Selecting an Initial ART Regimen

Medical Care Criteria Committee, updated June 2018

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Purpose of this Guideline

Medical Care Criteria Committee, updated June 2018

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

- Provide a clear and concise roadmap to choosing from among several equally efficacious ART regimens based on individual patient characteristics and preferences.
- Provide a list of regimens to avoid.
- Provide dosing considerations for patients 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 managing patients with extensive co-morbidities.
- Integrate current evidence-based clinical recommendations into the healthcare-related implementation strategies of the Ending the Epidemic (ETE) initiative, which seeks to end the AIDS epidemic in NYS by the end of 2020.

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

**Introduction:** The New York State (NYS) Department of Health (DOH) AIDS Institute (AI) Medical Care Criteria Committee (MCCC) recommendations for prescribing antiretroviral therapy (ART) regimens for treatment-naïve, nonpregnant adults (age ≥18 years) with HIV-1 infection and without acquired resistance are based on a comprehensive review of available clinical trial data. (For guidelines specific to treatment of adolescents with HIV, please consult Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV at AIDSinfo.gov.) 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 patients to manage. 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 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 tenofovir disoproxil fumarate (TDF) and the conflicting data on cardiac risk with abacavir (ABC); see Specific Factors to Consider and Discuss with Patients.
**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, please refer to the DHHS guideline, Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1–Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. Please refer to the NYSDOH AI guideline HIV-2 Infection for recommendations regarding treatment of HIV-2 infection. For recommendations regarding second-line regimens, please refer to the DHHS guideline on management of the treatment-experienced patient.

For the NYSDOH definition of “experienced HIV care provider,” see HIV Care Provider Definitions.

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### Updates to this Guideline

**June 2018**

**Available Antiretroviral Agents: Single-Tablet Regimens versus Multi-Tablet Regimens**

- Bictegravir (BIC; Biktarvy) added as a preferred initial ART regimen for patients with CrCl > 30 mL/min, with related updates throughout all sections of the guideline.
- New footnote (6) added to all regimen tables: "When a ‘rapid start’ or ‘test and treat’ initiation of ART occurs before baseline laboratory test results are available, avoid use of abacavir until a patient’s HLA-B*5701 is confirmed negative.”

**General Principles in Choosing an Initial ART Regimen**

- New citations of evidence added to general conclusions that can be drawn based on currently available evidence: 1) “In a study of ART-naïve patients RAL HD 1200 mg once daily was non-inferior to 400 mg tablets dosed twice daily [Cahn et al. 2017]”; and 2) “In two separate trials of treatment-naïve individuals, TAF/FTC/BIC was non-inferior to both TAF/FTC and DTG [Sax et al. 2017] and ABC/3TC/DTG [Gallant J et al. 2017].”

**May 2018**

Changes made in the Available ART Regimens section in May 2018 are described below.

**Added the following note at the beginning of the section:**

**Dolutegravir (DTG) Safety Statement, May 2018**

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

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

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

**Revised the sixth recommendation:**

- Clinicians should:
  - Ask women and men about their reproductive plans and discuss the use of contraception (AIII). Refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential who are not using effective contraception: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1–Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States
Table 1. Preferred Initial ART Regimens for Non-Pregnant Adults:
- To all dolutegravir-containing regimens, added the following comment: Clinicians should refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1–Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.

Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults:
- To all dolutegravir-containing regimens, added the following comment: Clinicians should refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1–Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.

Table 3. Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults:
- To all efavirenz-containing regimens, added the following comment: Clinicians should refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1–Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.

November 2017
Changes made in the Available ART Regimens section in November 2017 are described below.

Revisions:
- Revised the fifth recommendation to add active opportunistic infections to the list of extensive comorbidities that should prompt consultation with a care provider experienced in ART management when selecting an initial ART regimen.
- Revised text to state that with full adherence, any of the preferred or alternative regimens should lead to full suppression, including MTRs, which can be used when an STR is not possible or not tolerated. For example, a patient who is HLA-B*5701 positive on medications that have significant drug interactions with cobicistat and who did not tolerate DTG could use TAF/FTC with RAL.

Table 1: Preferred Initial ART Regimens for Non-Pregnant Adults
- Added the regimen “Tenofovir alafenamide/emtricitabine and raltegravir (TAF 25 mg/FTC and RAL HD; Descovy and Isentress HD)” to the “Available as Multi-Tablet Regimens with Once-Daily Dosing” section of table 1.
- Added footnote 5: “When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg.”

Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults
- Moved the regimen “Tenofovir disoproxil fumarate/emtricitabine and raltegravir (TDF/FTC and RAL HD; Truvada and Isentress HD)” to the “Available as Multi-Tablet Regimen with Once-Daily Dosing” section of table 2.
- The rating was changed from a BI to BIII for the regimen “Tenofovir alafenamide/emtricitabine and raltegravir (TAF 25 mg/FTC and RAL; Descovy and Isentress)” in the “Available as Multi-Tablet Regimen with Twice-Daily Dosing” section of table 2.
- Added footnote 5: “For once daily dosing of RAL, use the HD formulation dosed at 1200 mg (2 x 600 mg tablets).”

Table 3: Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults:
- Moved the regimen “Abacavir/lamivudine and raltegravir (ABC/3TC and RAL HD; Epzicom and Isentress HD)” to the “Available as Multi-Tablet Regimen with Once-Daily Dosing” section of table 3.
- Added footnote 5: “For once daily dosing of RAL, use the HD formulation dosed at 1200 mg (2 x 600 mg tablets).”
Available ART Regimens
Medical Care Criteria Committee, updated June 2018

Note: The recommendations in this guideline pertain to initial antiretroviral therapy (ART) regimens for adults with HIV infection who are not pregnant.

Dolutegravir (DTG) Safety Statement, May 2018

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

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

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

RECOMMENDATIONS
Available ART Regimens

▪ Clinicians should involve their patients when deciding which ART regimen is most likely to result in patient adherence. (A3)
▪ Clinicians should perform the following when initiating ART:
  ▫ Assessment for comorbidities that may affect the choice of regimen for initial therapy (A3)
  ▫ Genotypic resistance testing for the protease and reverse transcriptase genes at diagnosis or at the initial visit if not done previously (A2)
    ▫ See Specific Factors to Consider and Discuss with Patients
▪ Baseline testing is not recommended for either integrase resistance or tropism. (A3)
▪ For patients who have delayed initiation of ART and have engaged in high-risk behaviors associated with acquisition of HIV superinfection, genotypic resistance testing should be repeated before choosing the ART regimen. (B3)
▪ Clinicians should consult with a care provider experienced in ART management when:
  ▫ Baseline resistance requires treatment with a regimen other than the listed preferred or alternative regimens (A3)
  ▫ Selecting a regimen for patients with extensive comorbidities (B3), impaired renal function (B3), HBV or HCV co-infections (B3), active opportunistic infections (B3), or very high viral loads (B3)
▪ Clinicians should:
  ▫ Ask individuals about their reproductive plans and discuss the use of contraception (A3)
  ▫ Refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.
▪ A single-tablet regimen or regimen with once-daily dosing is preferred unless contraindicated by drug-drug interactions, intolerance, allergy, or access. (A2)
▪ For ART-naive patients, clinicians should: (A1)
  ▫ Select an initial ART regimen that is preferred; see Table 1. Preferred Initial ART Regimens for Non-Pregnant Adults
  ▫ Select an alternative or other regimen only when a preferred initial regimen cannot be used; see Table 2. Alternative Initial ART Regimens for Non-Pregnant Adults or Table 3. Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults
**RECOMMENDATIONS continued**

Available ART Regimens, continued

- Two-drug regimens are not recommended as initial therapy. (A2)
- Clinicians or clinical staff should follow up, by telephone or other methods, within 2 weeks after treatment initiation to assess tolerance and adherence. Adherence should be reinforced at regular intervals. (A3)
- Clinicians should obtain a viral load test within 4 weeks after initiation to assess response to therapy. (A3)
  - See NYSDOH AI guideline *Virologic and Immunologic Monitoring > Viral Load*

Available Antiretroviral Agents and Regimens

Each regimen listed below in Tables 1 and 2, preferred and alternative initial ART regimens, and in Table 3, *Other ART Regimens, Not Preferred or Alternative*, is expected to have excellent efficacy, but they differ in tolerability, possible toxicities, convenience, and the potential for drug–drug interactions, all of which can affect overall adherence and suppression rates.

