RAL; Descovy or Truvada *and* Isentress)	• For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min [c]. • For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min [c]. • For TDF/FTC, use with caution in patients with or at risk for osteoporosis. • 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.	B3

Table 2: Alternative Initial ART Regimens for Nonpregnant Adults [a] (listed alphabetically; for specific details, see guideline section Specific Factors to Consider and Discuss With Patients and drug package inserts)		
Tenofovir alafenamide/emtricitabine or tenofovir disoproxil fumarate/ emtricitabine *and* raltegravir HD [b] (TAF 25 mg/FTC or TDF 300 mg/FTC *and* RAL HD; Descovy or Truvada *and* Isentress HD)	• For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min [c]. • Contains 25 mg of TAF, unboosted [b]. • For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min [c]. • For TDF/FTC, use with caution in patients with or at risk for osteoporosis. • Administer as TAF/FTC or TDF/FTC once daily and RAL HD 1,200 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.	A2

Abbreviations: ART, antiretroviral therapy; CrCl, creatinine clearance; CYP, cytochrome P450; DHHS, U.S. Department of Health and Human Services.

Notes:

a. In choosing ART regimens for individuals of childbearing potential, refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
b. Substitutions:
   - In all cases, FTC and 3TC are interchangeable.
   - TAF 10 mg and TAF 25 mg are not interchangeable.
   - COBI and RTV should not be considered interchangeable because of their drug-interaction profiles.
c. For dose adjustments, see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment.

Table 3: Other Initial ART Regimens Not Included as Preferred or Alternative for Nonpregnant Adults [a] (listed alphabetically; for specific details, see guideline section Specific Factors to Consider and Discuss With Patients and drug package inserts)		
Regimen	**Comments**	**Rating**
Available as a Single-Tablet Formulation		
Abacavir/lamivudine/dolutegravir [b] (ABC/3TC/DTG; Triumeq)	• Initiate ***only*** in patients confirmed to be negative for HLA-B*5701. ABC-containing regimens are not recommended for rapid-start or test-and-treat initiation of ART. • Initiate ***only*** in patients with CrCl ≥30 mL/min [d]. • ABC is likely associated with CVD, even among individuals with low-to-moderate atherosclerotic CVD. • 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.	B1
Tenofovir disoproxil fumarate/ emtricitabine/efavirenz [c] (TDF/FTC/EFV; Atripla)	• Initiate ***only*** in patients with CrCl ≥50 mL/min [d]. • Use with caution in patients with depression or a history of suicidality. • Use with caution in patients with or at risk for osteoporosis.	B1

Table 3: Other Initial ART Regimens Not Included as Preferred or Alternative for Nonpregnant Adults [a]
(listed alphabetically; for specific details, see guideline section Specific Factors to Consider and Discuss With Patients and drug package inserts)

Regimen	Comments	Rating
Tenofovir disoproxil fumarate/ emtricitabine/rilpivirine [c] (TDF/FTC/RPV; Complera)	• Initiate ***only*** in patients confirmed to have a CD4 count ≥200 cells/mm^3 *and* HIV RNA level <100,000 copies/mL [e]. • Initiate ***only*** in patients with CrCl ≥50 mL/min [d]. • Use with caution in patients with depression or a history of suicidality. • Contraindicated with PPIs. • Use H_2-blockers with caution and separate dosing by 12 hours. • Must take with food. • Use with caution in patients with or at risk for osteoporosis.	B1
Available as a Multi-Tablet Regimen With Once-Daily Dosing		
Tenofovir alafenamide/emtricitabine *and* efavirenz [c] (TAF 25 mg/FTC *and* EFV; Descovy *and* Sustiva)	• Initiate ***only*** in patients with CrCl ≥50 mL/min [d]. • Use with caution in patients with depression or a history of suicidality. • Contains 25 mg of TAF, unboosted [c].	B3
Available as a Multi-Tablet Regimen With Twice-Daily Dosing		
Tenofovir disoproxil fumarate/ emtricitabine *and* raltegravir [c] (TDF/FTC *and* RAL; Truvada and Isentress)	• Initiate ***only*** in patients with CrCl ≥50 mL/min [d]. • Use with caution in patients with or at risk for osteoporosis. • TDF/FTC once daily and RAL 400 mg twice daily. • Magnesium- or aluminum-containing antacids are contraindicated; calcium-containing antacids are acceptable with RAL.	B1

Abbreviations: ART, antiretroviral therapy; CrCl, creatinine clearance; CVD, cardiovascular disease; DHHS, U.S. Department of Health and Human Services; PPI, proton pump inhibitor..

Notes:

a. In choosing ART regimens for individuals of childbearing potential, refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
b. 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 has been removed. DTG has been shown to be safe throughout pregnancy [Zash, et al. 2022]. See the MCCC's statement on Use of Dolutegravir in Individuals of Childbearing Capacity for further discussion.
c. Substitutions:
   – In all cases, FTC and 3TC are interchangeable.
   – TAF 10 mg and TAF 25 mg are not interchangeable.
   – COBI and RTV should not be considered interchangeable because of their drug-interaction profiles.
d. For dose adjustments, see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment.
e. When a rapid-start or test-and-treat initiation of ART occurs before viral load and CD4 count are available, avoid use of RPV.

General Principles in Choosing an Initial ART Regimen

Goals of ART: The issue of when to start ART was settled with the publication of the START and TEMPRANO studies early in 2015 [Danel, et al. 2015; Lundgren, et al. 2015]. Treatment is now recommended for all individuals with confirmed HIV regardless of CD4 cell count or viral load.

The goal of ART is complete and durable suppression of plasma viremia while minimizing toxicity and maximizing quality of life. Properly selected ART may never require a change or adjustment once started. Treatment interruptions should be avoided [El-Sadr, et al. 2006].

Since the approval of ZDV on March 19, 1987, there have been 30 individual agents approved for the treatment of HIV and 1 pharmacokinetic enhancer or "booster," COBI, which is currently used to enhance the pharmacokinetics of EVG, ATV, or DRV.

