



# CLINICAL GUIDELINES PROGRAM

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

## When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

**Lead authors:** Asa Radix, MD, MPH, and Noga Shalev, MD, with the Medical Care Criteria Committee, updated October 2021

### Contents

<b>Purpose of This Guideline</b> .....	<b>2</b>
<b>Benefits and Risks of Antiretroviral Therapy</b> .....	<b>3</b>
Benefits of ART .....	3
Risks of ART .....	4
Risks of Untreated HIV .....	4
<b>Rationale for Rapid ART Initiation</b> .....	<b>5</b>
Reduced Treatment Delays and Loss to Follow-Up.....	6
Benefits for the Patient With HIV.....	6
Rapid ART Initiation Is Safe .....	7
<b>Counseling and Education before Initiating ART</b> .....	<b>7</b>
<b>Protocol for Rapid ART Initiation</b> .....	<b>8</b>
<i>Figure 1: Protocol for Rapid ART Initiation</i> .....	9
Reactive HIV Screening Test Result.....	9
Counseling.....	10
Medical and Psychosocial Assessment.....	11
<i>Box 1: Medical History Checklist</i> .....	11
Baseline Laboratory and Resistance Testing .....	11
<i>Box 2: Baseline Laboratory Testing Checklist</i> .....	12
<b>General Principles in Choosing a Regimen for Rapid ART Initiation</b> .....	<b>12</b>
Choosing a Regimen for Rapid ART Initiation .....	12
Preferred and Alternative Regimens for Rapid ART Initiation .....	13
<i>Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults</i> .....	13
<i>Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults</i> .....	14
Rapid ART Initiation Follow-Up .....	15
Paying for Rapid ART Initiation.....	15
<b>Special Considerations</b> .....	<b>16</b>
Long-Term Nonprogressors and Elite Controllers.....	17
Barriers to Adherence .....	17
Patients With Acute Opportunistic Infections .....	17
<b>All Recommendations</b> .....	<b>24</b>
<b>All Good Practices</b> .....	<b>26</b>
<b>Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity</b> .....	<b>27</b>
<b>Supplement: Guideline Development and Recommendation Ratings</b> .....	<b>29</b>

### Guideline Information

- Developer and funding source: *New York State Department of Health AIDS Institute (NYSDOH AI)*
- Intended users: NYS clinicians who are initiating ART at the time of HIV diagnosis in ART-naïve adults
- Development: See *Supplement: Guideline Development and Recommendation Ratings*

### Update: October 8, 2021

- **New in the section General Principles in Choosing a Regimen for Rapid ART Initiation:** The 2-drug ART regimen of dolutegravir/lamivudine (DTG/3TC) cannot be used for rapid ART because a baseline HIV genotypic resistance profile and hepatitis B virus status are required prior to prescription of this regimen (see the NYSDOH AI guideline *Selecting an Initial ART Regimen* for more information.) One alternative regimen (tenofovir alafenamide/emtricitabine/cobicistat/darunavir [TAF/FTC/COBI/DRV]) has been studied formally in the setting of rapid ART initiation, in a phase 3, open-label, single-arm, prospective, multicenter study without the benefit of resistance testing, and produced high rates (96%) of viral suppression (HIV RNA <50 copies/mL) at 48 weeks.
- **Removed from the table of preferred and alternative regimens for rapid ART:** Tenofovir alafenamide/emtricitabine and raltegravir HD (TAF 25 mg/FTC and RAL HD; Descovy and Isentress HD)



# When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

## → A NEW HIV DIAGNOSIS IS A CALL TO ACTION

- In support of the October 30, 2019, NYSDOH and NYC Health confirmation of rapid ART initiation as the standard of care for HIV treatment in New York, this committee supports rapid, and ideally, same-day initiation of ART in patients newly diagnosed with HIV.
- In support of the [NYSDOH AIDS Institute's January 2018 call to action](#) for patients newly diagnosed with HIV, this committee stresses the following:
  - Immediate linkage to care is essential for any person diagnosed with HIV.
  - For the person with HIV, antiretroviral therapy (ART) dramatically reduces HIV-related morbidity and mortality.
  - Viral suppression helps to prevent HIV transmission to sex partners of people with HIV and prevents perinatal transmission of HIV.
- The urgency of ART initiation is even greater if the newly diagnosed patient is pregnant, has acute HIV infection, is ≥50 years of age, or has advanced disease. For these patients, every effort should be made to initiate ART immediately, and ideally, on the same day as diagnosis.
- All clinical care settings should be prepared, either on-site or with a confirmed referral, to support patients in initiating ART as rapidly as possible after diagnosis.
- For HIV therapy to be successful over time, the initiation of ART should involve both the selection of the most appropriate regimen and the acceptance of the regimen by the patient, bolstered by education and adherence counseling. All are critical in achieving the goal of durable and complete viral suppression.
  - See the NYSDOH AI guideline [Selecting an Initial ART Regimen](#).

## 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 to encourage initiation of antiretroviral therapy (ART) at the time of HIV diagnosis in ART-naïve adults, and ideally, on the same day, or within 72 hours, an approach referred to as “rapid initiation of ART.” The NYSDOH AI [January 2018 call to action](#) emphasized the importance of starting ART at the time of HIV diagnosis and promotes scale-up of this approach to treating people newly diagnosed with HIV. The [NYSDOH and NYC Health Dear Colleague Letter of October 30, 2019](#), confirms that initiation of ART on the same day that an individual has a reactive result on an HIV screening test, or is diagnosed with HIV, or on the first clinic visit is the recommended standard of care for HIV treatment in New York. To support the standard of ART initiation upon diagnosis, toward that end, this guideline:

- Provides guidance for choosing safe and efficacious ART regimens based on known patient characteristics, before results of recommended resistance testing or baseline laboratory testing are available.
- Identifies antiretroviral regimens to avoid for rapid ART initiation.
- Provides guidance for recognizing when rapid initiation is not appropriate.
- Encourages clinicians to seek the assistance of an [experienced HIV care provider](#) when managing patients with extensive comorbidities.
- Integrates current evidence-based clinical recommendations into the healthcare-related implementation strategies of the [NYS Ending the Epidemic initiative](#), which seeks to end the AIDS epidemic in NYS by the end of 2020.
- Provides guidance on funding sources for sustainable access to ART.

# Benefits and Risks of Antiretroviral Therapy

## ☑ RECOMMENDATION: Benefits and Risks of ART

- Clinicians should recommend antiretroviral therapy to all patients with HIV infection. (A1)

Antiretroviral therapy (ART) refers to the use of pharmacologic agents that have specific inhibitory effects on HIV replication. The use of fewer than three agents is not recommended for initiating rapid treatment. These agents belong to six distinct classes of drugs: the nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs, NtRTIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs), the protease inhibitors (PIs), the fusion inhibitors (FIs), the CCR5 co-receptor antagonists, and the integrase strand transfer inhibitors (INSTIs). See all commercially available [antiretroviral drugs that are approved by the U.S. Food and Drug Administration \(FDA\) for the treatment of HIV/AIDS](#).

## Benefits of ART

ART has led to dramatic reductions in HIV-associated morbidity and mortality [CDC 2017]. In resource-rich settings, life expectancy of patients with HIV infection with access to early ART is approaching that of the general population [Siddiqi, et al. 2016]. A number of randomized clinical trials have demonstrated the benefits of ART in reducing HIV-related morbidity and mortality, irrespective of the degree of immune suppression at treatment initiation [Severe, et al. 2010; Lundgren, et al. 2015]. Thus, ART should be recommended to all individuals with HIV infection.

With proper selection of an initial regimen (see the NYSDOH AI guideline [Selecting an Initial ART Regimen](#)) and good patient adherence, durable virologic suppression (i.e., lifetime control of viral load) is achieved in virtually all patients with HIV infection. Virologic suppression almost invariably leads to immunological recovery, followed by reductions in the incidence of opportunistic infections and malignancies.

The measurable goals of treatment include:

- Viral suppression as measured by HIV-1 RNA level below the limits of detection.
- Immune reconstitution as measured by an increase in or maintenance of the CD4 cell count.
- Reduction in HIV-associated complications, including AIDS- and non-AIDS-related conditions.

ART also reduces morbidity and mortality from non-HIV-related causes. In a randomized study comparing continuous ART with CD4-guided treatment interruption, a mortality benefit was observed in subjects on continuous ART [El-Sadr, et al. 2006]. This benefit was attributed to a reduction in deaths from cardiovascular, renal, and hepatic causes. ART decreases the inflammatory milieu associated with ongoing HIV replication. It is postulated that ART-mediated reductions in proinflammatory cytokines lead to lower rates of clinical complications associated with the proinflammatory state [Hileman and Funderburg 2017].