**KEY POINT**

- In general, a preferred regimen should be selected (Table 1, below), although there may be times when an alternative regimen may be a better choice for an individual patient (Table 2, below).

Based on renal and bone mineral density data from randomized trials of tenofovir alafenamide/emtricitabine/cobicistat/elvitegravir (TAF/FTC/COBI/EVG) versus tenofovir disoproxil fumarate/emtricitabine/cobicistat/elvitegravir (TDF/FTC/COBI/EVG) in ART-naïve patients or previously suppressed patients on TDF/FTC/COBI/EVG [Sax et al. 2015; Mills et al. 2016a; Pozniak et al. 2016], this Committee recommends TAF over TDF as part of the backbone in preferred regimens. These data, combined with bioequivalence and switch studies [Zack et al. 2016a; Zack et al. 2016b], provide support for the use of TAF/FTC rather than TDF/FTC when combined with dolutegravir (DTG) or raltegravir (RAL) as part of a preferred regimen. In a study of ART-naïve patients RAL HD 1200 mg once daily was non–inferior to 400 mg tablets dosed twice daily and is thus preferred [Cahn et al. 2017]. This Committee does not yet recommend TAF/FTC in combination with boosted protease inhibitors (PIs), as noted below (see Specific Factors to Consider and Discuss with Patients). TDF-containing regimens remain safe and efficacious as alternative regimens (Table 2, below). An integrase strand transfer inhibitor (INSTI) as the third drug is preferred over PIs and non–nucleoside reverse transcriptase inhibitors (NNRTIs) based on tolerability and a lower incidence of drug–drug interactions. Because the use of tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV) is limited by viral load and CD4 parameters and is contraindicated with proton–pump inhibitors (PPIs), this regimen is listed as an alternative regimen (Table 3, below).

Efavirenz (EFV)-containing regimens (see Table 3, below), although efficacious, have been shown to be less well–tolerated than the preferred or alternative regimens in Tables 1 and 2, below. Lopinavir/ritonavir (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.

When initiating ART at the time of diagnosis (i.e., “rapid start” or “test and treat”), avoid regimens containing abacavir unless results of HLA B*5701 testing are known to be negative. Similarly, rilpivirine is not appropriate for patients whose viral load has not been confirmed to be <100,000 copies/mL and CD4 count confirmed to be ≥200 cells/mm³.

Initial regimens should be selected on the basis of patient preferences and clinical characteristics, and a preferred regimen should be used whenever possible (Table 1, below). Regimens in the tables below are listed alphabetically.

(For more information, including drug trade names, see All FDA-Approved HIV Medications.)

**Single-Tablet Regimens versus Multi-Tablet Regimens**

The advantages of single–tablet regimens (STR) compared with multi–tablet regimens (MTR) include simplicity, convenience, and lower chance of selective non–adherence [Gardner et al. 2008]. A recent meta–analysis demonstrated that STR regimens had better adherence rates when compared with MTRs of any frequency (daily...
or twice daily) and had higher 48-week viral suppression rates with comparable side 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–based INSTI therapy was more durable [Mills et al. 2016b]. In the same study, STR for NNRTI–based therapy led to greater rates of suppression than MTR NNRTI therapy [Mills et al. 2016b]. Other studies have demonstrated better efficacy and adherence, lower costs to patients, and fewer hospital admissions associated with single–tablet regimens [Mills et al. 2016b; Armstrong et al. 2015; Sweet et al. 2014; Hanna et al. 2014; Cohen et al. 2013; Raboud et al. 2011; Bangalore et al. 2007; Maggiolo et al. 2015; Colombo et al. 2013; Griffith et al. 2016; Nachega et al. 2014]. Another study examined once–daily dosing of LPV/RTV and found better adherence than with twice–daily dosing [Molina et al. 2007].

There are three STRs listed as preferred regimens, ABC/3TC/DTG, TAF/FTC/COBI/EVG, and TAF/FTC/bictegrevir (BIC). It is possible that these regimens may contain one or more components that are not appropriate for the individual patient, do not allow for adjustment of individual components for renal function, have significant 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, including 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. (For more detailed instructions on dosage adjustments for impaired renal function, see Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment.)

Table 1, below, 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 insert for the drugs listed below.

<table>
<thead>
<tr>
<th>Table 1: Preferred Initial ART Regimens for Non–Pregnant Adults</th>
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<tr>
<td>(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)</td>
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<tr>
<td><strong>Regimen</strong></td>
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<tr>
<td>Abacavir/lamivudine/ dolutegravir (ABC/3TC/DTG; Triumeq)</td>
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<tr>
<td>Tenofovir alafenamide/ emtricitabine/bictegrevir (TAF 25 mg/FTC/BIC; Biktarvy)</td>
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<tr>
<td>Tenofovir alafenamide/ emtricitabine/cobicistat/ elvitegravir (TAF 10 mg/FTC/COBI/EVG; Genvoya)</td>
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Table 1: Preferred Initial ART Regimens for Non-Pregnant Adults, Continued
(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
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</thead>
</table>
| Tenofovir alafenamide/emtricitabine and dolutegravir (TAF 25 mg/FTC and DTG; Descovy and Tivicay) | • Initiate only in patients with CrCl ≥30 mL/min.  
• Documented DTG resistance after initiation in treatment-naive patients is rare.  
• Contains 25 mg of TAF, unboosted.  
• Clinicians should refer to the DHHS Perinatal Guideline when choosing an initial regimen for individuals of childbearing potential. | A1 |
| Tenofovir alafenamide/emtricitabine and raltegravir (TAF 25 mg/FTC and RAL HD; Descovy and Isentress HD) | • Initiate only in patients with CrCl ≥30 mL/min.  
• To date, no clinical trials have been conducted with TAF; data are based on bioequivalence pharmacokinetic studies.  
• Contains 25 mg of TAF, unboosted.  
• TAF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets. | A2 |

Notes: 1) In all cases, FTC and 3TC are interchangeable when not being used in fixed-dose combinations; 2) Because of their drug–interaction profiles, COBI and RTV should not be considered interchangeable; 3) TAF 10 mg and TAF 25 mg are not interchangeable; 4) Refer to Table 8. ARV Dose Adjustments for Renal and Hepatic Impairment for adjustment based on renal or hepatic function; 5) When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg; 6) When a “rapid start” or “test and treat” initiation of ART occurs before baseline laboratory test results are available, avoid use of abacavir until a patient’s HLA-B*5701 is confirmed negative.

Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults
(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
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</table>
| Tenofovir alafenamide/emtricitabine/raltegravir (TAF 25 mg/FTC/RPV; Odefsey) | • Initiate only in patients confirmed to have a CD4 count ≥200 cells/mm³ and viral load <100,000 copies/mL.  
• Initiate only in patients with CrCl of ≥30 mL/min  
• Use with caution in patients with depression or a history of suicidality.  
• To date, no clinical trials have been conducted; data are based on bioequivalence pharmacokinetic studies.  
• Contraindicated with PPIs.  
• Use H2-blockers with caution and separate dosing by 12 hours.  
• Must take with food.  
• Contains 25 mg of TAF, unboosted. | B3 |
### Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults, *Continued*
(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
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<tbody>
<tr>
<td><strong>Available as a Single-Tablet Formulation</strong></td>
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</tbody>
</table>
| Tenofovir disoproxil fumarate/emtricitabine/cobicistat/elvitegravir   | - Initiate *only* in patients with CrCl ≥ 70 mL/min.  
- Carefully consider drug–drug interactions with COBI.  
- Consider bone mineral density.                                                                                 | B1     |
| *(TDF/FTC/COBI/EVG; Stribild)*                                         |                                                                                                                                                                                                        |        |
| **Available as Multi-Tablet Regimen with Once-Daily Dosing**           |                                                                                                                                                                                                        |        |
| Tenofovir disoproxil fumarate/emtricitabine and darunavir/cobicistat  | - Initiate *only* in patients with CrCl ≥ 70 mL/min.  
- Carefully consider drug–drug interactions with COBI.  
- Consider bone mineral density.                                                                                 | B2     |
| *(TDF/FTC and DRV/COBI; Truvada and Prezcobix)*                        |                                                                                                                                                                                                        |        |
| Tenofovir disoproxil fumarate/emtricitabine and darunavir and ritonavir | - Initiate *only* in patients with CrCl ≥ 50 mL/min.  
- Carefully consider drug–drug interactions with RTV.  
- Consider bone mineral density.                                                                                 | B1     |
| *(TDF/FTC and DRV and RTV; Truvada and Prezista and Norvir)*           |                                                                                                                                                                                                        |        |
| Tenofovir disoproxil fumarate/emtricitabine and dolutegravir          | - Initiate *only* in patients with CrCl ≥ 50 mL/min.  
- Documented DTG resistance after initiation in treatment-naïve patients is rare.  
- Consider bone mineral density.                                                                                 | B1     |
| *(TDF/FTC and DTG; Truvada and Tivicay)*                               | - Clinicians should refer to the DHHS Perinatal Guideline when choosing an initial regimen for individuals of childbearing potential.                                                                    |        |
| **Available as Multi-Tablet Regimen with Twice-Daily Dosing**          |                                                                                                                                                                                                        |        |
| Tenofovir disoproxil fumarate/emtricitabine and raltegravir           | - Initiate *only* in patients with CrCl ≥ 50 mL/min.  
- Consider bone mineral density.  
- TDF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets.                                      | B1     |
| *(TDF/FTC and RAL HD; Truvada and Isentress HD)*                       |                                                                                                                                                                                                        |        |
| Tenofovir alafenamide/emtricitabine and raltegravir                   | - Initiate *only* in patients with CrCl ≥ 50 mL/min.  
- TDF/FTC once daily and RAL twice daily.                                                                               | B3     |
| *(TAF 25 mg/FTC and RAL; Descovy and Isentress)*                       |                                                                                                                                                                                                        |        |

**Notes:** 1) In all cases, FTC and 3TC are interchangeable when not being used in fixed-dose combinations; 2) Because of their drug–interaction profiles, COBI and RTV should not be considered interchangeable; 3) TAF 10 mg and TAF 25 mg are not interchangeable; 4) Refer to Table 8. ARV Dose Adjustments for Renal and Hepatic Impairment for adjustment based on renal or hepatic function; 5) When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg; 6) When a “rapid start” or “test and treat” initiation of ART occurs before a patient’s viral load and CD4 count are available, avoid use of rilpivirine.
Table 3: Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults
(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)

<table>
<thead>
<tr>
<th>Regimen</th>
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<tbody>
<tr>
<td><strong>Available as a Single-Tablet Formulation</strong></td>
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</tr>
</tbody>
</table>
| Tenofovir disoproxil fumarate/ emtricitabine/efavirenz (TDF/FTC/EFV; Atripla) | • Initiate only in patients with CrCl ≥50 mL/min.  
• Use with caution in patients with depression or a history of suicidality.  
• Consider bone mineral density.  
• Clinicians should refer to the DHHS Perinatal Guideline when choosing an initial regimen for individuals of childbearing potential. | B1     |
| Tenofovir disoproxil fumarate/ emtricitabine/rilpivirine (TDF/FTC/RPV; Complera) | • Initiate only in patients with CrCl ≥50 mL/min.  
• Use with caution in patients with depression or a history of suicidality.  
• Contraindicated with PPIs.  
• Use H2-blockers with caution and separate dosing by 12 hours.  
• Must take with food.  
• Consider bone mineral density. | B1     |
| **Available as Multi-Tablet Regimen with Once-Daily Dosing**            |                                                                                                                                                                                                         |        |
| Abacavir/lamivudine and atazanavir and ritonavir (ABC/3TC and ATV and RTV; Epzicom and Reyataz and Norvir) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
• Initiate only in patients with viral load <100,000 copies/mL.  
• Carefully consider drug-drug interactions with RTV.  
• Consider underlying risk of coronary heart disease.  
• Scleral icterus from benign hyperbilirubinemia may be a patient concern. | C1     |
| Abacavir/lamivudine and darunavir/cobicistat (ABC/3TC and DRV/COBI; Epzicom and Prezobix) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
• Carefully consider drug-drug interactions with COBI.  
• Consider underlying risk of coronary heart disease. | B3     |
| Abacavir/lamivudine and darunavir and ritonavir (ABC/3TC and DRV and RTV; Epzicom and Prezista and Norvir) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
• Carefully consider drug-drug interactions with RTV.  
• Consider underlying risk of coronary heart disease. | B2     |
| Abacavir/lamivudine and efavirenz (ABC/3TC and EFV; Epzicom and Sustiva) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
• Initiate only in patients with viral load <100,000 copies/mL.  
• Use with caution in patients with depression or a history of suicidality.  
• Consider underlying risk of coronary heart disease.  
• Clinicians should refer to the DHHS Perinatal Guideline when choosing an initial regimen for individuals of childbearing potential. | C1     |
### Table 3: Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults

(listed alphabetically; for specific details, see Specific Factors to Consider and Discuss with Patients or drug package inserts)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Available as Multi-Tablet Regimen with Once-Daily Dosing</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Tenofovir alafenamide/ emtricitabine and efavirenz (TAF 25 mg/FTC and EFV; Descovy and Sustiva) | • Initiate only in patients with CrCl ≥50 mL/min.  
  • Use with caution in patients with depression or a history of suicidality.  
  • Contains 25 mg of TAF, unboosted.  
  • Clinicians should refer to the DHHS Perinatal Guideline when choosing an initial regimen for individuals of childbearing potential. | B3 |
| Tenofovir disoproxil fumarate/ emtricitabine and atazanavir/ cobicistat (TDF/FTC and ATV/COBI; Truvada and Evotaz) | • Initiate only in patients with CrCl ≥70 mL/min.  
  • Scleral icterus from benign hyperbilirubinemia may be a patient concern.  
  • Carefully consider drug-drug interactions with COBI.  
  • Consider bone mineral density. | B1 |
| Tenofovir disoproxil fumarate/ emtricitabine and atazanavir and ritonavir (TDF/FTC and ATV and RTV; Truvada and Reyataz and Norvir) | • Initiate only in patients with CrCl ≥50 mL/min.  
  • Scleral icterus from benign hyperbilirubinemia may be a patient concern.  
  • Carefully consider drug-drug interactions with RTV.  
  • Consider bone mineral density. | B1 |
| Abacavir/lamivudine and raltegravir (ABC/3TC and RAL HD; Epzicom and Isentress HD) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
  • Consider underlying risk of coronary heart disease.  
  • ABC/3TC once daily, RAL HD 1200 mg once daily dosed as two 600 mg HD tablets. | B3 |

| Available as Multi-Tablet Regimen with Twice-Daily Dosing | | |
| Tenofovir disoproxil fumarate/ emtricitabine and raltegravir (TDF/FTC and RAL; Truvada and Isentress) | • Initiate only in patients with CrCl ≥50 mL/min.  
  • Consider bone mineral density.  
  • TDF/FTC once daily and RAL 400 mg twice daily. | B1 |
| Abacavir/lamivudine and raltegravir (ABC/3TC and RAL; Epzicom and Isentress) | • Initiate only in patients confirmed to be negative for HLA-B*5701.  
  • Consider underlying risk of coronary heart disease.  
  • ABC/3TC once daily and RAL 400 mg twice daily. | B1 |

**Notes:** 1) In all cases, FTC and 3TC are interchangeable when not being used in FDCs; 2) Because of their drug–interaction profiles, COBI and RTV should not be considered interchangeable; 3) TAF 10 mg and TAF 25 mg are not interchangeable; 4) Refer to Table 8. ARV Dose Adjustments for Renal and Hepatic Impairment for adjustment based on renal or hepatic function; 5) When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg; 6) When a “rapid start” or “test and treat” initiation of ART occurs before a patient’s viral load and CD4 count are available, avoid use of rilpivirine; if a patient has not been confirmed to be HLA-B*5701 negative, avoid use of abacavir.
References


General Principles in Choosing an Initial ART Regimen

Medical Care Criteria Committee, June 2018

Goals of ART: The issue of when to start ART was settled with the publication of the START (Strategic Timing of Antiretroviral Treatment) and TEMPRANO (Early Antiretroviral Treatment and/or Early Isoniazid Prophylaxis Against Tuberculosis in HIV-infected Adults) studies early in 2015 [INSIGHT START 2015; TEMPRANO ANRS 12136 2015]. Treatment is now recommended for all patients with confirmed HIV infection regardless of CD4 cell count or viral load (see NYSDOH AI guideline When to Initiate ART). 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 [SMART 2006].