RTV at treatment doses is poorly tolerated and is used only at lower doses for pharmacokinetic boosting of PIs. An additional 18 FDA-approved FDCs are also available. These FDCs include STRs, of which there are 9 currently available that provide a complete and effective treatment regimen for HIV that is combined into 1 pill for use in properly selected individuals. The goal of initial therapy is to start a regimen that suits an individual's lifestyle and is appropriate given existing baseline medical comorbidities (see Table 4, below).

Active drugs from 2 different classes: Although regimen options for treatment-naive, nonpregnant adults are constantly evolving, the same general principles that were established with the first effective and durable therapies are still true today [Gulick, et al. 2000]. The backbone of therapy has traditionally been 2 NRTIs paired with 1 of the following: an NNRTI, a boosted PI, or a boosted or unboosted INSTI. In a large meta-analysis, INSTIs were superior to other drug classes as a third drug [Lee, et al. 2014], and DTG may have specific advantages because documented resistance developing in ART-naive patients who initiate DTG-containing regimens is rare [Henegar, et al. 2023; Tao, et al. 2023; Wainberg and Mesplede 2015]. The entry inhibitors and fusion inhibitors are not recommended for initial therapy (see Table 5: Selected Drug-Drug Interactions to Discuss Before Initiating ART in Treatment-Naive Patients), but they may have a role in ART for treatment-experienced patients with extensive drug resistance (see All FDA-Approved HIV Medications, including generic and trade names).

The only 2-drug regimen that this committee recommends for ART initiation is DTG/3TC, although other dual- and even monotherapy regimens have been and continue to be studied [Cahn, et al. 2020; Cahn, et al. 2019; Cahn(a), et al. 2017; Baril, et al. 2016; Maggiolo, et al. 2016; Bedimo, et al. 2014; Cahn, et al. 2014; Raffi, et al. 2014; Taiwo, et al. 2011]. Importantly, use of DTG/3TC is recommended only after the result of HIV resistance and HBV testing are known. Further, this committee recommends against the use of DTG/3TC in patients with relevant NRTI resistance mutations, including the M184V/I mutation.

If DTG/3TC is started in a patient with HBV infection, a third antiviral agent with activity against HBV should be added. Because the Gemini 1 and 2 studies restricted entry to patients with HIV-1 RNA ≤500,000 copies/mL, this committee recommends against use of DTG/3TC in patients with HIV-1 RNA >500,000 copies/mL.

TAF, a prodrug formulation for tenofovir, was developed as an alternative to TDF and has been approved as part of the following STRs:

- TAF 10 mg/FTC/COBI/EVG
- TAF 25 mg/FTC/RPV
- TAF 25 mg/FTC/BIC [FDA 2025; FDA(a) 2024; FDA(b) 2022]
- TAF 10 mg/FTC/COBI/DRV [FDA(b) 2023] and the FDC TAF 25 mg/FTC [FDA(a) 2022]

Oral administration of TAF results in lower circulating levels of tenofovir in plasma and affects markers of renal toxicity and bone mineral density less adversely than does TDF [Mills(a), et al. 2016; Pozniak, et al. 2016; Sax, et al. 2015]. Bioequivalence studies in healthy volunteers show that the TAF 10 mg dose administered with COBI 150 mg is equivalent to the TAF 25 mg dose without COBI [Zack(a), et al. 2016; Zack(b), et al. 2016].

A switch study showed good maintenance of viral suppression when changing from TDF/FTC to TAF 10 mg/FTC if the third drug was a boosted PI, or to TAF 25 mg/FTC if the third drug was an unboosted NNRTI or INSTI [Gallant, et al. 2016]. Note that TAF 10 mg alone and TAF 10 mg/FTC are not currently FDA-approved.

Until further safety data are available, this committee has not included TAF 25 mg/FTC in combination with COBI or RTV as recommended regimens and recommends caution when using TAF 25 mg/FTC with regimens that contain either COBI or RTV in the setting of CrCl <50 mL/min.

COBI-boosted DRV was approved based on bioavailability studies [FDA(a) 2023; Kakuda, et al. 2014]. DRV/COBI has demonstrated comparable efficacy to RTV-boosted DRV in a single-arm study [Tashima, et al. 2014]. However, because randomized clinical trials that compare COBI- versus RTV-boosted DRV are not yet available, it has a lower strength of evidence rating. COBI-boosted ATV showed noninferiority when compared with RTV-boosted ATV with a TDF/FTC backbone in a randomized, double-blind study [Gallant, et al. 2013].

→ KEY POINT

- INSTI-based regimens are generally the best choice for most individuals because of tolerability and durability.

All of the currently recommended preferred regimens have similar virologic efficacy when measured by an "on-treatment" metric, but adherence, the potential for drug interactions, and tolerability under real-life conditions may inform the choice of preferred versus alternative versus other regimens.

The following general conclusions can be drawn based on currently available evidence from several pivotal studies:

- DTG is as efficacious as (i.e., noninferior to) RAL [Raffi, et al. 2013] and superior to both DRV/RTV [Molina, et al. 2014] and coformulated TDF/FTC/EFV [Walmsley, et al. 2015]. DTG was superior at 48 weeks when combined with ABC/3TC as compared to TDF/FTC/EFV [Walmsley, et al. 2013].
- In a study of ART-naive individuals, RAL HD 1,200 mg once daily was noninferior to RAL 400 mg tablets dosed twice daily [Cahn(b), et al. 2017].
- TAF/FTC/COBI/EVG as an STR was noninferior to the STR TDF/FTC/COBI/EVG, with fewer adverse effects on kidney function and bone mineral density [Sax, et al. 2015].
- In 2 separate trials of treatment-naive individuals, TAF/FTC/BIC was noninferior to both TAF/FTC and DTG [Sax, et al. 2017] and ABC/3TC/DTG [Gallant, et al. 2017].
- RPV has equivalent efficacy relative to EFV when baseline viral load is <100,000 copies/mL and is better tolerated [van Lunzen, et al. 2016; Behrens, et al. 2014; Cohen, et al. 2014; Cohen(b), et al. 2013; Cohen, et al. 2012]. But RPV should not be initiated in individuals with baseline viral load >100,000 copies/mL or CD4 counts <200 cells/mm^3.
- In 2 separate trials of treatment-naive individuals, TDF/3TC/DOR was noninferior to TDF/FTC/EFV, or DRV/RTV with either TDF/FTC or ABC/3TC [Orkin, et al. 2019; Molina, et al. 2018].
- DRV/RTV once daily is better tolerated and noninferior to either ATV/RTV or LPV/RTV [Lennox, et al. 2014; Orkin, et al. 2013], although LPV/RTV shows excellent efficacy when combined with either commonly used NRTI backbone [Smith, et al. 2009] and when compared with ATV/RTV [Molina, et al. 2008]. One open-label study using ABC/3TC as the backbone combined with DRV/RTV showed good safety and efficacy [Trottier, et al. 2012].