**Reducing HIV transmission:** In addition to its direct health benefit to the individual with HIV infection, ART is a critical component of the overarching public health goal of eliminating HIV transmission. Antiretroviral treatment as prevention (TasP) is associated with greater reductions in HIV transmission than any preventative modality studied to date. In HPTN 052, a large randomized clinical trial of serodiscordant couples, early treatment of the infected partner was associated with a 96% reduction in HIV transmission compared with a delayed treatment approach [Cohen, et al. 2011]. In long-term follow-up of study participants, linked transmissions between partners were thought to occur only when the index partner was viremic [Cohen, et al. 2016]. In the observational PARTNERS study, no phylogenetically linked HIV transmission was observed in serodiscordant couples in which the index partner was virologically suppressed on ART [Rodger, et al. 2016]. The evidence thus suggests that the risk of sexual transmission of HIV during virological suppression is negligible. ART should be recommended to all patients with HIV infection to prevent transmission to sex partners and, by extrapolation, to needle-sharing partners. Despite its potent benefit in reducing HIV transmission, ART does not obviate the use of condoms or clean syringes. Those harm reduction measures, along with the use of PrEP for partners who do not have HIV infection, will help reduce the incidence of other STIs and viral hepatitis and should be integrated into patient counseling at ART initiation.

**Reduced complications:** Accumulating evidence suggests that patients who initiate ART earlier or spend less cumulative time with detectable plasma viremia are less likely to suffer certain complications, such as cardiovascular disease [El-Sadr, et al. 2006; Marin, et al. 2009; Ho, et al. 2010; Lichtenstein, et al. 2010; Ho, et al. 2012], neurocognitive dysfunction [Tozzi, et al. 2007; Ellis, et al. 2011; Garvey, et al. 2011; Winston, et al. 2012], decreased risk of severe bacterial infections

[O'Connor, et al. 2017], and some non-HIV-related malignancies [Bruyand, et al. 2009; Guiguet, et al. 2009; Silverberg, et al. 2011; Sigel, et al. 2012]. Cohort data also demonstrate that although older patients are likely to achieve virologic suppression, they are less likely to achieve an immunologic response, as measured by an increase of CD4 count by 100 cells/mm<sup>3</sup>, and that patients >55 years old may be at higher clinical risk even after starting therapy [Sabin, et al. 2008]. The poor immunologic recovery seen in older patients is associated with higher morbidity and mortality, particularly cardiovascular events [van Lelyveld, et al. 2012]. In one study, men ≥50 years of age who initiated ART with CD4 counts in the 351 to 500 cells/mm<sup>3</sup> range were able to achieve similar immunologic responses as younger men who initiated at lower CD4 counts [Li X, et al. 2011].

**Reduced perinatal transmission of HIV:** Studies have shown that for pregnant women with HIV, the administration of ART during pregnancy or intrapartum significantly reduces the risk of mother-to-child transmission (MTCT) of HIV [Connor, et al. 1994; Guay, et al. 1999]. In addition, a large study showed a 96% reduction in transmission between serodiscordant heterosexual couples when the positive partner was receiving ART [Cohen, et al. 2011], adding to the body of evidence that lower viral load reduces transmission risk. ART is now part of the established strategy aimed at reducing HIV transmission and is an essential component of prevention interventions along with risk-reduction counseling, safer-sex practices, and avoidance of needle-sharing. Although the majority of patients both in New York and worldwide present later in the course of their HIV infection [Althoff, et al. 2010; CDC 2010, 2011], ongoing efforts to offer universal HIV testing to all patients over age 13 may begin to identify patients earlier in their disease who can benefit from immediate treatment.

## Risks of ART

Despite the excellent tolerability of contemporary ART regimens, adverse reactions, side effects, long-term drug toxicities, and drug-drug interactions continue to pose some relative or limited risks. Patients must be counseled about the potential for ART-associated adverse events in the short and long term. These risks include tolerability issues, which may affect quality of life, as well as possible long-term toxicities—primarily a low relative risk of renal and cardiovascular disorders or decreased bone density of uncertain clinical significance [Friis-Moller, et al. 2010; Monteiro, et al. 2014; Hoy, et al. 2017]. Renal and bone density issues are largely eliminated with newer formulations of ARVs. Fatal drug reactions from ART are exceedingly rare.

Many ART combinations are now available in single-pill, fixed-dose combination formulations. Thus, the pill burden associated with early antiretroviral regimens has been largely eliminated. Nevertheless, lifelong adherence to medications may constitute a challenge to some, particularly when treatment with a single daily tablet is not feasible.

When compared with early antiretroviral combinations, contemporary ART regimens (see the NYSDOH AI guideline *Selecting an Initial ART Regimen*) are associated with higher rates of durable virologic suppression. Lack of virologic suppression in a patient on ART should prompt the clinician to evaluate patient adherence and provide intensive support for those reporting challenges in this domain. Failure to achieve and maintain virologic suppression may lead to the emergence of resistance-associated mutations (RAMs). A large cohort study has demonstrated that virologic failure with contemporary ART regimens is associated with the infrequent emergence of RAMs [Scherrer, et al. 2016]. Nevertheless, RAMs can emerge with current first-line therapies. Resistance to antiretroviral medications may compromise the potential for long-term virologic suppression, simple dosing schedules, and the tolerability of future treatment options.

ART initiation is associated with a risk of immune reconstitution inflammatory syndrome (IRIS). IRIS is a clinical syndrome characterized by new or worsening infectious and non-infectious complications observed after the initiation of ART (see the NYSDOH AI guideline *Management of IRIS*). The risk of IRIS increases when ART is begun at low CD4 cell counts (<100 cells/mm<sup>3</sup>) or with the presence of specific opportunistic infections. Although the risk of IRIS is not a contraindication to initiating ART, clinicians and patients should be aware that the risk of developing IRIS is increased among individuals with lower CD4 counts. Patients at increased risk should be informed of the potential for a paradoxical clinical worsening after ART initiation.

## Risks of Untreated HIV

Results from the START trial [Lundgren, et al. 2015] and strong cohort data show that untreated HIV infection leads to increased morbidity and mortality from both HIV-related and non-HIV-related conditions, even at high CD4 counts. Together with the dramatic reduction of transmission risk with effective treatment, these data support the initiation of ART regardless of CD4 count in all adequately prepared patients, including patients diagnosed with acute HIV infection (for more discussion see the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*). Patients in care who are

documented *long-term nonprogressors* or *elite controllers* are a group that may warrant special consideration (see the *Special Considerations* section of this guideline).

In START, a randomized trial initiating ART in treatment-naïve patients with CD4 counts >500 cells/mm<sup>3</sup> versus waiting for a decrease to ≤350 cells/mm<sup>3</sup> before initiation showed a 53% reduction in serious illness and death in the early ART group [Lundgren, et al. 2015]. Data from NA-ACCORD, a large observational cohort study, showed that both morbidity and mortality were improved by initiation of ART in patients with CD4 counts in the high or even normal range [Kitahata, et al. 2009]. A significantly decreased risk of death was observed in patients who initiated therapy at CD4 counts >500 cells/mm<sup>3</sup> compared to those who deferred to <500 cells/mm<sup>3</sup>, as well as in the cohort who initiated ART in the 350 to 500 cells/mm<sup>3</sup> range compared with those deferring to <350 cells/mm<sup>3</sup> [Kitahata, et al. 2009]. Although other cohort studies demonstrated only a minimal survival advantage [Wright, et al. 2011] or no survival advantage among those starting ART at the highest CD4 counts, they did confirm the benefits of initiating ART at levels ≤500 cells/mm<sup>3</sup> [Cain, et al. 2011; CASCADE Collaboration 2011; Young, et al. 2012]. Another showed an approximately 33% reduction in the risk of death from end-stage liver disease, non-AIDS infections, and non-AIDS-defining cancers with each 100 cells/mm<sup>3</sup> increase in CD4 count [Marin, et al. 2009]. A randomized study of early versus deferred therapy in patients with CD4 counts in the 350-550 cells/mm<sup>3</sup> range showed no mortality benefit [Cohen, et al. 2011]; however, this study has significant limitations, most notably a relatively brief follow-up period.

## Rationale for Rapid ART Initiation

### RECOMMENDATIONS: Rationale for Rapid ART Initiation

- Clinicians should recommend antiretroviral therapy (ART) for all patients with a diagnosis of HIV infection. (A1)
- Clinicians should offer rapid initiation of ART—preferably on the same day (A1) or within 72 hours—to all individuals who are candidates for rapid ART initiation (see text) and who have:
  - A confirmed HIV diagnosis (A1), *or*
  - A reactive HIV screening result pending results of a confirmatory HIV test (A2), *or*
  - Suspected acute HIV infection, i.e., HIV antibody negative and HIV RNA positive (A2).
- Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk after effective ART is initiated and viral suppression is achieved, and should strongly recommend ART for patients with seronegative partners. (A1)
- Clinicians should evaluate and prepare patients for ART initiation as soon as possible; completion of the following should not delay initiation:
  - Discuss **benefits and risks of ART** with the patient. (A3)
  - Assess patient readiness. (A3)
  - Identify and ameliorate factors that might interfere with successful adherence to treatment, including inadequate access to medication, inadequate supportive services, psychosocial factors, active substance use, or mental health disorders. (A2)
- Clinicians should refer patients for supportive services as necessary to address modifiable barriers to adherence. An ongoing plan for coordination of care should be established. (A3)
- Clinicians should involve patients in the decision-making process regarding initiation of ART and which regimen is most likely to result in adherence. The patient should make the final decision of whether and when to initiate ART. (A3)
- If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible.
- In patients with advanced HIV (or AIDS), ART should be initiated even if barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support. (A2)
- After ART has been initiated, response to therapy should be monitored by, or in consultation with, a clinician with **experience in managing ART**. (A2)



The New York State Department of Health (NYSDOH) HIV Clinical Guidelines Program and the U.S. Department of Health and Human Services (DHHS) recommend initiation of ART for all patients with a confirmed HIV diagnosis regardless of their CD4 cell count or viral load, for the benefit of the individual with HIV (reduced morbidity and mortality) [Zolopa, et al. 2009; Lundgren, et al. 2015] and to reduce the risk of transmission to others [Cohen, et al. 2016]. Initiating ART during early HIV infection may improve immunologic recovery (CD4 T cell counts) and reduce the size of the HIV reservoir [Jain, et al. 2013]; there is also evidence that initiating ART at the time of diagnosis reduces treatment delays and improves retention in care and viral suppression at 12 months [Ford, et al. 2018].