Since the approval of zidovudine (ZDV) on March 19, 1987, there have been 28 individual agents approved for the treatment of HIV and one pharmacokinetic enhancer (or booster), cobicistat (COBI), which is currently used to enhance the pharmacokinetics of elvitegravir (EVG), atazanavir (ATV), or darunavir (DRV). Ritonavir (RTV) at treatment doses is poorly tolerated and is used only at lower doses for pharmacokinetic boosting of PIs. An additional 16 FDA-approved fixed-dose combination tablets (FDCs) are also available. These FDCs include so-called “single-tablet regimens,” of which there are seven currently available that provide a complete and effective treatment regimen for HIV that is combined into one pill for use in properly selected individuals. The goal of initial therapy is to start a regimen that suits a patient’s lifestyle and is appropriate given existing baseline medical comorbidities.

Three active drugs from at least two different classes: Although regimen options for treatment-naïve, nonpregnant patients 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]. Patients should receive three active drugs from at least two different classes. The “backbone” of therapy remains two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) paired with one of the following: an NNRTI, a boosted PI, or a boosted or unboosted INSTI. In one large meta-analysis, integrase strand inhibitors (INSTIs), were superior to other drug classes as a third drug [Lee et al. 2014], and dolutegravir (DTG) may have specific advantages because of the lack, to date, of documented resistance developing in ART-naïve patients who initiate DTG-containing regimens [Wainberg and Mesplede 2015]. Two other classes of approved medications, entry inhibitors and fusion inhibitors, are not recommended for initial therapy (see Table 5, below) but may have a role in treatment-experienced patients with extensive drug resistance (see All FDA-Approved Medications, including generic and trade names).

0→ KEY POINT

- Although dual or even monotherapy regimens have been and continue to be studied [Bedimo et al. 2014; Taiwo et al. 2011; Raffi et al. 2014; Cahn et al. 2014; Maggiolo et al. 2016; Cahn et al. 2016; Baril et al. 2016], they cannot be recommended currently as initial therapy until more data are available. Existing studies show limitations with these regimens in ART-naïve individuals based on pill burden, toxicities, and efficacy, particularly in patients with viral loads >100,000 copies/mL or CD4 counts <200 cells/mm³, compared with recommended therapy.

TAF, which is a newer pro-drug formulation for tenofovir, was developed as an alternative to TDF and has been approved as part of three single-tablet regimens, TAF 10 mg/FTC/COBI/EVG, TAF 25 mg/FTC/RPV, TAF 25 mg/FTC/BIC [Genvoya 2016; Odefsey 2016], and the fixed-dose combination TAF 25 mg/FTC [Descovy 2016]. 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 [Sax et al. 2015; Mills et al. 2016; Pozniak et al. 2016]. 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 et al 2016a; Zack et al. 2016b]. A switch study showed good maintenance of viral suppression when changing TDF/FTC to TAF 10 mg/FTC if the third drug was a boosted PI or 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 creatinine clearance (CrCl) <50 mL/min.
COBI-boosted DRV was approved based on bioavailability studies [Prescobicx 2018; Kakuda et al. 2014] and has demonstrated comparable efficacy to RTV-boosted DRV in a single-arm study [Tashima et al. 2014]. However, because COBI-boosted DRV has not yet been studied in randomized clinical trials, it has a lower evidence strength. COBI-boosted ATV showed non-inferiority when compared with RTV-boosted ATV with a TDF/FTC backbone in a randomized double-blind study [Gallant et al. 2013].

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 (see Available ART Regimens).

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

- When abacavir/lamivudine (ABC/3TC) is used as a backbone with EFV or boosted ATV, time to failure was shorter in the ≥100,000 copies/mL viral load stratum when compared with a backbone of TDF/FTC [Sax et al. 2011; Post et al. 2010; Sax et al. 2009].
- DTG is as efficacious as (i.e., non-inferior to) raltegravir (RAL) [Raffi et al. 2013] and superior to both RTV-boosted DRV [Molina et al. 2014] and co-formulated TDF/FTC/EFV [Walmsley et al. 2015]. DTG was superior at 48 weeks when combined with ABC/3TC as compared to TDF/FTC [Walmsley et al. 2013].
- RAL, although dosed twice daily, has a favorable tolerability profile and provides durable virologic control [Lennox et al. 2014; DeJesus et al. 2012b; Young et al. 2010] and was superior to both RTV-boosted DRV and RTV-boosted ATV based on the cumulative incidence of virologic failure and tolerability [Lennox et al. 2014].
- In a study of ART-naive patients, RAL HD 1200 mg once daily was non-inferior to 400 mg tablets dosed twice daily [Cahn et al. 2017].
- TAF/FTC/COBI/EVG as a single-tablet regimen was non-inferior to the single-tablet regimen TDF/FTC/COBI/EVG, with fewer adverse effects on kidney function and bone mineral density [Sax et al. 2015].
- RPV has excellent efficacy relative to EFV when baseline viral load is <100,000 copies/mL and is better tolerated [Cohen et al. 2012, 2013, 2014; van Lunzen et al. 2016; Behrens et al. 2014] but should not be initiated in patients with baseline viral load >100,000 copies/mL or CD4 counts <200 cells/mm³.
- Co-formulated TDF/FTC/COBI/EVG was non-inferior to both TDF/FTC with RTV-boosted ATV at 48 and 96 weeks [Dejesus et al. 2012a; Rockstroh et al. 2013] and co-formulated TDF/FTC/EFV [Sax et al. 2012; Zolopa et al. 2013].
- RTV-boosted DRV once daily is better tolerated and non-inferior to either RTV-boosted ATV 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 RTV-boosted ATV [Molina et al. 2008]. One open-label study using ABC/3TC as the backbone combined with RTV-boosted DRV showed good safety and efficacy [Trottier et al. 2012].
- In two separate trials of treatment-naive individuals, TAF/FTC/BIC was non-inferior to both TAF/FTC and DTG [Sax et al. 2017] and ABC/3TC/DTG [Gallant J et al. 2017].

<table>
<thead>
<tr>
<th>ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine (NVP; Viramune)</td>
<td>Life-threatening rash: Stevens-Johnson syndrome and toxic epidermal necrolysis are possible</td>
</tr>
<tr>
<td>Stavudine (d4T; Zerit)</td>
<td>Serious toxicities: Potentially fatal lactic acidosis, peripheral neuropathy, pancreatitis, lipoatrophy, and hepatic steatosis are possible</td>
</tr>
<tr>
<td>Didanosine (ddl; Videx)</td>
<td>Serious toxicities: Potentially fatal lactic acidosis, peripheral neuropathy, pancreatitis, lipoatrophy, and hepatic steatosis are possible</td>
</tr>
<tr>
<td>Delavirdine (DLV; Rescriptor)</td>
<td>Thrice-daily dosing and inferior efficacy</td>
</tr>
<tr>
<td>Etravirine (ETR; Intelence)</td>
<td>ETR does not have an FDA indication in ART-naive patients</td>
</tr>
<tr>
<td>Maraviroc (MVC; Selzentry) NRTI-only regimens, either triple or quadruple</td>
<td>Inferior efficacy and durability</td>
</tr>
</tbody>
</table>
Table 4: Individual ARVs or Combinations to Avoid in Initial Therapy for Non-Pregnant Adults, continued

<table>
<thead>
<tr>
<th>ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (ZDV; Retrovir)</td>
<td>Not well tolerated because of bone marrow suppression (notably anemia), headache, myopathies</td>
</tr>
<tr>
<td>Unboosted PIs</td>
<td>Inferior efficacy relative to boosted PIs</td>
</tr>
<tr>
<td>• Fosamprenavir (FPV; Lexiva)</td>
<td>Either not well studied or limited by dosing and side effects relative to recommended PIs</td>
</tr>
<tr>
<td>• Indinavir (IDV; Crixivan)</td>
<td></td>
</tr>
<tr>
<td>• Tipranavir (TPV; Aptivus)</td>
<td></td>
</tr>
<tr>
<td>• Nelfinavir (NFV; Viracept)</td>
<td></td>
</tr>
</tbody>
</table>

References


General Considerations with Initial ART Regimens

Medical Care Criteria Committee, April 2017

The recommended antiretroviral therapy (ART) regimens should work well for the majority of properly selected patients, but some circumstances may make one regimen more favorable than another for a given individual. In general, an integrase strand transfer inhibitor (INSTI)–based regimen will be the best option for most patients [Lee et al. 2014; Mills et al. 2016]. To date, no resistance has been reported in ART-naïve patients treated with dolutegravir (DTG), suggesting that this ARV may be an excellent choice, particularly given its tolerability and lack of drug–drug interactions [Wainberg and Mesplede 2015]. Regimens containing a boosted-PI or DTG may be more appropriate when adherence is a concern given the higher barrier to resistance. For urgent treatment when genotypic information is not yet available, for example acute symptomatic infection, or advanced HIV with an opportunistic infection, some experts would use both DTG and boosted-DRV together with the NRTI backbone given the possibility of transmitted NRTI–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 co–infections, or very high viral loads.