Table 4: Individual Antiretroviral Medications or Combinations to Avoid in Initial Therapy for Nonpregnant Adults

Antiretroviral Medication	Comments
Abacavir (ABC; Ziagen)	Likely associated with CVD, even among individuals with low-to-moderate risk for atherosclerotic CVD and should be avoided in an initial ART regimen.
Nevirapine (NVP; Viramune)	**Life-threatening rash:** Stevens-Johnson syndrome and toxic epidermal necrolysis are possible.
Etravirine (ETR; Intelence)	ETR does not have an FDA indication in ART-naive patients.
• Maraviroc (MVC; Selzentry) • NRTI-only regimens, either triple or quadruple	Inferior efficacy and durability.
Zidovudine (ZDV; Retrovir)	Not well tolerated because of bone marrow suppression (notably anemia), headache, and myopathies.
Unboosted PIs	Inferior efficacy relative to boosted PIs.
• Fosamprenavir (FPV; Lexiva) • Indinavir (IDV; Crixivan) • Tipranavir (TPV; Aptivus) • Nelfinavir (NFV; Viracept)	Either not well studied or limited by dosing and side effects relative to recommended protease inhibitors.

Abbreviations: ART, antiretroviral therapy; CVD, cardiovascular disease; FDA, U.S. Food and Drug Administration; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor.

General Considerations With Initial ART Regimens

The recommended ART regimens should work well for the majority of patients, but some circumstances may make 1 regimen more favorable than another for a given individual. In general, an INSTI-based regimen will be the best option for most patients [Mills(b), et al. 2016; Lee, et al. 2014]. To date, rare cases of resistance to DTG have been reported in real-world settings [Henegar, et al. 2023] and in individuals naive to INSTI-based regimens [Tao, et al. 2023]. Despite these uncommon instances, DTG remains an excellent choice for ART-naive patients because of its high barrier to resistance, tolerability, and minimal drug-drug interactions [Cevik, et al. 2020; Wainberg and Mesplede 2015]. Regimens containing BIC (as part of TAF/FTC/BIC), DTG, or a boosted PI may be more appropriate when adherence is a concern, given the higher barrier to resistance. Consultation with an experienced HIV care provider is recommended when choosing a regimen for patients with extensive comorbidities, impaired renal function, HBV or HCV coinfection, or very high viral loads.

Early clinical trials in HIV used surrogate markers, such as viral load and CD4 cell count, or clinical endpoints, such as morbidity and mortality, to demonstrate superiority of new therapies over the "gold standard" treatment of the era. One of the trials that led to the 1996 approval of IDV compared IDV alone versus ZDV/3TC versus ZDV/3TC/IDV in ZDV- treatment-experienced patients, given that, at the time, dual NRTI treatment was considered acceptable [Gulick, et al. 1997].

As treatment has evolved and become more effective, the use of clinical end points has become challenging; most trials in the current era of HIV therapy are powered to detect noninferiority when compared with standard of care. For a variety of reasons, including cost and complexity, it would be impractical to conduct head-to-head comparisons of all available regimens. Some STRs and FDCs have been approved primarily based on bioequivalence studies when compared with the individual components, such as TDF/FTC/EFV, ABC/3TC/DTG, TAF/FTC/RPV, TAF/FTC, and DRV/COBI.

Some of the cutoff values used for comparisons, such as viral load <100,000 copies/mL or CD4 count ≥200 cells/mm^3, are somewhat arbitrary. For example, most studies including RPV show that its efficacy is diminished when initiated at viral loads ≥100,000 copies/mL, and 1 study showed that RPV worked less well than EFV-based therapy at a viral load of ≥500,000 copies/mL [Domingo and Ribera 2013].

Some agents have been approved based on noninferiority to the relatively less well-tolerated TDF/FTC/EFV regimen, which is, nevertheless, a potent and effective regimen for those who tolerate it well. The higher prevalence of NNRTI resistance mutations when transmitted drug resistance occurs has prompted most experts to avoid NNRTI-based regimens if treatment is indicated before genotypic resistance testing results are available [Panichsillapakit, et al. 2016; Rhee, et al. 2015; Stekler, et al. 2015]. Although coformulated TAF/FTC/COBI/EVG is approved for use at any starting viral load, reports of failure using TDF/FTC/COBI/EVG, with resistance, have been documented in individuals with very high baseline viral loads >1,000,000 copies/mL [Adams, et al. 2016; Rhee, et al. 2015].

A paucity of data is available demonstrating how different ARV medications perform based on race and gender, although studies have suggested, for instance, that DRV/RTV is less well tolerated in women than in men and that discontinuation of DRV/RTV occurs at a higher rate among Black patients than among others [Smith, et al. 2012; Currier, et al. 2010].

Long-acting injectable therapy: An injectable long-acting formulation of the INSTI CAB and the NNRTI RPV (CAB/RPV LA) has been approved by the FDA as replacement ART for adults and adolescents ≥12 years old who [FDA(b) 2024]:

- Weigh ≥35 kg
- Do not have chronic HBV infection
- Are virally suppressed (HIV-1 RNA level <50 copies/mL) on a stable ART regimen
- Have no history of treatment failure
- Have no known or suspected resistance to either CAB or RPV

The use of CAB/RPV LA as replacement ART in virally suppressed patients engaged in care may be a suitable option for those who would prefer an alternative to daily oral therapy.