#### → KEY POINTS

- Rapid ART initiation, the standard of care in New York State, is efficacious, safe, and highly acceptable, with few patients declining the offer of immediate ART.
- Patients with active substance use, untreated mental health conditions, immigration issues or unstable housing deserve the highest standard of HIV care, including the option of rapid initiation of ART. Potential barriers to medication adherence and care continuity can be addressed with appropriate counseling and linkage to support services.

## Reduced Treatment Delays and Loss to Follow-Up

Standard practice protocols for ART initiation have produced preventable delays, and the required wait for confirmatory HIV diagnostic and baseline laboratory test results (including resistance testing) along with required medical visits can unnecessarily delay the start of treatment by as long as 4 weeks. Problems in accessing insurance or waiting for activation of public benefits may also cause delays. It is estimated that in 2016, only 75.9% of individuals diagnosed with HIV in the U.S. HIV care continuum were linked to care within 1 month [CDC 2018]. Individuals with HIV who are not linked to care are at risk of having sustained viral loads and ongoing HIV transmission.

Rapid initiation of ART may reduce delays and improve viral suppression rates in people with HIV. Rapid or same-day ART initiation, which is preferable, or initiation within 3 days of a newly positive HIV test is the strategy endorsed by the World Health Organization [WHO 2017] and is an essential component of the *New York State Ending the Epidemic initiative*. Mathematical modeling demonstrates that a test-and-treat strategy, with immediate initiation of ART and prevention approaches, could lead to elimination of new HIV infections [Granich, et al. 2009].

## Benefits for the Patient With HIV

Several observational and clinical trials have demonstrated the individual-level benefits of rapid ART initiation [Ford, et al. 2018]. An early pilot of this approach in San Francisco, California, demonstrated that patients initiating ART within 1 or 2 days had a shorter time (median, 1.8 months) to viral suppression (HIV RNA  $\leq 200$  copies/mL) than those offered the standard of care (4.3 months) or than historical controls (7.2 months) [Pilcher, et al. 2017]. A longer-term follow-up of 225 patients at the same center found that, of patients who had access to rapid initiation, 95.8% had achieved viral suppression at least once and 92.1% had achieved it at the last recorded visit [Coffey, et al. 2019]. These individual-level benefits have been replicated in other U.S. and international studies that demonstrated improved viral suppression with shortened time to ART initiation [Rosen, et al. 2016a; Koenig, et al. 2017; Colasanti, et al. 2018]. After implementing rapid ART initiation at a hospital clinic in Atlanta, Georgia, time to viral suppression fell from 77 days, before the intervention, to 57 days [Lundgren, et al. 2015], and average time to ART initiation decreased from 21 to 7 days; both findings were statistically significant [Colasanti, et al. 2018].

Another demonstrated benefit is an improved rate of retention in care [Amanyire, et al. 2016; Rosen, et al. 2016a; Koenig, et al. 2017]. In the RapIT trial in South Africa, patients newly diagnosed with HIV were randomized to rapid ART initiation or standard of care [Rosen, et al. 2016b]. The participants in the rapid initiation arm had higher rates of ART initiation at 90 days (97% vs. 72%) and higher rates of retention in care and viral suppression (HIV RNA  $\leq 400$  copies/mL) at 10 months (relative risk, 1.26 [1.05–1.50]). The average cost per patient to achieve viral suppression was lower in the intervention arm, demonstrating that this strategy of care may also be cost-effective [Long, et al. 2017]. Studies conducted in China and South Africa support the cost-effectiveness of rapid ART initiation [Zulliger, et al. 2014; Wu, et al. 2015; Ford, et al. 2018]. Rapid ART initiation is efficacious, safe, and highly acceptable, with few patients declining the offer of immediate ART [Pilcher, et al. 2017; Coffey, et al. 2019].

Modeling evidence suggests the potential for rapid ART initiation to significantly reduce HIV transmission in the community, although this has been directly modeled only in the context of South Africa [Granich, et al. 2009]. In the United States, linkage to and retention in HIV care are significant gaps in the HIV care continuum, with an estimated 64% of individuals with HIV receiving any HIV care and 49% being retained in care during 2016 [CDC 2019]. Models have translated these gaps in care to their effect on HIV transmission in the United States, demonstrating that between 43% and 49% of new HIV transmissions are attributable to individuals who have been diagnosed with HIV but are not receiving ART and have not been retained in care [Skarbinski, et al. 2015; Li Z, et al. 2019]. Because it is designed to help close this care gap, rapid ART initiation greatly reduces new HIV infections, hastening the achievement of [HIV incidence reduction goals in New York State](#).

## Rapid ART Initiation Is Safe

In the San Francisco study discussed above [Pilcher, et al. 2017], 89.7% of patients used integrase strand transfer inhibitor (INSTI)-containing regimens and 12.8% used protease inhibitor–containing regimens. The predominant INSTI-based regimen was dolutegravir plus emtricitabine/tenofovir disoproxil fumarate. The clinic did not have any cases of major resistance mutations to the prescribed ART regimen, and no regimen switches were made because of resistance. Two patients had their regimens changed because of rash, and in 10 cases, the regimen was simplified to a single-tablet regimen.

Of 149 patients initiating ART through a program in New York City, only 1 required a regimen change because of subsequently detected resistance [Blank, et al. 2018].

Rapid ART initiation is safe. Most designated regimens for rapid ART initiation are the same regimens that are recommended as initial treatment in the existing [NYSDOH](#), [International Antiviral Society–USA](#), and [DHHS](#) guidelines. These regimens are well-tolerated and effective, and the likelihood of drug resistance is low based on the current prevalence of drug resistance [NYCDHMH 2018].

### → RESOURCES

- The CEI Line provides primary care providers in New York State the opportunity to consult with [clinicians who have experience managing ART](#). The CEI Line can be reached at 1-866-637-2342 or 1-585-273-2793.
- The AIDS Institute maintains a voluntary [NYSDOH AIDS Institute Provider Directory](#) to assist with identification of experienced providers in New York State.
- Experienced care providers can also be identified through the [American Academy of HIV Medicine \(AAHIVM\)](#) and the [HIV Medicine Association \(HIVMA\)](#).

## Counseling and Education before Initiating ART

### RECOMMENDATIONS: Counseling and Patient Education

- Counseling and education should include the following:
  - Basic education about HIV, CD4 cells, viral load, and resistance. (A3)
  - Available treatment options and potential risks and benefits of therapy (see text). (A3)
  - The need for strict adherence to avoid the development of viral drug resistance. (A2)
  - Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection. (A3)
- Clinicians should involve the patient in the decision-making process regarding initiation of ART. (A3)

Discussion of ART should occur when a positive HIV test result is obtained, regardless of CD4 count. The clinician and patient should discuss the benefits of early ART (see below) and individual factors that may affect the decision to initiate, such as patient readiness or reluctance and adherence barriers. Clinicians should involve the patient in the decision-making process regarding initiation of ART [Salzberg Global Seminar 2011]. When clinicians and patients engage in shared decision-making, patients are more likely to choose to initiate ART and to achieve an undetectable viral load [Beach, et al.

2007]. Misconceptions about treatment initiation should be addressed, including the implication that starting ART represents advanced HIV illness or that taking ART may adversely affect therapeutic levels of gender-affirming hormones [Braun, et al. 2017]. Initiating ART before symptoms occur allows patients to stay healthier and live longer.

The risks and benefits of early ART to discuss with patients when making the decision of whether and when to initiate ART are outlined below. It should be emphasized that the START trial provided definitive evidence that the benefits of early initiation of ART outweigh the potential disadvantages.

**Benefits of early ART in asymptomatic patients:**

(early therapy = initiation at CD4 counts >500 cells/mm<sup>3</sup>)

- Reduction in HIV-related and non-HIV-related morbidity and mortality [Phillips, et al. 2007; Kitahata, et al. 2009; Marin, et al. 2009; Sterne, et al. 2009; Ray, et al. 2010; Silverberg, et al. 2011; Ho, et al. 2012; Lewden, et al. 2012; Lundgren, et al. 2015].
- Delay or prevention of immune system compromise [Lewden, et al. 2007].
- Possible lower risk of antiretroviral resistance [Uy, et al. 2009].
- Decreased risk of *sexual* transmission of HIV [Quinn, et al. 2000; Castilla, et al. 2005; Donnell, et al. 2010; Cohen, et al. 2011]. HIV cannot be transmitted *sexually* when the plasma viral load is undetectable; ART is not a substitute for primary HIV prevention measures, such as avoidance of needle sharing [Politch, et al. 2012].
- Decreased risk of several severe bacterial infections [O'Connor, et al. 2017].
- Potential decrease in size of viral reservoir and preservation of gut-associated lymphoid tissue with initiation during acute HIV, i.e., within the first 6 weeks [Jain, et al. 2013; Novelli, et al. 2018].