KEY POINT

• INSTI–based regimens are generally the best choice for most patients because of tolerability and durability.

Early clinical trials in HIV used surrogate markers, such as viral load and CD4 cell count, or clinical end points, 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 indinavir (IDV) compared IDV alone versus zidovudine (ZDV) plus lamivudine (3TC) versus ZDV plus 3TC plus indinavir (IDV) in ZDV treatment–experienced patients, given that, at the time, dual–nucleoside (or nucleotide) analogue reverse transcriptase inhibitor (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 non–inferiority 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 single–tablet regimens and fixed–dose combinations (FDCs) have been approved primarily based on bioequivalence studies when compared with the individual components, such as tenofovir disoproxil fumarate/emtricitabine/efavirenz (TDF/FTC/EFV), abacavir/lamivudine/dolutegravir (ABC/3TC/DTG), tenofovir alafenamide/emtricitabine/rlipivirine (TAF/FTC/RPV), TAF/FTC, and cobicistat/darunavir (COBI/DRV).

Some of the cutoff values used for comparisons, such as viral load <100,000 copies/mL or CD4 cell 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 one showed that RPV worked even 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 non–inferiority 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 non–nucleoside reverse transcriptase inhibitor (NNRTI) resistance mutations when transmitted drug resistance occurs has prompted most experts to avoid NNRTI–based regimens if treatment is indicated prior to the availability of genotypic information [Panichsillapakit et al. 2016; Rhee et al. 2015; Stekler et al. 2015]. Although co–formulated TDF/FTC/COBI/EVG is approved for use at any starting viral load, reports of failure, with resistance, have been documented at very high baseline viral loads over 1,000,000 copies/mL [Rhee et al. 2015; Adams et al. 2016].

A paucity of data is available demonstrating how different antiretrovirals (ARVs) perform based on race and gender, although studies have suggested, for instance, that ritonavir (RTV)–boosted DRV is less well tolerated in women than in men and that blacks have higher discontinuation rates on RTV–boosted DRV compared with other populations [Smith et al. 2012; Currier et al. 2010].
References


Specific Factors to Consider and Discuss with Patients

Medical Care Criteria Committee, June 2018

Before initiating antiretroviral therapy (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 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 patients over 50 years of age, careful regimen selection with the use of integrase strand inhibitors (INSTIs) when possible, rather than cytochrome P450 inhibitors such as cobicistat (COBI) or ritonavir (RTV), can help minimize interactions, while using tenofovir alafenamide (TAF) 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.

**Cost:** Single-tablet regimens 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 versus twice daily):** Most patients express a preference for once-daily dosing, especially those who are not taking other medications or are taking other medications that are dosed once daily. If patients are already on twice-daily dosing of other medications and report no adherence issues, twice-daily dosing is an acceptable option.

**Drug–drug interactions:** Some key interactions exist (Table 5, below), such as avoiding use of proton-pump inhibitors (PPIs) with rilpivirine (RPV), which is especially important to discuss with patients, given the availability of over-the-counter PPIs and the possibility that these drugs may be prescribed by someone other than the HIV care provider. To avoid unnecessary regimen changes once started, even patients who are not currently on PPIs should be asked whether they have needed PPIs in the past or may need them in the future.

RTV and COBI have many significant and important interactions, including with cardiac medications. Methadone maintenance requirements may also change with some antiretroviral agents (ARVs). A detailed review of all medications, including over-the-counter medications or supplements, is mandatory. Using automated drug–drug interaction software embedded in the electronic medical record or consulting an up-to-date database, such as HIV InSite’s Database of Antiretroviral Drug Interactions, for interactions with currently prescribed medications BEFORE prescribing a regimen, can help avoid serious problems.
Table 5: Select Drug-Drug Interactions to Discuss before Initiating ART in Treatment-Naive Patients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>ARV(s): Comments</th>
</tr>
</thead>
</table>
| **H₂ -blockers**           | • **ATV:** In treatment-naïve patients on boosted ATV, H₂-blockers should be either taken simultaneously with ATV or, if simultaneous dosing is not possible, separated from ATV by 10 hours; prescribe no more than 20 mg of famotidine or equivalent for one dose and no more than 40 mg twice daily of famotidine or equivalent for daily dose  
  • **RPV:** Use with caution; administer at least 12 hours before or at least 4 hours after RPV |
| **Inhaled steroids; statins** | • **COBI; RTV:** Alternatives or dose adjustments may be needed  
  • Consult the package inserts for drug-drug interactions between specific statins and ARVs |
| **Polyvalent cations [a]** | • **DTG:** Take 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food  
  • **RAL:** Magnesium- or aluminum-containing antacids are contraindicated; calcium-containing antacids are acceptable  
  • **RAL HD:** Magnesium- or aluminum-containing antacids are contraindicated; co-administration of calcium-containing antacids is not recommended  
  • **EVG:** Separate dosing by 2 hours, either before or after dose of EVG |
| **PPIs**                   | • **ATV:** Contraindicated with ATV in treatment-experienced patients; in treatment-naïve patients, use no more than equivalent of 20 mg of omeprazole with ATV, separated by 12 hours  
  • **RPV:** Contraindicated |
| **Metformin**              | • **DTG:** Metformin levels are significantly raised when co-administered with DTG. The dose of metformin should not exceed 1,000 mg. |
| **Ethinyl estradiol and norethindrone [b]** | • **EFV; COBI/ATV; COBI/DRV; RTV and DRV:** Use alternative or additional (e.g. barrier) contraceptive methods or choose alternative ART regimen  
  • **ATV; RTV and ATV:** Use with caution; see manufacturer's package insert for specific dosing information |
| **Factor Xa inhibitors**   | • **COBI; RTV:**  
  ▫ Apixiban: Reduce dose by 50% if patient is on 5 mg twice daily; avoid use if the indicated dose is 2.5 mg twice daily (based on age, weight, creatinine)  
  ▫ Dabigatran: No adjustment needed if CrCl ≥50 mL/min; avoid if CrCl <50 mL/min  
  ▫ Rivaroxaban: Avoid use |
| **Platelet inhibitors**    | • **COBI; RTV:**  
  ▫ Clopidogrel: Avoid use  
  ▫ Prasugrel: No adjustment needed  
  ▫ Ticagrelor: Avoid use |

Drug name abbreviations: atazanavir (ATV); cobicistat (COBI); darunavir (DRV); dolutegravir (DTG); efavirenz (EFV); raltegravir (RAL); rilpivirine (RPV); ritonavir (RTV)  
  a. Aluminum, calcium, magnesium, or iron in some antacids or vitamin preparations.  
  b. For emergency contraception, other oral combinations, and patch, ring, or injectable formulations, please refer to package insert for specific ARV for dosing instructions and safety information.
**Food requirements:** Because patients may have a strong preference for taking medication with or without food, it is important to discuss which pills 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 1, below.