There is currently no evidence supporting the use of CAB/RPV LA as initial ART, and it is not FDA-approved for initial ART or individuals with detectable viremia. However, CAB/RPV LA may be considered as an early transition option for patients who are virologically suppressed on their initial oral regimen. Planning an early transition to CAB/RPV LA could potentially improve adherence and motivate patients to continue treatment.

Specific Factors to Consider and Discuss With Patients

Before initiating ART, the following factors are important to consider and discuss with patients.

Age: As individuals with HIV age, they have a higher prevalence of comorbidities than younger patients with HIV and are likely to be on more non–HIV-specific medications, particularly cardiovascular or gastrointestinal agents, posing a higher risk for adverse interactions [Marzolini, et al. 2011]. For individuals older than 50 years, careful regimen selection, with the use of INSTIs when possible rather than cytochrome P450 inhibitors, such as COBI or RTV, can help minimize interactions. In addition, use of TAF rather than TDF can lower the risk of renal and bone toxicity.

Comorbidities: Assessment for existing cardiovascular risk, renal disease, or risk factors for the development of renal disease, hepatic disease, bone health, mental health, and substance use should be performed. Additionally, the risk for greater weight gain and potential exacerbation of metabolic complications with TAF- versus TDF-containing regimens, especially when combined with certain INSTI-based regimens, should be discussed before initiation of ART.

Cost: STRs may be favorable because of the lower copays that could be associated with fewer prescriptions. Conversely, the individual components of these regimens may be available generically as separate pills.

Dosing requirements (daily vs. twice daily): Most patients express a preference for once-daily dosing, especially if they are not taking other medications or are taking other medications that are dosed once daily. If individuals are already taking other medications that are dosed twice daily and report no adherence issues, twice-daily dosing is an acceptable option.

Drug-drug interactions: Because of some key drug-drug interactions, coadministration of some medications is to be avoided (see Table 5, below). For instance, PPIs should not be coadministered with oral RPV; however, injectable RPV can be used with PPIs. Given the availability of over-the-counter PPIs and the possibility that these drugs may be prescribed by a different care provider, this interaction is especially important to discuss with patients. In this case, to avoid unnecessary regimen changes once started, even patients who are not currently taking a PPI should be asked whether they have needed PPIs in the past or may need them in the future. Dose limitations for metformin may also be required when combined with DTG and possibly BIC.

RTV and COBI have many significant interactions, including with cardiac medications. Methadone maintenance requirements may also change with some ARV agents. A detailed review of all of a patient's medications, including over-the-counter medications or supplements, is essential.

Before prescribing an ART regimen, using an automated interaction checker embedded in the electronic medical record or tools such as the following to check for potential drug-drug interactions with currently prescribed medications can help avoid serious problems:

- University of Liverpool HIV Drug Interactions Checker
- NYSDOH AI Resource: ART Drug-Drug Interactions

Table 5: Selected Drug-Drug Interactions to Discuss Before Initiating ART in Treatment-Naive Patients

Drug Class	Drug(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 equivalent 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.

Table 5: Selected Drug-Drug Interactions to Discuss Before Initiating ART in Treatment-Naive Patients	
Drug Class	**Drug(s): Comments**
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	• **ATV:** Contraindicated with ATV in treatment-experienced patients; in treatment-naive patients, use no more than the 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, the 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 an alternative or additional (e.g., barrier) contraceptive methods or choose an 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 the 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.

Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral medication; ATV, atazanavir; BIC, bictegravir; COBI, cobicistat; CrCl, creatinine clearance; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; RAL, raltegravir; RAL HD, RAL high-dose; RPV, rilpivirine; RTV, ritonavir.

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 the package insert for specific ARV for dosing instructions and safety information.

Food requirements: Because an individual may have a strong preference for taking medication with or without food, it is important to discuss which medications must be taken on an empty stomach, which must be taken with food, and which can be taken with or without food, as listed in Box 2, below.

Box 2: Antiretroviral Medications That Can Be Taken With or Without Food, Must Be Taken With Food, or Must Be Taken on an Empty Stomach		
Take With or Without Food	**Take With Food**	**Take on an Empty Stomach**
• 3TC • ABC • DOR • DTG • FTC • RAL • TAF • TDF • DTG/3TC • TAF/FTC/BIC • TAF/FTC/DOR	• ATV/COBI • ATV/RTV • DRV/COBI • DRV/RTV • EVG • RPV • TAF/FTC/EVG/COBI • TAF/FTC/DRV/COBI	• EFV
Abbreviations: 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.		

Known adverse effects and toxicities: Review the known and potential adverse effects in advance.

Number of pills: Some patients feel strongly that the fewer the number of pills, the better. For others, the greatest concern may be the ability to take all pills (regardless of the number) together once daily. Sometimes using individual agents rather than a multi-agent FDC or STR may be attractive depending on pill size. In rare cases, individuals who either cannot or will not swallow pills may need liquid formulations or pill crushing. Table 6, below, presents an abbreviated summary of commonly used ARVs and their availability in liquid formulation and/or the acceptability of crushing or dissolving them before ingestion.

Table 6: Acceptable Alternative Formulations and Methods of Administration of Antiretroviral Medications		
Drug	**Available as Liquid, Powder, or Chewable Tablet?**	**Can Tablet Be Split, Crushed, or Dissolved?**
Single-Table Formulations		
Abacavir/lamivudine/dolutegravir (ABC/3TC/DTG; Triumeq)	No	Probably acceptable to split/crush
Tenofovir alafenamide/emtricitabine/bictegravir (TAF/FTC/BIC; Biktarvy)	No	No data; not recommended
Tenofovir alafenamide/emtricitabine/darunavir/cobicistat (TAF/FTC/DRV/COBI; Symtuza)	No	No data; not recommended
Tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat (TAF/FTC/EVG/COBI; Genvoya)	No	No data; not recommended
Tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV; Odefsey)	No	No data; not recommended
Tenofovir disoproxil fumarate/lamivudine/doravirine (TDF/3TC/DOR; Delstrigo)	No	No data; not recommended
Tenofovir disoproxil fumarate/emtricitabine/efavirenz (TDF/FTC/EFV; Atripla)	No	No data; not recommended
Dolutegravir/lamivudine (DTG/3TC; Dovato)	No	No data; not recommended
Tenofovir disoproxil fumarate/emtricitabine/rilpivirine (TDF/FTC/RPV; Complera)	No	No data; not recommended