**Disadvantages of early ART in asymptomatic patients:**

- Possibility of greater cumulative side effects from ART [Volberding and Deeks 2010].
- Possibility for earlier development of drug resistance and limitation in future [Barth, et al. 2012] antiretroviral options if adherence and viral suppression are suboptimal.
- Possibility for earlier onset of treatment fatigue.

→ RESOURCES

- Patients who do not have health insurance may qualify for Medicaid or the [NYSDOH HIV Uninsured Care Program](#), which provides access to free health care (HIV drugs, primary care, home care, and the ADAP Plus Insurance Continuation Program, or APIC) for residents who have HIV and are uninsured or underinsured. The program is open Monday-Friday, 8:00AM-5:00PM and can be reached: in state 1-800-542-2437; out-of-state 1-518-459-1641; TDD 1-518-459-0121. If eligible, patients may also consider treatment options through enrollment in clinical trials. A resource that may help with this process is the [AIDS Clinical Trials Information Service \(1-800-TRIALS-A\)](#).

## Protocol for Rapid ART Initiation

**☑ RECOMMENDATIONS: Protocol for Rapid ART Initiation**

- To determine whether a patient is a candidate for rapid antiretroviral therapy (ART) initiation, the clinician should confirm that the individual has any of the following (A1):
  - A reactive point-of-care HIV test result, or confirmed HIV diagnosis, or suspected acute HIV infection, or known HIV infection, and
  - No prior ART (i.e., treatment naive) or limited prior use of antiretroviral medications, and
  - No medical conditions or opportunistic infections that require deferral of rapid ART initiation, including suspected cryptococcal or tuberculous meningitis.
- Clinicians should perform baseline laboratory testing listed in *Box 2: Baseline Laboratory Testing Checklist* for all patients who are initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)



→ SELECTED GOOD PRACTICE REMINDERS

- For patients with a reactive HIV antibody screening test that is pending confirmation, make sure the patient understands the benefits of rapid ART initiation and the following:
  1. Reactive screening test results are not formally diagnostic, because false-positive results are still possible;
  2. A confirmatory (diagnostic) HIV test will be performed;
  3. ART will be discontinued if the confirmatory test result is negative and continued if it is positive;
  4. The benefit of starting ART early, after a presumptive positive screening test, outweighs the negligible risk of taking ART for a few days and then stopping it if confirmed HIV negative.
- Provide the result of the confirmatory HIV test as soon as it is available; discontinue ART if the result is negative and reinforce adherence and next steps if it is positive.
- If a patient declines rapid ART initiation, discuss options for deferred initiation of ART, link the patient with HIV primary care, and outline next steps.

Figure 1: Protocol for Rapid ART Initiation

Identify Rapid ART Candidates	Counseling and Education	Assess and Refer	Baseline Lab Testing	Initiate ART	Payment Assistance?	Follow-Up	Adjust ART
Candidates have: <ul style="list-style-type: none"> <li>• A new reactive POC HIV test result, new HIV diagnosis, acute HIV, or known HIV, <i>and</i></li> <li>• No or limited prior ARV use, <i>and</i></li> <li>• No medical conditions or OIs that require deferral of ART initiation</li> </ul>	<ul style="list-style-type: none"> <li>• HIV diagnosis</li> <li>• Disclosure</li> <li>• Adherence</li> <li>• Side effects and management of</li> <li>• Management of lifelong medications</li> </ul>	<ul style="list-style-type: none"> <li>• Health literacy</li> <li>• Identify and address medical and psychosocial barriers to treatment and adherence</li> <li>• As indicated, refer for substance use treatment, behavioral health services, housing assistance</li> </ul>	<ul style="list-style-type: none"> <li>• Confirm HIV diagnosis</li> <li>• Viral load</li> <li>• Resistance testing</li> <li>• CD4 count</li> <li>• HAV, HBV, HCV testing</li> <li>• Metabolic panel</li> <li>• STIs</li> <li>• Urinalysis</li> <li>• Pregnancy test for individuals of childbearing potential</li> </ul>	<ul style="list-style-type: none"> <li>• Choose a preferred regimen based on patient characteristics and preference</li> <li>• Initiate ART immediately—preferably on the same day—or within 72 hours</li> <li>• Administer the first dose on site if possible</li> </ul>	<ul style="list-style-type: none"> <li>• Assess need for payment assistance</li> <li>• Refer patients with no insurance to NYS UCP</li> <li>• Provide resources for payment assistance</li> </ul>	<ul style="list-style-type: none"> <li>• Contact the patient within 24 to 48 hours by phone (or other preferred method)</li> <li>• Assess medication tolerance and adherence</li> <li>• If feasible, schedule in-person visit with medical care provider within 7 days</li> <li>• Reinforce adherence</li> </ul>	<ul style="list-style-type: none"> <li>• Change or adjust the initial ART regimen based on results of initial lab and resistance testing</li> </ul>

NYSDOH AI Clinical Guidelines Program [www.hivguidelines.org](http://www.hivguidelines.org)

## Reactive HIV Screening Test Result

When the result of a patient’s initial HIV point-of-care screening test is reactive, established practice is to obtain a blood specimen for diagnostic HIV testing because of the possibility of false-positive screening results. This is particularly important for individuals who are not at high risk of acquiring HIV. However, supplemental testing results may not be available for several days, introducing the risk that a patient will not return. The goal of the rapid ART initiation protocol is to assess whether a person with a reactive HIV screening test result (or a confirmed HIV diagnosis) is also a candidate for same-day initiation of ART. If so, then the rapid ART initiation protocol is to provide counseling on HIV transmission and the benefits of ART, initiate ART that day or within 3 days, and link the person expeditiously to HIV primary care. Thus, the protocol recommends immediate initiation of ART while awaiting confirmatory HIV test results.

Patients who are candidates for rapid ART initiation:

- Have a new reactive point-of-care HIV test result or a new HIV diagnosis (confirmed through the *Centers for Disease Control and Prevention HIV testing algorithm*) or acute HIV infection (HIV antibody negative and HIV RNA positive) or known HIV, *and*
- Are treatment-naïve, *or*

- Have a history of limited ART use (e.g., a person who stopped first-line therapy for reasons other than regimen failure), as long as concern for acquired drug resistance is low (requires a case-by-case determination).

Patients with a new reactive HIV test result can be retested using a second point-of-care test from a manufacturer different from that of the first test to further minimize the possibility of a false-positive result. It is not necessary to retest with a second point-of-care test before providing ART, but given the possibility of a false-positive screening result, a laboratory-based confirmatory HIV test should always be performed to establish a diagnosis of HIV. If the confirmatory HIV test result is negative, ART can be discontinued.

→ **KEY POINT**

- Patients with a new reactive HIV test result can be retested using a second point-of-care test from a different manufacturer than that of the first test, if available, to further minimize the possibility of a false-positive result.
  - See the NYSDOH AI guideline *HIV Testing > Characteristics of FDA-Approved Rapid HIV Tests* for a list of available point-of-care HIV tests.

## Counseling

A reactive HIV screening result should prompt a care provider to counsel the patient about the benefits and risks of ART and about HIV transmission risk, including the consensus that *Undetectable Equals Untransmittable (U=U)*. When patients are initiated on ART on the same day as their reactive HIV test result, the priorities for patient education and counseling include:

- Confirming the diagnosis of HIV.
- Managing disclosure, if indicated.
- Adhering to the ART regimen.
- Recognizing and responding to side effects.
- Following through with clinic visits.
- Assessing health literacy.
- Managing lifelong ART: Navigating acquisition of and paying for medications required for lifelong therapy, including pharmacy selection, insurance requirements and restrictions, co-pays, and prescription refills.
- Identifying and addressing psychosocial issues that may pose barriers to treatment.
- Referring for substance use and behavioral health counseling if indicated.
- Referring for housing assistance if indicated.
- Ensuring the patient knows how to reach the care team if needed, to address the adverse effects of medications or other concerns.

→ **KEY POINT: HEALTH LITERACY**

- According to the *National Network of Libraries of Medicine*, health literacy requires:
  - The ability to understand instructions on prescription drug bottles, appointment slips, medical education brochures, and doctor’s directions and consent forms.
  - The ability to negotiate complex healthcare systems.
  - Reading, listening, analytical, and decision-making skills, and the ability to apply these skills to health situations.
- Resources:
  - *AHRQ Short Assessment of Health Literacy–Spanish and English*
  - *AHRQ Rapid Estimate of Adult Literacy in Medicine–Short Form*
  - *AHRQ Short Assessment of Health Literacy for Spanish Adults*
  - *Health Literacy Tool Shed (funded by the U.S. National Libraries of Medicine)*

## Medical and Psychosocial Assessment

Medical assessment of a patient with a new reactive HIV test result should include history or signs or symptoms of opportunistic infection(s). ART should be delayed and appropriate medical management initiated if tuberculous (TB) meningitis or cryptococcal meningitis are suspected (see below) [WHO 2017], if cytomegalovirus retinitis is suspected, or if the patient has any evidence of advanced HIV disease on clinical exam.