<table>
<thead>
<tr>
<th>Box 1: Food Requirements for Antiretroviral Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Take with or without food</strong></td>
</tr>
<tr>
<td>• 3TC</td>
</tr>
<tr>
<td>• ABC</td>
</tr>
<tr>
<td>• BIC/TAF/FTC</td>
</tr>
<tr>
<td>• DTG</td>
</tr>
<tr>
<td>• FTC</td>
</tr>
<tr>
<td>• RAL</td>
</tr>
<tr>
<td>• TAF</td>
</tr>
<tr>
<td>• TDF</td>
</tr>
</tbody>
</table>

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

**Known side effects and toxicities:** Review known and potential side effects in advance.

**Number of pills:** Some patients feel strongly that the fewer the number of pills, the better. For other patients, 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 single-tablet regimen may be attractive depending on pill size. In rare cases, patients 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 prior to ingestion. A full list that gives greater detail is available.

<table>
<thead>
<tr>
<th>Table 6: Alternatives to the Tablet Form of ART Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td><strong>Single-Tablet Formulations</strong></td>
</tr>
<tr>
<td>Abacavir/lamivudine/dolutegravir (ABC/3TC/DTG; Triumeq)</td>
</tr>
<tr>
<td>Bictegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC; Biktarvy)</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (EVG/COBI/TAF/FTC; Genvoya)</td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV; Odefsey)</td>
</tr>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>Single-Tablet Formulations</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/efavirenz (TDF/FTC/EFV; Atripla)</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/rilpivirine (TDF/FTC/RPV; Complera)</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/cobicistat/elvitegravir (TDF/FTC/COBI/EVG; Stribild)</td>
</tr>
<tr>
<td>Fixed-Dose Combinations</td>
</tr>
<tr>
<td>Abacavir/lamivudine (ABC/3TC; Epzicom)</td>
</tr>
<tr>
<td>Darunavir/cobicistat (DRV/COBI; Prezcobix)</td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine (TAF/FTC; Descovy)</td>
</tr>
<tr>
<td>(Tenofovir disoproxil fumarate/emtricitabine) (TDF/FTC; Truvada)</td>
</tr>
<tr>
<td>Zidovudine/lamivudine (ZDV/3TC; Combivir)</td>
</tr>
<tr>
<td>Individual Drugs</td>
</tr>
<tr>
<td>Abacavir (ABC; Ziagen)</td>
</tr>
<tr>
<td>Atazanavir (ATV; Reyataz)</td>
</tr>
<tr>
<td>Darunavir (DRV; Prezista)</td>
</tr>
<tr>
<td>Dolutegravir (DTG; Tivicay)</td>
</tr>
<tr>
<td>Efavirenz (EFV; Sustiva)</td>
</tr>
<tr>
<td>Elvitegravir (EVG; Vitekta)</td>
</tr>
<tr>
<td>Emtricitabine (FTC; Emtriva)</td>
</tr>
</tbody>
</table>
### Table 6: Alternatives to the Tablet Form of ART Medications, continued

<table>
<thead>
<tr>
<th>Drug</th>
<th>Available as Liquid, Powder, or Chewable Tablet</th>
<th>Can Tablet be Split/ Crushed/Dissolved?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individual Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine (3TC; Epivir)</td>
<td>Oral solution (10 mg/mL)</td>
<td>Acceptable to crush or split</td>
</tr>
<tr>
<td>Raltegravir (RAL; Isentress)</td>
<td>Chewable tablet (25 mg, 100 mg); oral powder for suspension (100 mg/packet); neither is bioequivalent to the 400 mg adult dose</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Raltegravir HD (RAL HD; Isentress HD)</td>
<td>No</td>
<td>No data, not recommended</td>
</tr>
<tr>
<td>Rilpivirine (RPV; Edurant)</td>
<td>No</td>
<td>No data, not recommended</td>
</tr>
<tr>
<td>Ritonavir (RTV; Norvir)</td>
<td>Oral solution (80 mg/mL)</td>
<td>No</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate (TDF; Viread)</td>
<td>Oral powder mixed with soft food only (40 mg/1 g)</td>
<td>Acceptable to dissolve in water</td>
</tr>
</tbody>
</table>

**Pill size:** Use images or real examples to give patients an idea of pill size BEFORE they fill the prescription (examples of visual guides include those of AIDSinfo and HIV i-Base). TAF/FTC/BIC and TAF/FTC/RPV are the smallest single-tablet regimens.

**Pregnancy or conception planning:** Patients of childbearing age 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, clinicians should consult the Department of Health and Human Services (DHHS) guideline, Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. All patients should be assessed for conception plans; this can be an opportunity to discuss pre-exposure prophylaxis (PrEP) for uninfected partners (see NYSDOH AI guideline *PrEP to Prevent HIV Acquisition*).

**Reference**

Special Considerations for Comorbid Conditions

Medical Care Criteria Committee, June 2018

**Bone disease:** TDF causes a decrease in bone mineral density in all patients after initiation of therapy and should be used with caution in patients with pre-existing severe osteoporosis [Stellbrink et al. 2010; McComsey et al. 2011; 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 tenofovir alafenamide (TAF) formulation available currently in tenofovir alafenamide/emtricitabine (TAF/FTC), tenofovir alafenamide/emtricitabine/cobicistat/elvitegravir (TAF/FTC/COBI/EVG), tenofovir alafenamide/emtricitabine/bictegravir (TAF/FTC/BIC), and tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV), is a better alternative with less bone toxicity [Pozniak et al. 2016; Bonora et al. 2016].

**Cardiovascular Risks:** Cobicistat (COBI)– or ritonavir (RTV)–containing regimens typically elevate lipids; tenofovir disoproxil fumarate (TDF)–containing regimens can have a beneficial effect [Souza et al. 2013]. Abacavir (ABC) has been associated with a higher risk of myocardial infarction in some studies [D:A:D Study Group et al. 2008; SMART/INSIGHT Study Groups et al. 2008; Obel et al. 2010; Choi et al. 2011; Marcus et al. 2016], whereas other studies have not confirmed this association [Bedimo et al. 2011; Ribaudo et al. 2011; Ding et al. 2012; Brothers et al. 2009]. Based on the available data, ABC should be used with caution in those with multiple cardiac risk factors or known coronary heart disease; however, the absolute risk of myocardial infarction remains low, and no clear causality has been established. In the appropriate clinical setting, such as a patient with impaired renal function, the use of ABC would be acceptable [Llibre and Hill 2016]. Clinicians should be made aware of the conflicting study data and share this information with patients.

**Liver disease:** In patients with existing liver disease of any etiology, dose adjustment of antiretrovirals (ARVs) may be required depending on the severity of hepatic impairment (see Table 8. ARV Dose Adjustments for Renal and Hepatic Impairment).

**Mental health and substance use:** Modifiable factors that may influence adherence should be addressed.

---

**KEY POINT**

- Neither mental health nor substance use disorders are contraindications to initiating therapy, although, in some cases, delay of initiation may be appropriate (see NYSDOH AI guideline *When to Initiate ART*).

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**Renal function:** TDF can cause renal tubular dysfunction, such as acquired Fanconi syndrome [Karras et al. 2003; Zimmermann et al. 2006]. The risk of renal impairment has been shown to be elevated in patients with pre-existing renal disease, longer treatment duration, low body weight, and when used in conjunction with RTV– or COBI–boosted regimens [Gervasoni et al. 2013; Mocroft et al. 2016]. In general, full-dose TDF should be used with caution in patients with baseline creatinine clearance (CrCl) <70 mL/min and should be adjusted or changed to an alternative agent if CrCl decreases to <50 mL/min. Use of the TAF formulation 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 RTV–boosted atazanavir (ATV/r) and lopinavir/RTV (LPV/r) have also been independently associated with a greater decrease in renal function over time compared with NNRTI–based regimens [Goicoechea et al. 2008; Quesada et al. 2015]. COBI, and to a lesser extent dolutegravir (DTG), can inhibit the excretion of creatinine, with expected elevations of creatinine at initiation of therapy. However, such increases are not clinically relevant and do not significantly affect glomerular filtration rate [German et al. 2012; Lepist et al. 2014; Koteff et al. 2013].

Although DTG is highly bound to plasma proteins and therefore is unlikely to be removed by dialysis, it has not been studied in this population [Tivicay 2013]; therefore, raltegravir (RAL) or a boosted-protease inhibitor (PI) with renally-adjusted lamivudine (3TC) lamivudine and either ABC or once weekly TDF are usually the regimens of choice in this setting.
Additional information on prescribing agents in the setting of reduced renal function is available in Table 8. ARV Dose Adjustments for Renal and Hepatic Impairment.