Table 6: Acceptable Alternative Formulations and Methods of Administration of Antiretroviral Medications		
Drug	**Available as Liquid, Powder, or Chewable Tablet?**	**Can Tablet Be Split, Crushed, or Dissolved?**
Fixed-Dose Combinations		
Darunavir/cobicistat (DRV/COBI; Prezcobix)	No	No
Tenofovir alafenamide/emtricitabine (TAF/FTC; Descovy)	No	No
Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC; Truvada)	See individual components below	Acceptable to crush or dissolve
Zidovudine/lamivudine (ZDV/3TC; Combivir)	See individual components below	Probably acceptable to split or crush
Individual Drugs		
Abacavir (ABC; Ziagen)	Oral solution (20 mg/mL)	No data
Atazanavir (ATV; Reyataz)	Oral dispersible powder (50 mg/packet)	Okay to open capsule and sprinkle contents
Darunavir (DRV; Prezista)	Oral suspension (100 mg/mL)	Probably acceptable to crush
Doravirine (DOR; Pifeltro)	No	No data
Dolutegravir (DTG; Tivicay)	No	Acceptable to crush
Efavirenz (EFV; Sustiva)	No	No
Elvitegravir (EVG; Vitekta)	No	No data
Emtricitabine (FTC; Emtriva)	Oral solution (10 mg/mL)	Acceptable to open and dissolve in water
Lamivudine (3TC; Epivir)	Oral solution (10 mg/mL)	Acceptable to crush or split
Raltegravir (RAL; Isentress)	Chewable tablet (25 mg, 100 mg); oral powder for suspension (100 mg/packet); neither is bioequivalent to the 400 mg adult dose	Not recommended
Raltegravir HD (RAL HD; Isentress HD)	No	No data; not recommended
Rilpivirine (RPV; Edurant)	No	No data; not recommended
Ritonavir (RTV; Norvir)	Oral solution (80 mg/mL)	No
Tenofovir alafenamide (TAF; Vemlidy)	No	Acceptable to crush
Tenofovir disoproxil fumarate (TDF; Viread)	Oral powder mixed with soft food only (40 mg/1 g)	Acceptable to dissolve in water

Pill size: Use images or real examples to give patients an idea of pill size ***before*** they fill the prescription. TAF/FTC/BIC and TAF/FTC/RPV are the smallest STR pills.

Pregnancy or conception planning: Individuals of childbearing potential should receive a pregnancy test and be assessed for use of contraception. When selecting an initial regimen for those who are not using effective contraception or who are contemplating pregnancy, clinicians should consult DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.

All patients should be assessed for conception plans, which also provides an opportunity to discuss PrEP for partners without HIV. Additionally, all individuals with HIV should be informed that maintaining a plasma HIV RNA level of <200 copies/mL with ART prevents sexual transmission of HIV to their partners.

Special Considerations for Comorbid Conditions

Bone disease: TDF causes a decrease in bone mineral density in all patients after initiation of ART and should be used with caution in patients with or at risk for osteoporosis [McComsey, et al. 2011; Stellbrink, et al. 2010; Perrot, et al. 2009]. Some experts recommend baseline bone densitometry screening for osteoporosis in postmenopausal women and in men and transgender women older than 50 years who have HIV [Aberg, et al. 2014]. The TAF formulation available currently in TAF/FTC, TAF/FTC/EVG/COBI, TAF/FTC/BIC, TAF/FTC/RPV, and TAF/FTC/DRVc is an alternative, with lower markers of bone turnover in clinical trials [Bonora, et al. 2016; Pozniak, et al. 2016].

Cardiovascular risks: COBI- or RTV-containing regimens typically elevate lipids; TAF and certain INSTIs can cause greater weight gain than other ART regimens, with the potential for increased risk of metabolic complications [Łomiak, et al. 2021; Surial, et al. 2021; Bourgi(a), et al. 2020; Bourgi(b), et al. 2020; Calmy, et al. 2020; Lake, et al. 2020; Sax, et al. 2020; Venter, et al. 2020; Venter, et al. 2019]. TDF-containing regimens can have a beneficial effect on lipids [Souza, et al. 2013].

Recent studies, including the large-scale REPRIEVE trial, have strengthened the association between ABC use and increased cardiovascular disease (CVD) risk in people with HIV [Fichtenbaum, et al. 2024; Jaschinski, et al. 2023; Varriano, et al. 2021; Dorjee, et al. 2018]. The REPRIEVE study found a 37% higher risk of major adverse cardiovascular events in participants using ABC-containing regimens, even though participants were at low risk for CVD and had normal kidney function. This is consistent with other studies showing increased CVD incidence with ABC use [Marcus, et al. 2016; Choi, et al. 2011; Obel, et al. 2010; Sabin, et al. 2008; SMART/INSIGHT and D:A:D Study Groups 2008]. Although some earlier studies did not confirm this association [Ding, et al. 2012; Bedimo, et al. 2011], the preponderance of recent evidence, including meta-analyses [Dorjee, et al. 2018], supports a link between ABC use and increased cardiovascular risk. Given this evidence, ABC should be avoided in an initial ART regimen.

Liver disease: In patients with existing liver disease of any etiology, dose adjustment of ARVs may be required depending on the severity of hepatic impairment (see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment).

Mental health and substance use: Factors that may influence adherence should be addressed. There are also potential interactions between illicit (e.g., methamphetamine) and licit substances (e.g., methadone) and ARVs [Kumar, et al. 2015].

→ KEY POINT

- 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.

Renal function: TDF can cause renal tubular dysfunction, such as acquired Fanconi syndrome [Zimmermann, et al. 2006; Karras, et al. 2003]. The risk of renal impairment is elevated in patients with preexisting renal disease, longer treatment duration, low body weight, and when used in conjunction with RTV- or COBI-boosted regimens [Mocroft, et al. 2016; Gervasoni, et al. 2013]. In general, full-dose TDF should be used with caution in patients with baseline CrCl <70 mL/min and should be adjusted or changed to an alternative agent if CrCl decreases to <50 mL/min; TAF is a better choice in these patients. As noted above, TAF 25 mg/FTC should be used with caution in boosted regimens when CrCl is <50 mL/min.