To identify the potential for pre-existing drug-resistant virus, the initial assessment should also include the patient's history of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) use and previous ART use for people who are re-engaging in care [Ford, et al. 2018]. See *Box 1: Medical History Checklist*, below.

### Box 1: Medical History Checklist

When taking a medical history before rapid ART initiation, ask about:

- Date and result of last HIV test
- Serostatus of sex partners and their ART regimens if known
- Previous use of antiretroviral medications, including as PrEP or PEP, with dates of use
- Comorbidities, including a history of renal or liver disease, particularly hepatitis B infection
- Prescribed and over-the-counter medications
- Drug allergies
- Substance use
- Symptoms, to assess for active cryptococcal and TB meningitis
- Psychiatric history, particularly depressive or psychotic symptoms or any history of suicidality
- Possible pregnancy and childbearing plans in individuals of childbearing potential

**Deferral of ART initiation:** If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible. In some circumstances, such as in the rare case of suspected cryptococcal or TB meningitis, rapid ART is not recommended (see the *Patients With Acute Opportunistic Infections* section of this guideline). Patients who present with signs and symptoms suggestive of pulmonary or intracranial and ophthalmologic infections should receive further assessment before initiating ART on the same day as a reactive HIV screening test result.

ART initiation should be delayed in any person presenting with signs or symptoms suggestive of meningitis, including headache, nausea or vomiting, light sensitivity, and changes in mental status. Treatment of TB meningitis was investigated in a clinical trial in Vietnam in which immediate initiation of ART was compared with ART initiated 2 months after TB treatment [Torok, et al. 2011]. There were significantly more grade 4 adverse effects in individuals who initiated ART immediately than in those who delayed. Among patients with cryptococcal meningitis, early initiation of ART has been associated with adverse outcomes, including death [Boulware, et al. 2014]; therefore, it is recommended that ART be deferred until after the induction phase of treatment for cryptococcal meningitis has been completed (see *DHHS: Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV*).

It is clear that co-treatment of HIV and pulmonary TB improves survival. In the SAPIT trial in South Africa, there was a 56% relative reduction in mortality when ART was initiated within 4 weeks of TB treatment initiation, compared with when it was started after TB treatment was completed (hazard ratio, 0.44; 95% confidence interval, 0.25–0.79;  $P=.003$ ), although symptoms of immune reconstitution inflammatory syndrome (IRIS) were greater in patients who started ART earlier [Abdool Karim, et al. 2010]. However, it is not clear that ART initiation prior to initiation of pulmonary TB treatment is the best course of action. Care providers should weigh the benefits of rapid ART initiation against the potential drawbacks of pill burden, *drug interactions*, and the risk of IRIS.

## Baseline Laboratory and Resistance Testing

All patients with a reactive HIV test result should undergo the baseline laboratory testing listed in Box 2, below. For discussion of baseline testing, see the NYSDOH AI guideline *Selecting an Initial ART Regimen > ART-Initiation Laboratory Testing*. It is not necessary to wait for these test results before initiating ART.

**Box 2: Baseline Laboratory Testing Checklist**

- HIV-1/2 antigen/antibody assay
- HIV quantitative viral load
- Baseline HIV genotypic resistance profile
- Baseline CD4 cell count
- Testing for hepatitis A, B, and C viruses
- Comprehensive metabolic panel (creatinine clearance, hepatic profile)
- See [CDC > Sexually Transmitted Infections Treatment Guidelines, 2021 > Screening](#)
- Urinalysis
- Pregnancy test for individuals of childbearing potential

## General Principles in Choosing a Regimen for Rapid ART Initiation

**RECOMMENDATIONS: General Principles in Choosing a Regimen for Rapid ART Initiation**

- Clinicians should involve their patients when deciding which antiretroviral therapy (ART) regimen is most likely to result in adherence. (A3)
- Before initiating ART, clinicians should:
  - Assess the patient’s prior use of antiretroviral medications, including pre-exposure prophylaxis (PrEP), which may increase the risk for baseline resistance. (A2)
  - Assess for any comorbidities and chronic coadministered medications that may affect the choice of regimen for initial ART. (A2)
  - At the time of HIV diagnosis, obtain genotypic resistance testing for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes.
  - Ask individuals of childbearing potential about the possibility of pregnancy, their reproductive plans, and their use of contraception. (A3)
- For ART-naïve patients, clinicians should select an initial ART regimen that is preferred; see *Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults*. (A1)
- Clinicians should reinforce medication adherence regularly. (A3)
- Clinicians should obtain a viral load test 4 weeks after ART initiation to assess the response to therapy. (A3)
  - See the NYSDOH AI guideline *Virologic and Immunologic Monitoring* for more information.

**→ SELECTED GOOD PRACTICE REMINDERS**

- Follow up within 24 to 48 hours, by telephone or another preferred method, with a patient who has initiated ART to assess medication tolerance and adherence.
- If feasible, schedule an in-person visit for 7 days after ART initiation.

## Choosing a Regimen for Rapid ART Initiation

The preferred medications for rapid ART initiation are based on the established regimens for individuals who are ART-naïve and are restricted to those that can be safely initiated in the absence of readily available baseline laboratory testing results, such as viral load, CD4 count, and HLA-B\*5701. The preferred regimens have a high barrier to resistance, are well tolerated, and limit the potential for **drug-drug interactions**. Initial regimens should be selected on the basis of patient preferences and clinical characteristics, and a preferred regimen should be used whenever possible (see *Table 1*, below).

The 2-drug ART regimen of dolutegravir/lamivudine (DTG/3TC) cannot be used for rapid ART because a baseline HIV genotypic resistance profile and hepatitis B virus status are required prior to prescription of this regimen (see the NYSDOH AI guideline *Selecting an Initial Antiretroviral Therapy Regimen* for more information.)

One alternative regimen (tenofovir alafenamide/emtricitabine/darunavir/cobicistat [TAF/FTC/DRV/COBI]) has been studied formally in the setting of rapid ART initiation, in a phase 3, open-label, single-arm, prospective, multicenter study without the benefit of resistance testing, and produced high rates (96%) of viral suppression (HIV RNA level <50 copies/mL) at 48 weeks [Huhn, et al. 2019].

When following a rapid ART initiation protocol, care providers should avoid regimens containing abacavir because results of HLA-B\*5701 testing are not likely to be available. Similarly, rilpivirine should be avoided in any patient who has a viral load >100,000 copies/mL and in any patient whose viral load is unknown.

Efavirenz is associated with a higher risk of central nervous system side effects and of transmitted drug resistance mutations [Kagan, et al. 2019]; therefore, it is not recommended for rapid ART initiation.

Clinics that have implemented rapid ART initiation frequently design pre-approved regimens that consider local patterns of transmitted drug resistance and drug toxicity [Pilcher, et al. 2017].

There is a greater possibility that HIV drug resistance mutations may emerge and reduce the efficacy of an initial ART regimen in patients with a new reactive HIV screening test or a new HIV diagnosis who have taken tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide fumarate/emtricitabine (TAF/FTC) as PrEP since their last negative HIV test. Results of a recent study in New York City demonstrated that individuals who had taken PrEP in the 3 months prior to a new HIV diagnosis were significantly more likely than those who never used PrEP (26% vs. 2%;  $P<.0001$ ) to have resistance mutations (M184I/V/IV/MV) to lamivudine/emtricitabine (3TC/FTC) [Misra, et al. 2019]. For such patients, the initial regimen should consist of an integrase strand transfer inhibitor plus a boosted protease inhibitor and 2 nucleoside reverse transcriptase inhibitors. An option for treatment in this scenario is provided in *Table 1*, below. The initial regimen may be simplified once results of baseline genotypic testing have been reviewed.

- See the NYSDOH AI guideline *Selecting an Initial ART Regimen* for more information.

## Preferred and Alternative Regimens for Rapid ART Initiation

*Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults*, below, includes initial preferred and alternative regimens for rapid ART initiation in nonpregnant adults. The regimens are listed alphabetically. For specific details on choosing a regimen, see the discussions in other sections of this guideline and the [package inserts](#) for the drugs listed below.

**Providing ART:** Some clinics provide patients with the first dose of ART and a 30-day prescription when a rapid ART initiation protocol is being followed [Pilcher, et al. 2017]. Others may provide a 7-day ART starter pack or a 30-day prescription.

Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults		
Regimen	Comments	Rating
<i>Preferred Regimens</i>		
Tenofovir alafenamide/emtricitabine/bictegravir (TAF 25 mg/FTC/BIC; Biktarvy)	<ul style="list-style-type: none"> <li>• Available as a single-tablet formulation, taken once daily.</li> <li>• TAF/FTC should not be used in patients with a creatinine clearance (CrCl) &lt;30 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>• Contains 25 mg of TAF, unboosted.</li> <li>• 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.</li> </ul>	A1
Tenofovir alafenamide/emtricitabine and dolutegravir [a] (TAF 25 mg/FTC and DTG; Descovy and Tivicay)	<ul style="list-style-type: none"> <li>• TAF/FTC should not be used in patients with CrCl &lt;30 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>• Contains 25 mg of TAF, unboosted.</li> <li>• Two tablets once daily.</li> <li>• 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.</li> </ul>	A1



Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults		
Regimen	Comments	Rating
Tenofovir alafenamide/emtricitabine/darunavir/cobicistat (TAF 10 mg/FTC/DRV/COBI; Symtuza)	<ul style="list-style-type: none"> <li>Available as a single-tablet formulation, taken once daily.</li> <li>Contains 10 mg TAF, boosted.</li> <li>TAF/FTC should not be used in patients with CrCl &lt;30 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>Pay attention to <a href="#">drug-drug interactions</a>.</li> </ul>	A2
<p><i>Regimen for Patients With Exposure to TDF/FTC as PrEP Since Their Last Negative HIV Test</i> Note: The initial ART regimen may be simplified based on results of genotypic resistance testing.</p>		
Dolutegravir and darunavir/cobicistat/tenofovir alafenamide/emtricitabine [a] (DTG/DRV/COBI/TAF/FTC 10 mg/FTC; Tivicay and Symtuza)	<ul style="list-style-type: none"> <li>TAF/FTC should not be used in patients with CrCl &lt;30 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>Documented DTG resistance after initiation in treatment-naive patients is rare.</li> <li>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.</li> <li>Tenofovir disoproxil fumarate (TDF) may be substituted for TAF; TDF/FTC is available as a single tablet (brand name, Truvada).</li> <li>Lamivudine (3TC) may be substituted for FTC.</li> <li>3TC/TDF is also available as a single tablet.</li> </ul>	A3
<p><i>Medications to Avoid</i></p>		
<ul style="list-style-type: none"> <li>Abacavir (ABC)</li> <li>Rilpivirine (RPV)</li> <li>Efavirenz (EFV)</li> </ul>	<ul style="list-style-type: none"> <li>ABC should be avoided unless a patient is confirmed to be HLA-B*5701 negative.</li> <li>RPV should be administered <b>only</b> in patients confirmed to have a CD4 cell count <math>\geq 200</math> cells/mm<sup>3</sup> and a viral load &lt;100,000 copies/mL.</li> <li>EFV is not as well tolerated as other antiretroviral medications, and nonnucleoside reverse transcriptase inhibitors have higher rates of resistance.</li> </ul>	A3
<p><b>Note:</b> a. See <a href="#">Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity</a>.</p>		

Reducing the risk of perinatal transmission of HIV requires timely identification of HIV infection in a pregnant individual and 3-drug ART initiated as soon as possible after diagnosis. Pregnancy is not a contraindication to rapid ART initiation. Adherence to an ART regimen during pregnancy should be encouraged, as should coordination among HIV and obstetric care providers (see the NYSDOH AI guideline [Prevention of Mother-to-Child HIV Transmission](#)).

Table 2, below, includes initial preferred regimens for rapid ART initiation in pregnant adults.

Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults		
<p>See also: <a href="#">DHHS: Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infections and Interventions to Reduce Perinatal HIV Transmission in the United States</a>.</p>		
Regimen	Comments	Rating
Tenofovir disoproxil fumarate/emtricitabine and dolutegravir [a] (TDF/FTC and DTG; Truvada and Tivicay)	<ul style="list-style-type: none"> <li>Should not be initiated during the first trimester (&lt;14 weeks), gestational age measured by last menstrual period.</li> <li>TDF/FTC should not be used in patients with creatinine clearance (CrCl) &lt;50 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>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.</li> </ul>	A1

**Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults**

See also: *DHHS: Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infections and Interventions to Reduce Perinatal HIV Transmission in the United States.*

Regimen	Comments	Rating
Tenofovir disoproxil fumarate/ emtricitabine <i>and</i> atazanavir <i>and</i> ritonavir (TDF/FTC <i>and</i> ATV <i>and</i> RTV; Truvada <i>and</i> Reyataz <i>and</i> Norvir)	<ul style="list-style-type: none"> <li>TDF/FTC should not be used in patients with CrCl &lt;50 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>Carefully consider <a href="#">drug-drug interactions</a> with RTV.</li> <li>Scleral icterus from benign hyperbilirubinemia due to ATV may be a patient concern.</li> <li>The recommended dose of ATV is 300 mg once daily in the first trimester; the dose increases to 400 mg once daily in the second and third trimesters when used with either TDF or a histamine-2 receptor antagonist.</li> <li>This regimen can be initiated in the first trimester.</li> </ul>	A2
Tenofovir disoproxil fumarate/ emtricitabine <i>and</i> darunavir <i>and</i> ritonavir (TDF/FTC <i>and</i> DRV/RTV; Truvada <i>and</i> Prezista <i>and</i> Norvir)	<ul style="list-style-type: none"> <li>Twice-daily DRV/RTV dosing (DRV 600 mg plus RTV 100 mg with food) is recommended in pregnancy.</li> <li>TDF/FTC should not be used in patients with CrCl &lt;50 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>Twice-daily DRV/RTV dosing (DRV 600 mg plus RTV 100 mg with food) is recommended in pregnancy.</li> <li>Regimen can be initiated in the first trimester.</li> </ul>	A2
Tenofovir disoproxil fumarate/ emtricitabine <i>and</i> raltegravir (TDF/FTC <i>and</i> RAL; Truvada <i>and</i> Isentress)	<ul style="list-style-type: none"> <li>RAL 400 mg twice daily is recommended in pregnancy, <i>not</i> once-daily RAL HD.</li> <li>TDF/FTC should not be used in patients with CrCl &lt;50 mL/min; re-evaluate after baseline laboratory testing results are available.</li> <li>Administer as TDF/FTC once daily and RAL 400 mg twice daily.</li> <li>The recommended dose of RAL is 400 mg twice daily without regard to food.</li> <li>This regimen can be initiated in the first trimester.</li> </ul>	A2

**Note:**

a. See [Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity](#).

## Rapid ART Initiation Follow-Up

Standard good practice is to follow up by telephone or in-person within 48 hours after a person initiates ART, to assess for adverse effects, answer questions, and encourage adherence. If feasible, based on clinic protocol and individual patient needs, an in-person follow-up visit with a medical care provider is encouraged within 7 days of ART initiation. If an in-person visit is not feasible, then follow-up by telephone is encouraged.

Once laboratory test results are available, ART should be discontinued if an HIV diagnosis is not confirmed. In this case, the patient may be assessed or referred for PrEP if there is ongoing risk of HIV exposure (see the NYSDOH AI guideline [PrEP to Prevent HIV and Promote Sexual Health > Candidates for PrEP](#)). If the HIV diagnosis is confirmed, the ART regimen may be adjusted if necessary (e.g., if there is significant renal disease). Further adjustments may be required if major resistance mutations are found that will compromise the effectiveness of the initial regimen. Arrangements should be made for a viral load test 4 weeks after ART initiation to assess adherence and troubleshoot any problems with maintaining treatment. See the NYSDOH AI guideline [Virologic and Immunologic Monitoring](#) for more information.

## Paying for Rapid ART Initiation

Lack of insurance coverage for antiretroviral therapy (ART), a high co-pay, or large out-of-pocket costs may pose a significant barrier to rapid ART initiation for some patients. Addressing financial requirements for ART initiation and helping patients identify sources of payment assistance is an essential component of the rapid ART initiation protocol. Options for residents of New York State (NYS), regardless of immigration status, are described below.

**For patients who are underinsured or uninsured:** The [NYS Department of Health Uninsured Care Programs \(UCP\)](#) provide access to free medications, outpatient primary care, home care, and insurance premium payments for NYS residents who

are uninsured or underinsured. Acknowledging the critical need for rapid access to ART, UCP has revised the enrollment process to facilitate same-day enrollment.

NYS residents who do have health insurance but need help with out-of-pocket costs (co-pays, deductibles, etc.) and meet eligibility criteria may be eligible for help from the UCP.

Information for contacting the new enrollment unit is listed below.

→ **RESOURCE: NYSDOH UNINSURED CARE PROGRAMS**

- Hours of Operation: Monday – Friday, 8:00 AM – 5:00 PM
- Telephone:
  - In state, toll free: 1-800-542-2437 or 1-844-682-4058
  - Out of state: 1-518-459-1641
  - TDD: 1-518-459-0121
- Address: Empire Station, P.O. Box 2052, Albany, NY 12220-0052

A care provider must be enrolled as an AIDS Drug Assistance Provider Plus provider on the day that services are provided to receive reimbursement. New York State Medicaid Program providers are eligible to enroll in the UCP. To become an enrolled provider, contact the UCP Provider Relations Department at 1-518-459-1641 or email [damarys.feliciano@health.ny.gov](mailto:damarys.feliciano@health.ny.gov). Eligible providers will be activated on the date the application is received.

**For patients with existing health insurance:** People who have insurance coverage may be eligible for medication and co-pay assistance to cover the cost of out-of-pocket expenses.

- For dolutegravir: <https://www.myviivcard.com/>.
- For emtricitabine, tenofovir disoproxil fumarate, and bicitgravir: <https://www.gileadadvancingaccess.com/get-started-advancing-access>.
- For darunavir/cobicistat/emtricitabine/tenofovir alafenamide: <https://www.janssencarepath.com/patient/symtuza/cost-support>.