**Very high viral loads (>750,000 copies/mL):** In some cases, experts will recommend use of both boosted DRV and DTG when the viral load is very high, with possible simplification once viral suppression is achieved. Numerous switch studies have demonstrated the safety of simplifying ART regimens in suppressed patients with no pre-existing resistance [Cazanave et al. 2015; Arribas et al. 2014; Mills et al. 2013; Fisher et al. 2009]. Consultation with an experienced HIV care provider in these situations is helpful.

<table>
<thead>
<tr>
<th>KEY POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ COBI and DTG can both cause decreased tubular excretion of creatinine and will dependably cause a slight increase in measured creatinine.</td>
</tr>
<tr>
<td>▪ ABC has been associated with a higher risk of myocardial infarction in some studies, although not in others. No clear causal link has been established.</td>
</tr>
<tr>
<td>▪ Boosted PIs and COBI-boosted EVG are associated with more hyperlipidemia than unboosted INSTIs.</td>
</tr>
<tr>
<td>▪ Consultation with an experienced HIV care provider is advised when a patient’s baseline viral load is very high.</td>
</tr>
</tbody>
</table>

**References**


Pre-ART-Initiation Laboratory Testing

Medical Care Criteria Committee, June 2018

**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 in this population (see Table 7, below). When *Pneumocystis jiroveci* pneumonia (PCP) prophylaxis is indicated, it may be prudent to defer antiretroviral therapy (ART) for 7 to 10 days if 2 medications that may cause rash are going to be started, such as trimethoprim-sulfamethoxazole (TMP-SMX) and efavirenz (EFV).

**Baseline viral load:** Some regimens should not be used when the viral load is ≥100,000 copies/mL: see Table 7, below; comments in Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults; and Table 3: Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults.

**Co-infections:** Hepatitis B virus (HBV), hepatitis C virus (HCV), and tuberculosis (TB) infection status should be assessed. The ART regimen for those with chronic HBV infection should treat both HIV and HBV when possible (see NYSDOH AI guideline *HBV–HIV Coinfection*). 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.

**Creatinine clearance:** Some antiretroviral agents (ARVs) are contraindicated below a given creatinine clearance (CrCl) level, and some may need adjustments that require the use of individual elements of fixed-dose combination or a single-tablet regimen rather than the single-tablet version of the drug. See Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment for more information.

**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 Special Considerations for Comorbid Conditions and Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment.

**HIV genotypic resistance profile:** Genotypic resistance testing that includes the protease and reverse transcriptase genes should be obtained at diagnosis (or initial visit if not done previously) [Borroto-Esoda et al. 2007; Kuritzkes et al. 2008]. 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 prior to the availability of genotypic resistance testing, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens should be avoided because of the higher prevalence of transmitted resistance in NNRTIs versus protease inhibitors (PIs) or integrase strand transfer inhibitors (INSTIs) [Panichsillapakit et al. 2016; Rhee et al. 2015; Stekler et al. 2015]. In this situation, for example symptomatic acute infection or advanced HIV with an opportunistic infection, some experts would include DTG, boosted-DRV or both together with the NRTI backbone given the possibility of transmitted NRTI-resistance, with possible simplification once genotypic information is available. Because of the low prevalence, to date, of transmitted integrase resistance in ART-naïve patients [Volpe et al. 2016; Garcia-Diaz et al. 2014], routine integrase resistance testing is not recommended in these patients. However, in cases where integrase resistance is suspected, this test can be ordered as a supplement to protease and reverse transcriptase testing.

**HLA-B*5701 testing:** To avoid potentially serious or life-threatening hypersensitivity reactions, HLA-B*5701 testing is mandatory before initiating ART that includes abacavir (ABC) [Saag et al. 2008; Mallal et al. 2008]. Initiation of the regimens listed in Table 7, below, is contraindicated based on the listed baseline laboratory parameters.
Table 7: Contraindicated ART Regimens Based on Routine Baseline\* Laboratory Parameters

<table>
<thead>
<tr>
<th>Lab Parameter</th>
<th>Contraindicated ART Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral load ≥100,000 copies/mL</td>
<td>• ABC/3TC and COBI/ATV (Epzicom and Evotaz)</td>
</tr>
<tr>
<td></td>
<td>• ABC/3TC and EFV (Epzicom and Sustiva)</td>
</tr>
<tr>
<td></td>
<td>• ABC/3TC and RTV and ATV (Epzicom and Norvir and Reyataz)</td>
</tr>
<tr>
<td></td>
<td>• RAL and RTV and DRV (Isentress and Norvir and Prezista)</td>
</tr>
<tr>
<td></td>
<td>• TAF/FTC/RPV (Odefsey)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC/RPV (Complera)</td>
</tr>
<tr>
<td>CD4 &lt;200 cells/mm(^3)</td>
<td>• TAF/FTC/RPV (Odefsey)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC/RPV (Complera)</td>
</tr>
<tr>
<td>CrCl &lt;70 mL/min</td>
<td>• TDF/FTC and COBI/ATV (Truvada and Evotaz)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC and COBI/DRV (Truvada and Prezcobix)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC/COBI/EVG (Stribild)</td>
</tr>
<tr>
<td>CrCl &lt;50 mL/min</td>
<td>• ABC/3TC (Epzicom)</td>
</tr>
<tr>
<td></td>
<td>• ABC/3TC/DTG (Triumeq)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC/EFV (Atripla)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC/RPV (Complera)</td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min</td>
<td>• TAF/FTC (Descovy)</td>
</tr>
<tr>
<td></td>
<td>• TAF/FTC/BIC (Biktarvy)</td>
</tr>
<tr>
<td></td>
<td>• TAF/FTC/COBI/EVG (Genvoya)</td>
</tr>
<tr>
<td></td>
<td>• TAF/FTC/RPV (Odefsey)</td>
</tr>
<tr>
<td></td>
<td>• TDF/FTC (Truvada)</td>
</tr>
</tbody>
</table>

Drug name abbreviations: abacavir (ABC); atazanavir (ATV); bictegravir (BIC); cobicistat (COBI); darunavir (DRV); dolutegravir (DTG); efavirenz (EFV); elvitegravir (EVG); emtricitabine (FTC); lamivudine (3TC); raltegravir (RAL); rilpivirine (RPV); ritonavir (RTV); tenofovir alafenamide (TAF); tenofovir disoproxil fumarate (TDF)

*For renal adjustment of FDCs and single-tablet regimens while on therapy, see Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment.

References


## ARV Dose Adjustments for Renal and Hepatic Impairment

Medical Care Criteria Committee, June 2018

<table>
<thead>
<tr>
<th>Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formulation and Usual Adult Dose</strong></td>
</tr>
<tr>
<td>Single-Tablet Regimens</td>
</tr>
<tr>
<td>Abacavir/lamivudine/dolutegravir (ABC/3TC/DTG; Triumeq)</td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine/bictegravir (TAF/FTC/BIC; Biktarvy)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine/cobicistat/elvitegravir (TAF/FTC/COBI/EVG; Genvoya)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV; Odefsey)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/cobicistat/elvitegravir (TDF/FTC/COBI/EVG; Stribild)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/efavirenz (TDF/FTC/EFV; Atripla)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once each night</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine/rilpivirine (TDF/FTC/RPV; Complera)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 pill once daily</td>
</tr>
</tbody>
</table>