Both ATV/RTV and LPV/RTV have also been independently associated with a greater decrease in renal function over time than NNRTI-based regimens [Quesada, et al. 2015; Goicoechea, et al. 2008]. COBI, and to a lesser extent DTG, can inhibit the excretion of creatinine, with expected elevations of creatinine at therapy initiation. However, such increases are not clinically relevant and do not significantly affect the glomerular filtration rate [Lepist, et al. 2014; Koteff, et al. 2013; German(a), et al. 2012].

TAF/FTC/BIC can be used in patients on hemodialysis, with administration after dialysis on dialysis days [Eron, et al. 2025; FDA(a) 2024; Sidman and Ondrush 2023]. For patients who cannot take TAF/FTC/BIC, alternatives include RAL or a boosted PI with renally adjusted 3TC and either ABC or once-weekly TDF. Although DTG is highly bound to plasma proteins and unlikely to be removed by dialysis, data in the dialysis population remain limited [FDA(c) 2024]. Additional information on prescribing

agents for patients with reduced renal function is available in the guideline section ARV Dose Adjustments for Hepatic or Renal Impairment.

→ KEY POINTS

- Both COBI and DTG can cause decreased tubular excretion of creatinine and may cause a slight increase in measured creatinine.
- Although no clear causal link has been established, ABC use has been associated with an increased risk of adverse cardiovascular events in multiple studies, including large cohorts and clinical trials, and should be avoided in an initial ART regimen.
- Boosted PIs and COBI-boosted EVG are associated with a higher incidence of hyperlipidemia than unboosted INSTIs.
- 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

Baseline CD4 cell count: Some regimens should not be used when the CD4 count is <200 cells/mm^3 because of an increased risk of treatment failure (see Table 7, below).

Baseline HIV genotypic resistance profile: Genotypic resistance testing that includes the protease, reverse transcriptase, and integrase genes should be obtained at diagnosis (or initial visit if not done previously), but ART initiation should not be delayed pending the results [Kuritzkes, et al. 2008; Borroto-Esoda, et al. 2007].

Transmitted integrase resistance was identified in 0.7% of genotypic resistance tests obtained within 3 months of HIV diagnosis from 2013 to2017 in New York State [Wang, et al. 2019]. Similarly, 0.8% of baseline genotypic resistance tests across 23 U.S. jurisdictions of the CDC reported INSTI resistance, which had a higher prevalence (1.6%) in metropolitan areas (population 50,000 to 500,000) [McClung, et al. 2022]. Although INSTI resistance overall remains rare, most experts believe that transmission of INSTI resistance will increase over time, given that this class of ARV has become the preferred therapy for ART initiation (including rapid ART initiation) in all major guidelines.

Consultation with a care provider experienced in ART management is warranted when patients have baseline resistance that requires treatment with a regimen other than the listed preferred or alternative regimens. If treatment is indicated before genotypic resistance testing results are available, NNRTI-based regimens should be avoided because of the higher prevalence of transmitted resistance in NNRTIs than in PIs or INSTIs [Panichsillapakit, et al. 2016; Rhee, et al. 2015; Stekler, et al. 2015]. In the case of, for example, a patient with symptomatic acute HIV or advanced HIV with an opportunistic infection, some experts would include a second-generation INSTI (DTG or BIC or boosted DRV, or both together) with the NRTI backbone, given the possibility of transmitted NRTI resistance, with possible simplification once genotypic information is available.

Baseline viral load: Some regimens should not be used when the HIV RNA level is ≥100,000 copies/mL (see Table 7, below, and comments in the tables of preferred and alternative ART regimens).

Coinfections: Patients should be assessed for chronic HBV, HCV coinfection, and TB. The ART regimen for individuals with chronic HBV should treat both HIV and HBV when possible. For those planning concurrent HCV treatment or treatment for active TB, drug-drug interactions will play an important role in the selection of a regimen. The University of Liverpool HEP Drug Interactions Checker is a useful resource for identifying drug-drug interactions.

Creatinine clearance level: Some ARVs are contraindicated below a given CrCl level, and some may need adjustments that require the use of individual elements of an FDC or STR rather than the single-tablet version of the drug (see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment).

Hepatic profile: Some ARVs require dose adjustment in the presence of impaired liver function; patients with abnormal liver enzyme levels or evidence of decreased synthetic function should be assessed for underlying liver disease (see guideline sections Special Considerations for Comorbid Conditions and ARV Dose Adjustments for Hepatic or Renal Impairment).

→ KEY POINTS

- When initiating ART at the time of HIV diagnosis (rapid start), it is not necessary to have the results of baseline laboratory tests immediately available. Laboratory tests, as indicated below, 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.

HLA-B*5701 testing: To avoid potentially serious or life-threatening hypersensitivity reactions, HLA-B*5701 testing is mandatory before initiating ART that includes ABC [Mallal, et al. 2008; Saag, et al. 2008].

Initiation of the regimens listed in Table 7, below, is contraindicated based on the listed baseline laboratory parameters.

Table 7: ART Regimens That Are Not Recommended Based on Routine Baseline Laboratory Parameters [a]

Laboratory Parameter	ART Regimens That Are Not Recommended
HIV RNA level ≥100,000 copies/mL	• TAF/FTC/RPV (Odefsey) • TDF/FTC/RPV (Complera)
CD4 count <200 cells/mm^3	• TAF/FTC/RPV (Odefsey) • TDF/FTC/RPV (Complera)
CrCl <50 mL/min	• ABC/3TC/DTG (Triumeq) • TDF/3TC/DOR (Delstrigo) • TDF/FTC/EFV (Atripla) • TDF/3TC/EFV (Symfi and Symfi Lo) • TDF/FTC/RPV (Complera)
CrCl <30 mL/min	• TAF/FTC (Descovy) • TAF/FTC/BIC (Biktarvy) [b] • TAF/FTC/DRV/COBI (Symtuza) • TAF/FTC/EVG/COBI (Genvoya) [b] • TAF/FTC/RPV (Odefsey) • TDF/FTC (Truvada) • DTG/3TC (Dovato)

Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; ATV, atazanavir; BIC, bictegravir; COBI, cobicistat; CrCl, creatinine clearance; 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.