## Special Considerations

**RECOMMENDATIONS: Special Considerations**

**Long-Term Nonprogressors and Elite Controllers**

- Decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3) should be individualized.
- Clinicians should consult with a provider experienced in the management of ART when considering whether to initiate ART in long-term nonprogressors and elite controllers. (A3)

**Patients With Acute Opportunistic Infections**

- Clinicians should recommend that patients beginning treatment for acute opportunistic infections (OIs) initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
- Clinicians should not immediately initiate ART in patients with tuberculous (TB) meningitis or cryptococcal meningitis. (A1)
- Consultation with a clinician with experience in management of ART in the setting of acute OIs is recommended. (A3)
- For all other manifestations of TB, clinicians should initiate ART in patients with HIV as follows:
  - For patients with CD4 counts  $\geq 50$  cells/mm<sup>3</sup>: as soon as they are tolerating anti-TB therapy and no later than 8 to 12 weeks after initiating anti-TB therapy. (A1)
  - For patients with CD4 counts  $< 50$  cells/mm<sup>3</sup>: within 2 weeks of initiating anti-TB therapy. (A1)

## ☑ RECOMMENDATIONS: Special Considerations

### Notes:

- a. For recommendations on initiating ART in pregnant women with HIV, refer to the *DHHS Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States*.
- b. Initial ART regimens for patients with chronic hepatitis B must include NRTIs that are active against hepatitis B. See the NYSDOH AI guideline *HBV-HIV Coinfection*.
- c. In co-infected patients with HCV, attention should be paid to interactions between the planned ART and HCV therapy.

## Long-Term Nonprogressors and Elite Controllers

- **Long-term nonprogressors** demonstrate a lack of disease progression, marked by no symptoms and low viral loads in the absence of therapy during long-term follow-up. Most published studies of long-term nonprogressors include 7-10 years of follow-up [Casado, et al. 2010].
- **Elite controllers** suppress HIV to low but detectable levels (<50-75 copies/mL) for many years [Okulicz, et al. 2010].

The role of early ART initiation in long-term nonprogressors or elite controllers is unclear. At this time, there are not enough data to recommend for or against initiation of ART in long-term nonprogressors and elite controllers. Close monitoring of CD4 count and viral load level may be an acceptable approach. Declines in CD4 count should prompt consideration of initiation of ART. Elite controllers have demonstrated CD4 cell increases after initiation of ART [Okulicz, et al. 2010]. Another study found higher rates of hospitalizations in elite controllers compared to treatment suppressed patients, particularly for cardiovascular and psychiatric conditions [Crowell, et al. 2015]; however, there were important limitations in this analysis and it does not provide definitive evidence in favor of treating this rare population based on current information [Karris and Haubrich 2015]. The clinician and patient should discuss the current data on the risks and benefits of early ART as well as individual factors that may affect the decision to initiate, such as patient readiness and reluctance, adherence barriers, CD4 cell count and viral load, comorbidities, age, and partner serodiscordance. If treatment is delayed, clinicians should counsel patients about the risk of HIV transmission to partners.

## Barriers to Adherence

Although the current first-line regimens used for ART are much easier to tolerate with fewer side effects than earlier combinations, they are not free of side effects (see the NYSDOH AI guideline *Selecting an Initial ART Regimen > Available ART Regimens*). Their use requires a lifelong commitment from the patient. Patients who prefer not to take medication, or who do not understand the significance of skipping doses, are at high risk for poor adherence and subsequent viral resistance. In patients with barriers to adherence, the risk of viral resistance and eventual treatment failure may outweigh any clinical benefit from earlier treatment [Politch, et al. 2012]. These patients should remain under particularly close observation for clinical and laboratory signs of disease progression [Wallis, et al. 2012]. ART should be initiated as soon as the patient seems prepared to adhere to a treatment regimen. When initiation of treatment is clinically urgent, such as for patients who are pregnant, have HIV-related malignancies, HIV-associated nephropathy, symptomatic HIV, older age, severe thrombocytopenia from HIV, chronic hepatitis, or advanced AIDS, it is appropriate to initiate ART even if some barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support.

Barriers such as alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system should not necessarily preclude rapid initiation of ART. The option of rapid initiation of ART should be offered to all individuals with HIV, except when medically contraindicated. Barriers to care can be addressed with appropriate counseling and support services. In some cases, patients will require ongoing attention and use of supportive services.

## Patients With Acute Opportunistic Infections

In a randomized study, patients who initiated ART at a median of 12 days from the start of OI therapy had better outcomes, as measured by disease progression and death, without an increase in adverse events, compared to those who initiated ART at a median of 45 days from presentation [Zolopa, et al. 2009]. Although this study excluded patients with active TB, three randomized controlled trials in patients newly diagnosed with HIV and pulmonary TB have demonstrated

a significant mortality benefit when ART was initiated during the first 2 months of starting anti-TB therapy and a further benefit when those who were severely immunocompromised initiated therapy in the first 2 weeks [Abdool Karim, et al. 2011; Blanc, et al. 2011; Havlir, et al. 2011]. Although antiretroviral agents and anti-TB medications can have overlapping toxicities, ART should be initiated within the first 8 to 12 weeks of starting anti-TB therapy. Patients with CD4 counts <50 cells/mm<sup>3</sup> should receive ART within the first 2 weeks of initiating anti-TB therapy.

Tuberculous meningitis and cryptococcal meningitis are exceptions; there are data showing that early initiation of ART increases adverse events and mortality in this setting [Lawn, et al. 2011; Torok, et al. 2011; NIAID 2012; Bisson, et al. 2013; Boulware, et al. 2014]. Close attention should be paid to possible drug-drug interactions between OI therapy and ART. In some cases, determining the optimal timing for initiating ART in patients with OIs can be complex and may require consultation with a clinician with experience in management of ART in this context.

After initiating ART, clinicians need to be alert to the possibility of immune reconstitution syndromes as CD4 cell counts are restored (see the NYSDOH AI guideline *Management of IRIS*).

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# All Recommendations

## All RECOMMENDATIONS: When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

### Benefits and Risks of ART

- Clinicians should recommend antiretroviral therapy to all patients with HIV infection. (A1)

### Rationale for Rapid ART Initiation

- Clinicians should recommend antiretroviral therapy (ART) for all patients with a diagnosis of HIV infection. (A1)
- Clinicians should offer rapid initiation of ART—preferably on the same day (A1) or within 72 hours—to all individuals who are candidates for rapid ART initiation (see text) and who have:
  - A confirmed HIV diagnosis (A1), *or*
  - A reactive HIV screening result pending results of a confirmatory HIV test (A2), *or*
  - Suspected acute HIV infection, i.e., HIV antibody negative and HIV RNA positive (A2).
- Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk after effective ART is initiated and viral suppression is achieved, and should strongly recommend ART for patients with seronegative partners. (A1)
- Clinicians should evaluate and prepare patients for ART initiation as soon as possible; completion of the following should not delay initiation:
  - Discuss **benefits and risks of ART** with the patient. (A3)
  - Assess patient readiness. (A3)
  - Identify and ameliorate factors that might interfere with successful adherence to treatment, including inadequate access to medication, inadequate supportive services, psychosocial factors, active substance use, or mental health disorders. (A2)
- Clinicians should refer patients for supportive services as necessary to address modifiable barriers to adherence. An ongoing plan for coordination of care should be established. (A3)
- Clinicians should involve patients in the decision-making process regarding initiation of ART and which regimen is most likely to result in adherence. The patient should make the final decision of whether and when to initiate ART. (A3)
- If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible.
- In patients with advanced HIV (or AIDS), ART should be initiated even if barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support. (A2)
- After ART has been initiated, response to therapy should be monitored by, or in consultation with, a clinician with **experience in managing ART**. (A2)

### Counseling and Patient Education

- Counseling and education should include the following:
  - Basic education about HIV, CD4 cells, viral load, and resistance. (A3)
  - Available treatment options and potential risks and benefits of therapy (see text). (A3)
  - The need for strict adherence to avoid the development of viral drug resistance. (A2)
  - Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection. (A3)
- Clinicians should involve the patient in the decision-making process regarding initiation of ART. (A3)

### Protocol for Rapid ART Initiation

- To determine whether a patient is a candidate for rapid antiretroviral therapy (ART) initiation, the clinician should confirm that the individual has any of the following (A1):
  - A reactive point-of-care HIV test result, or confirmed HIV diagnosis, or suspected acute HIV infection, or known HIV infection, and

## **☑ All RECOMMENDATIONS: When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation**

- No prior ART (i.e., treatment naive) or limited prior use of antiretroviral medications, and
- No medical conditions or opportunistic infections that require deferral of rapid ART initiation, including suspected cryptococcal or tuberculous meningitis.
- Clinicians should perform baseline laboratory testing listed in *Box 2: Baseline Laboratory Testing Checklist* for all patients who are initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)

### **General Principles in Choosing a Regimen for Rapid ART Initiation**

- Clinicians should involve their patients when deciding which antiretroviral therapy (ART) regimen is most likely to result in adherence. (A3)
- Before initiating ART, clinicians should:
  - Assess the patient’s prior use of antiretroviral medications, including pre-exposure prophylaxis (PrEP), which may increase the risk for baseline resistance. (A2)
  - Assess for any comorbidities and chronic coadministered medications that may affect the choice of regimen for initial ART. (A2)
  - At the time of HIV diagnosis, obtain genotypic resistance testing for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes.
  - Ask individuals of childbearing potential about the possibility of pregnancy, their reproductive plans, and their use of contraception. (A3)
- For ART-naive patients, clinicians should select an initial ART regimen that is preferred; see *Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults*. (A1)
- Clinicians should reinforce medication adherence regularly. (A3)
- Clinicians should obtain a viral load test 4 weeks after ART initiation to assess the response to therapy. (A3)
  - See the NYSDOH AI guideline *Virologic and Immunologic Monitoring* for more information.