Fixed-Dose Combinations

<table>
<thead>
<tr>
<th>Formulation and Usual Adult Dose</th>
<th>Renal Insufficiency Dosing</th>
<th>Hepatic Impairment Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir/lamivudine (ABC/3TC; Epzicom)</td>
<td><strong>CrCl &lt;50 mL/min: do not use</strong></td>
<td><strong>Child–Pugh A, B, C: do not use</strong></td>
</tr>
<tr>
<td>1 pill once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir alafenamide/emtricitabine (TAF/FTC; Descovy)</td>
<td><strong>CrCl &lt;30 mL/min: do not use</strong></td>
<td><strong>Child–Pugh A, B: no adjustment</strong></td>
</tr>
<tr>
<td>1 pill once daily</td>
<td></td>
<td><strong>Child–Pugh C: no data</strong></td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC Truvada)</td>
<td><strong>CrCl 30–49 mL/min: 1 pill every 48 hr</strong></td>
<td><strong>No adjustment</strong></td>
</tr>
<tr>
<td>1 pill once daily</td>
<td><strong>CrCl &lt;30 mL/min: do not use</strong></td>
<td></td>
</tr>
<tr>
<td>Individual Drug Components</td>
<td>Renal Insufficiency Dosing*</td>
<td>Hepatic Impairment Dosing*</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Abacavir (ABC; Ziagen)</td>
<td>• No adjustment</td>
<td>• Child–Pugh A: 200 mg twice daily as solution</td>
</tr>
<tr>
<td></td>
<td>• 300 mg twice daily or 600 mg once daily</td>
<td>• Child–Pugh B, C: do not use</td>
</tr>
<tr>
<td>Atazanavir (ATV; Reyataz)</td>
<td>• No adjustment, but use only 300 mg dose with 100 mg RTV</td>
<td>• Child–Pugh A, B: no adjustment</td>
</tr>
<tr>
<td></td>
<td>• 300 mg daily with RTV 100 mg once daily or 400 mg once daily</td>
<td>• Child–Pugh C: no data</td>
</tr>
<tr>
<td>Dolutegravir (DTG; Tivicay)</td>
<td>• No adjustment, but not studied in dialysis</td>
<td>• Child–Pugh A, B: no adjustment</td>
</tr>
<tr>
<td></td>
<td>• Treatment naïve or no DTG resistance mutations: 50 mg once daily</td>
<td>• Child–Pugh C: no data</td>
</tr>
<tr>
<td></td>
<td>• Known INSTI mutations or given with CYP3A inducers (e.g., EFV, LPV/RTV): 50 mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Darunavir (DRV; Prezista)</td>
<td>• CrCl &lt;70 L/min with TDF– containing regimen: do not use</td>
<td>• Child–Pugh A, B: no adjustment</td>
</tr>
<tr>
<td></td>
<td>• 800 mg daily with ritonavir 100 mg once daily</td>
<td>• Child–Pugh C: no data</td>
</tr>
<tr>
<td></td>
<td>• Treatment experienced or ≥1 mutation associated with DRV resistance: 600 mg twice daily with ritonavir 100 mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Darunavir/cobicistat (DRV/COBI; Prezobix)</td>
<td>• CrCl &lt;70 L/min with TDF– containing regimen: do not use</td>
<td>• Child–Pugh A, B: no adjustment</td>
</tr>
<tr>
<td></td>
<td>• Treatment naïve: 1 pill once daily</td>
<td>• Child–Pugh C: no data</td>
</tr>
<tr>
<td></td>
<td>• Treatment experienced or ≥1 mutation associated with DRV resistance: do not use</td>
<td></td>
</tr>
<tr>
<td>Efavirenz (EFV; Sustiva)</td>
<td>• No adjustment</td>
<td>No data; use with caution</td>
</tr>
<tr>
<td></td>
<td>• 600 mg daily or at night</td>
<td></td>
</tr>
<tr>
<td>Elvitegravir (EVG; Vitekta)</td>
<td>• No adjustment</td>
<td>• Child–Pugh A, B: no adjustment</td>
</tr>
<tr>
<td></td>
<td>• Not commonly used as single agent, see package insert for dosing with boosted PIs</td>
<td>• Child–Pugh C: no data</td>
</tr>
</tbody>
</table>
Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment, continued

<table>
<thead>
<tr>
<th>Individual Drug Components</th>
<th>Renal Insufficiency Dosing*</th>
<th>Hepatic Impairment Dosing*</th>
</tr>
</thead>
</table>
| **Emtricitabine (FTC; Emtriva)** | • CrCl 30–49 mL/min: 200 mg every 48 hr  
• CrCl 15–29 mL/min: 200 mg every 72 hr  
• CrCl <15 mL/min: 200 mg every 96 hr or solution 120/80/60 every 24 hr | • No adjustment |
| • 200 mg once daily or 240 mg once daily of suspension | | |
| **Lamivudine (3TC; Epivir)** | • CrCl > 50 mL/min: 150 mg twice daily or 300 mg once daily  
• 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: HD 50 mg first dose then 25 mg once daily | • No adjustment |
| • 150 mg twice daily or 300 mg once daily | | |
| **Raltegravir (RAL; Isentress)** | • No adjustment | • Child–Pugh A, B: no adjustment  
• Child–Pugh C: no data |
| • 400 mg twice daily | | |
| **Raltegravir (RAL; Isentress)** | • No adjustment | • No data; use with caution |
| • 600 mg twice daily | | |
| **Rilpivirine (RPV; Edurant)** | • No adjustment | • Child–Pugh A, B: no adjustment  
• Child–Pugh C: no data |
| • 25 mg once daily | | |
| **Tenofovir disoproxil fumarate (TDF; Viread)** | • 300 mg once daily  
• CrCl 30–49 mL/min: 300 mg every 48 hr  
• CrCl 10–29 mL/min: 300 mg every 72 to 96 hr  
• Dialysis: 300 mg every 7 days | • No adjustment |
| • 300 mg once daily | | |

*From drug package inserts
All Recommendations
Medical Care Criteria Committee, updated May 2018

Dolutegravir (DTG) Safety Statement, May 2018

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

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

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

 около

ALL RECOMMENDATIONS

Available ART Regimens
- Clinicians should involve their patients when deciding which ART regimen is most likely to result in patient adherence. (A3)
- Clinicians should perform the following when initiating ART:
  - Assessment for comorbidities that may affect the choice of regimen for initial therapy (A3)
  - Genotypic resistance testing for the protease and reverse transcriptase genes at diagnosis or at the initial visit if not done previously (A2)
    - See Specific Factors to Consider and Discuss with Patients
- Baseline testing is not recommended for either integrase resistance or tropism. (A3)
- For patients who have delayed initiation of ART and have engaged in high-risk behaviors associated with acquisition of HIV superinfection, genotypic resistance testing should be repeated before choosing the ART regimen. (B3)
- Clinicians should consult with a care provider experienced in ART management when:
  - Baseline resistance requires treatment with a regimen other than the listed preferred or alternative regimens (A3)
  - Selecting a regimen for patients with extensive comorbidities (B3), impaired renal function (B3), HBV or HCV co-infections (B3), active opportunistic infections (B3), or very high viral loads (B3)
- Clinicians should:
  - Ask individuals about their reproductive plans and discuss the use of contraception (A3)
  - Refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.
- A single-tablet regimen or regimen with once-daily dosing is preferred unless contraindicated by drug–drug interactions, intolerance, allergy, or access. (A2)
- For ART-naïve patients, clinicians should: (A1)
  - Select an initial ART regimen that is preferred; see Table 1. Preferred Initial ART Regimens for Non-Pregnant Adults
  - Select an alternative or other regimen only when a preferred initial regimen cannot be used; see Table 2. Alternative Initial ART Regimens for Non-Pregnant Adults or Table 3. Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults

Continued next page
ALL RECOMMENDATIONS – CONTINUED

- Two-drug regimens are not recommended as initial therapy. (A2)
- Clinicians or clinical staff should follow up, by telephone or other methods, within 2 weeks after treatment initiation to assess tolerance and adherence. Adherence should be reinforced at regular intervals. (A3)
- Clinicians should obtain a viral load test within 4 weeks after initiation to assess response to therapy. (A3)
  - See NYSDOH AI guideline Virologic and Immunologic Monitoring > Viral Load

See the following tables:
- Table 1: Preferred Initial ART Regimens for Non-Pregnant Adults
- Table 2: Alternative Initial ART Regimens for Non-Pregnant Adults
- Table 3: Other ART Regimens That Are Not Preferred or Alternative for Non-Pregnant Adults
- Table 4: Individual ARVs or Combinations to Avoid in Initial Therapy for Non-Pregnant Adults
- Table 5: Select Drug–Drug Interactions to Discuss before Initiating ART in Treatment-Naive Patients
- Table 6: Alternatives to the Tablet Form of ART Medications
- Table 7: Contraindicated ART Regimens Based on Routine Baseline Laboratory Parameters
- Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment

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