Notes:

a. For renal adjustment of fixed-dose combinations and single-tablet regimens while on therapy, see guideline section ARV Dose Adjustments for Hepatic or Renal Impairment.
b. Unless CrCl <15 mL/min and on chronic hemodialysis.

ARV Dose Adjustments for Hepatic or Renal Impairment

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Integrase Strand Transfer Inhibitors				
Abacavir/dolutegravir/ lamivudine (ABC/DTG/3TC; Triumeq)	**Child-Pugh A, B, C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **ABC:** No renal dose adjustment is needed. • **DTG:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30–49 mL/min:** 150 mg once daily – **CrCl 15–29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5–14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily	• **CrCl >30 mL/min:** Limited data to support use of FDC; 21 patients with CrCl >30 mL/min received full dose 3TC with minimal increases in AUC. No elevations in lactate or other ADRs reported [Fischetti, et al. 2018]. • **CrCl <30 mL/min, without HD:** Renal adjustment should be based on individual components; 13 patients with CrCl <30 mL/min not on HD received 100–150 mg of 3TC with minimal increases in AUC. No elevations in lactate or other ADRs reported [Fischetti, et al. 2018]. • **CrCl <30 mL/min, with HD:** Limited data to support use of FDC. Case series evaluating safety and efficacy of FDC in 9 patients with end-stage renal disease on HD reported viral suppression achieved in all 9 patients. No change in immune function. FDC generally well tolerated; 1 patient complained of nausea, which resolved without drug discontinuation [Michienzi, et al. 2019]. • **Note:** DTG serum concentrations appear to be reduced in uninfected healthy controls with eGFR <30 mL/min/m^2 compared to those with normal kidney function. This may increase the risk of therapeutic failure among patients with HIV drug resistance to INSTIs [FDA(c) 2024].

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Bictegravir/emtricitabine/ tenofovir alafenamide [b] (BIC/FTC/TAF; Biktarvy)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **BIC:** No renal adjustment is needed. • **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **CrCl 15–29 mL/min:** No BIC dose adjustment is needed. In a study of 10 patients with CrCl 15–29 mL/min compared to 8 patients with normal renal function who received a single dose of BIC 75 mg, severe renal impairment did not produce clinically relevant changes in BIC exposure [Zhang, et al. 2017].
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF; Stribild)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data; do not use.	• **CrCl <70 mL/min:** Do not initiate therapy. • **Drop in CrCl to <50 mL/min during treatment:** Discontinue therapy.	• **EVG:** No renal dose adjustment is needed. • **EVG/COBI:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30–49 mL/min:** 300 mg every 48 hours – **CrCl 10–29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	• **CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **EVG/COBI:** Dose adjustment not warranted. In 12 patients with eGFR <30 mL/min/m^2 (not on HD) and 12 controls with normal renal function given 7 days of EVG/COBI, lower EVG AUC, C_{max}, and C_{min} values and higher COBI AUC, C_{max}, and C_{min} values were observed in severe renal impairment, but values were not considered clinically relevant [German(b), et al. 2012].

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide [b] (EVG/COBI/FTC/TAF; Genvoya)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **EVG:** No renal dose adjustment is needed. • **EVG/COBI:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed. – **ESRD, with HD:** 1 tablet once daily; administer after HD on HD days.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <15 mL/min, with HD:** In a study of 55 patients on FDC for up to 96 weeks, 18 (33%) had grade 3 or higher ADR during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Dolutegravir/lamivudine (DTG/3TC; Dovato)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **DTG:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30–49 mL/min:** 150 mg once daily – **CrCl 15–29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5–14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily	**CrCl <50mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.
Dolutegravir/rilpivirine (DTG/RPV; Juluca)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data; do not use.	**CrCl <30 mL/min or ESRD:** No dose adjustment is needed; increased monitoring is recommended.	—	—

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment[a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Non-Nucleoside Reverse Transcriptase Inhibitor				
Emtricitabine/rilpivirine/ tenofovir alafenamide (FTC/RPV/TAF; Odefsey) [b]	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **RPV:** No renal dose adjustment needed. • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **CrCl <30 mL/min, with HD:** 1 FDC tablet once daily. On HD days, administer after dialysis [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Doravirine/lamivudine/ tenofovir disoproxil fumarate (DOR/3TC/TDF; Delstrigo)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **DOR:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30–49 mL/min:** 150 mg once daily – **CrCl 15–29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5–14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily • **TDF:** – **CrCl 30–49 mL/min:** 300 mg every 48 hours – **CrCl 10–29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Efavirenz/lamivudine/ tenofovir disoproxil fumarate (EFV/3TC/TDF; Symfi Lo)	• **Child-Pugh A:** No dose adjustment is needed. • **Child-Pugh B, C:** No data; do not use.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **EFV:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30–49 mL/min:** 150 mg once daily – **CrCl 15–29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5–14 mL/min:** 150 mg first dose, then 50 mg once daily • **TDF:** – **CrCl 30–49 mL/min:** 300 mg every 48 hours – **CrCl 10–29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.
Efavirenz/emtricitabine/ tenofovir disoproxil fumarate (EFV/FTC/TDF; Atripla)	• **Child-Pugh A:** No dose adjustment is needed. • **Child-Pugh B, C:** No data; do not use.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **EFV:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30–49 mL/min:** 300 mg every 48 hours – **CrCl 10–29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Protease Inhibitor				
Darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF; Symtuza) [b]	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **DRV; DRV/COBI:** No renal dose adjustment required unless when combined with TDF. Renal dose adjustment for CrCl <70 mL/min is recommended when combined with TDF. • **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <30mL/min, with HD:** 1 FDC tablet once daily. On HD days, administer after dialysis [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors				
Emtricitabine/tenofovir alafenamide (FTC/TAF; Descovy)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <30 mL/min, with HD:** 1 FDC once daily. On HD days, administer after HD [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].