### **Long-Term Nonprogressors and Elite Controllers**

- Decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3) should be individualized.
- Clinicians should consult with a provider experienced in the management of ART when considering whether to initiate ART in long-term nonprogressors and elite controllers. (A3)

### **Patients With Acute Opportunistic Infections**

- Clinicians should recommend that patients beginning treatment for acute opportunistic infections (OIs) initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
- Clinicians should not immediately initiate ART in patients with tuberculous (TB) meningitis or cryptococcal meningitis. (A1)
- Consultation with a clinician with experience in management of ART in the setting of acute OIs is recommended. (A3)
- For all other manifestations of TB, clinicians should initiate ART in patients with HIV as follows:
  - For patients with CD4 counts  $\geq 50$  cells/mm<sup>3</sup>: as soon as they are tolerating anti-TB therapy and no later than 8 to 12 weeks after initiating anti-TB therapy. (A1)
  - For patients with CD4 counts  $< 50$  cells/mm<sup>3</sup>: within 2 weeks of initiating anti-TB therapy. (A1)

### **Notes:**

- a. For recommendations on initiating ART in pregnant women with HIV, refer to the *DHHS: Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States*.
- b. Initial ART regimens for patients with chronic hepatitis B must include NRTIs that are active against hepatitis B. See the NYSDOH AI guideline *HBV-HIV Coinfection*
- c. In co-infected patients with HCV, attention should be paid to interactions between the planned ART and HCV therapy.

# All Good Practices

## All GOOD PRACTICES: When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

### Protocol for Rapid ART Initiation

- For patients with a reactive HIV antibody screening test that is pending confirmation, make sure the patient understands the benefits of rapid ART initiation and the following:
  5. Reactive screening test results are not formally diagnostic, because false-positive results are still possible;
  6. A confirmatory (diagnostic) HIV test will be performed;
  7. ART will be discontinued if the confirmatory test result is negative and continued if it is positive;
  8. The benefit of starting ART early, after a presumptive positive screening test, outweighs the negligible risk of taking ART for a few days and then stopping it if confirmed HIV negative.
- Provide the result of the confirmatory HIV test as soon as it is available; discontinue ART if the result is negative and reinforce adherence and next steps if it is positive.
- If a patient declines rapid ART initiation, discuss options for deferred initiation of ART, link the patient with HIV primary care, and outline next steps.

### General Principles in Choosing a Regimen for Rapid ART Initiation

- Follow up within 24 to 48 hours, by telephone or another preferred method, with a patient who has initiated ART to assess medication tolerance and adherence.
- If feasible, schedule an in-person visit for 7 days after ART initiation.

# Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity

**Lead author:** Geoffrey A. Weinberg, MD, with the *Medical Care Criteria Committee*, May 2021

Evidence from multiple studies indicates no difference in rates of total birth defects among infants exposed to antiretroviral (ARV) medications during the first trimester compared with infants exposed later in pregnancy. ARVs are generally considered safe and may be taken by pregnant patients with HIV without increasing the risk of infant birth defects. The MCCC is providing the following updated information for medical care providers concerning preliminary reports that previously had linked dolutegravir (DTG) to neural tube defects (NTDs) in infants exposed to dolutegravir during the periconception period [Zash, et al. 2018; Zash, et al. 2019; Reefhuis, et al. 2020].

**Potentially increased NTDs and DTG:** NTDs are birth defects, including meningocele and spina bifida, thought to occur early after conception during development of the embryonic neural tube. The neural tube closes by approximately 8 weeks gestational age, which is 8 weeks after the last menstrual period or approximately 6 weeks post-conception. Ingestion of folic acid or folate by a pregnant individual significantly lowers the rate of NTDs; all individuals in the United States who are pregnant or trying to conceive and engaged in prenatal care are routinely administered 400 µg of folic acid daily. The background rate of NTDs in the general population in the United States and other countries that routinely fortify food with folate or folic acid is low: approximately 0.07% of all births (7/10,000 births) [Reefhuis, et al. 2020].

In 2018, an unplanned interim analysis of a large observational clinical trial conducted in Botswana, a country where food is not routinely fortified with folate or folic acid, was performed. The researchers found NTDs in 0.94% of 426 infants exposed at conception to maternal DTG-based antiretroviral therapy (ART) compared with 0.12% of 11,300 infants exposed to non-DTG-based ART. Importantly, however, as more data were collected, the rates of infant NTDs markedly declined [Zash, et al. 2018; Zash, et al. 2019; Antiretroviral Pregnancy Registry Steering Committee 2020; Zash 2020; DHHS 2021]. The latest available data, through April 2020, now show that the rate of infant NTDs with maternal DTG-based ART use at conception is *not* any greater than it is in infants exposed to non-DTG-based ART at conception: 0.19% [Antiretroviral Pregnancy Registry Steering Committee 2020; Zash 2020; DHHS 2021]. No increases have been found in the registry data or through pharmacovigilance database studies from Europe and the United States [Vannappagari and Thorne 2019; van De Ven, et al. 2020]. Nor have any differences been found in the rates of NTDs among infants in a randomized controlled open-label phase 3 trial of DTG-based versus EFV-based ART in pregnant individuals, though the median gestational age at enrollment in this trial was 22 weeks, and all enrollees were at 14 weeks or more gestational age at enrollment [Lockman, et al. 2021].

**Benefits of DTG:** There are many known benefits of DTG as a component of ART for all adults, pregnant or not, and many children. DTG is potent, rapidly reduces viral load, has a high barrier to HIV genetic resistance, and is generally well-tolerated. Moreover, folate deficiency is uncommon in countries such as the United States. Thus, both the U.S. Department of Health and Human Services and the World Health Organization consider DTG a *preferred ARV drug* for individuals with HIV in all trimesters of pregnancy, and those with HIV who are trying to conceive. If an alternative ART regimen that does not include DTG is the best choice, alternatives to DTG during pregnancy include raltegravir, ritonavir-boosted atazanavir, or ritonavir-boosted darunavir (see the NYSDOH AI guideline *Selecting an Initial ART Regimen > Specific Factors to Consider and Discuss With Patients*). No data currently exist to support the use of bictegravir during pregnancy or the period surrounding conception. Further, cobicistat-boosted regimens containing elvitegravir, darunavir, or atazanavir are not recommended due to reduced levels of the integrase inhibitors given with cobicistat during pregnancy.

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# Supplement: Guideline Development and Recommendation Ratings

Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
<b>Developer</b>	<i>New York State Department of Health AIDS Institute (NYS DOH AI) Clinical Guidelines Program</i>
<b>Funding Source</b>	NYSDOH AI
<b>Program Manager</b>	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See <i>Program Leadership and Staff</i> .
<b>Mission</b>	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.
<b>Expert Committees</b>	<p>The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout NYS to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of NYS, all relevant clinical practice settings, key NYS agencies, and community service organizations.</p> <ul style="list-style-type: none"> <li>See <i>Expert Committees</i></li> </ul>
<b>Committee Structure</b>	<ul style="list-style-type: none"> <li>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</li> <li>Contributing members</li> <li>Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders</li> </ul>
<b>Conflicts of Interest Disclosure and Management</b>	<ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>Disclosures are listed for each committee member.</li> </ul>
<b>Evidence Collection and Review</b>	<ul style="list-style-type: none"> <li>Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update.</li> <li>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.</li> <li>A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years.</li> <li>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.</li> </ul>
<b>Recommendation Development</b>	<ul style="list-style-type: none"> <li>The lead author drafts recommendations to address the defined scope of the guideline based on available published data.</li> <li>Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations.</li> <li>When published data are not available, support for a recommendation may be based on the committee's expert opinion.</li> <li>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.</li> </ul>

**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 when required.
  - Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
- 
- External Reviewers**
- External peer reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
  - Peer reviewers may include nationally known experts from outside of New York State.
- 
- 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.
  - All contributing committee members review and approve substantive changes to, additions to, or deletions of recommendations; JHU editorial staff track, summarize, and publish ongoing guideline changes.

**Recommendation Ratings Scheme**

Strength		Quality of Evidence	
Rating	Definition	Rating	Definition
<b>A</b>	Strong	<b>1</b>	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
<b>B</b>	Moderate	<b>*</b>	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.
<b>C</b>	Optional	<b>2</b>	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
		<b>2†</b>	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.
		<b>3</b>	Based on committee expert opinion, with rationale provided in the guideline text.