Table 8: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment[a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Emtricitabine/tenofovir disoproxil fumarate (FTC/TDF; Truvada)	**Child-Pugh A, B, C:** No dose adjustment is needed.	• **CrCl 30–49 mL/min:** FTC 200 mg/TDF 300 mg every 48 hours • **CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30–49 mL/min:** 200 mg every 48 hours – **CrCl 15–29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30–49 mL/min:** 300 mg every 48 hours – **CrCl 10–29 mL/min:** 300 mg every 72 to 96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Abbreviations: ADR, adverse drug reaction; AUC, area under the curve; C_{max}, maximum plasma concentration; C_{min}, minimum plasma concentration; CrCl, creatinine clearance; FDC, fixed-dose combination; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HD, hemodialysis; INSTI, integrase strand transfer inhibitor.

Notes:

a. Per package inserts; see links.
b. Per package inserts, FTC can be used at standard dose in FDCs that contain FTC/TAF when CrCl is >30 mL/min. FTC as an individual component requires renal dose adjustment when CrCl is <50 mL/min.

Other ARVs, not included above:

- Tenofovir disoproxil fumarate/emtricitabine/rilpivirine (TDF/FTC/RPV; Complera):
  - Renal dose adjustment: CrCl <50 mL/min: Do not use.
  - Hepatic dose adjustment: Child-Pugh A, B—no adjustment; Child-Pugh C—no data.
- Atazanavir (ATV; Reyataz):
  - Renal dose adjustment: No adjustment, but use only 300 mg dose with 100 mg RTV; do not use in treatment-experienced patients on HD.
  - Hepatic dose adjustment: Child-Pugh A, B—no adjustment; Child-Pugh C—no data.
- Atazanavir/cobicistat (ATV/COBI; Evotaz):
  - Renal dose adjustment: Do not use in patients with CrCl <70 mL/min taking a TDF-containing regimen; do not use in treatment-experienced patients on HD.
  - Hepatic dose adjustment: No data; not recommended.
- Raltegravir (RAL; Isentress):
  - Renal dose adjustment: None.
  - Hepatic dose adjustment: 400 mg twice daily: Child-Pugh A, B—no adjustment; Child-Pugh C—no data. 600 mg once daily: No data; use with caution.

DRUG MANUFACTURER PACKAGE INSERTS

Atripla: FDA. Atripla (efavirenz, emtricitabine, and tenofovir disoproxil fumarate) tablets, for oral use. 2019 Oct. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021937s044lbl.pdf [accessed 2024 Oct 15]

Biktarvy: FDA. Biktarvy (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. 2024 Oct. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/210251Orig1s020lbl.pdf [accessed 2024 Oct 15]

Complera: FDA. Complera (emtricitabine, rilpivirine, tenofovir disoproxil fumarate) tablets, for oral use. 2019 Nov. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202123s031lbl.pdf [accessed 2024 Oct 15]

Delstrigo: FDA. Delstrigo (doravirine, lamivudine, and tenofovir disoproxil fumarate) tablets, for oral use. 2024 Nov. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/210807s013lbl.pdf [accessed 2024 Oct 15]

Descovy: FDA. Descovy (emtricitabine and tenofovir alafenamide) tablets, for oral use. 2022 Jan. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208215s020lbl.pdf [accessed 2024 Oct 15]

Dovato: FDA. Dovato (dolutegravir and lamivudine) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/211994s021lbl.pdf [accessed 2024 Oct 15]

Evotaz: FDA. Evotaz (atazanavir and cobicistat) tablets, for oral use. 2023 May. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/206353s008lbl.pdf [accessed 2024 Oct 15]

Genvoya: FDA. Genvoya (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets, for oral use. 2022 Jan. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/207561s029lbl.pdf [accessed 2024 Oct 15]

Isentress: FDA. Isentress (raltegravir) tablets, for oral use. 2021 May. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022145s044,203045s017,205786s009lbl.pdf [accessed 2024 Oct 15]

Juluca: FDA. Juluca (dolutegravir and rilpivirine) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/210192s014lbl.pdf [accessed 2024 Oct 15]

Odefsey: FDA. Odefsey (emtricitabine, rilpivirine, and tenofovir alafenamide) tablets, for oral use. 2025 Feb. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/208351s014s015lbl.pdf [accessed 2024 Oct 15]

Reyataz: FDA. Reyataz (atazanavir) capsules, for oral use. 2024 Dec. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021567s049,206352s011lbl.pdf [accessed 2024 Oct 15]

Stribild: FDA. Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate) tablets, for oral use. 2021 Sep. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/203100s036lblet.pdf [accessed 2024 Oct 15]

Symfi Lo: FDA. Symfi lo (efavirenz, lamivudine, and tenofovir disoproxil fumarate) tablets, for oral use. 2019 Oct. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208255s008lbl.pdf [accessed 2024 Oct 15]

Symtuza: FDA. Symtuza (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets, for oral use. 2023 Mar. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/210455s023lbl.pdf [accessed 2024 Oct 15]

Tivicay: FDA. Tivicay (dolutegravir) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/204790s031,213983s004lbl.pdf [accessed 2024 Oct 15]

Triumeq: FDA. Triumeq (abacavir, dolutegravir, and lamivudine) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/205551s032,215413s003lbl.pdf [accessed 2024 Oct 15]

Truvada: FDA. Truvada (emtricitabine and tenofovir disoproxil fumarate) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021752s064lbl.pdf [accessed 2024 Oct 15]

All Recommendations

☑ ALL RECOMMENDATIONS: SELECTING AN INITIAL ART REGIMEN

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 regimen options and engage in shared decision-making to optimize the likelihood of adherence. (A3)
  - Assess for comorbidities and chronic coadministered 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)
  - Recommend an STR 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 [a] and discuss the use of contraception. (A3)
- 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 HBV status are known. (A1)
  - Genotypic resistance testing results have confirmed that a patient does not have a relevant 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; HBV or HCV coinfection; or active opportunistic infections. (B3)
  - The NYSDOH Clinical Education Initiative provides access to HIV specialists through their toll-free line: 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)

Note:

a. In choosing an initial ART regimen for a patient who is pregnant or planning a pregnancy, refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.

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Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B: Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.