



CLINICAL GUIDELINES PROGRAM

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

Diagnosis and Management of HIV-2 in Adults

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Diagnosis and Management of HIV-2 in Adults

Purpose and Development of This Guideline

The New York State Department of Health (NYSDOH) AIDS Institute (AI) developed this guideline for primary care providers and other clinicians who may diagnose and treat patients with HIV-2 infection. The guideline is designed to achieve the following goals:

- Inform clinicians about when to suspect and how to diagnose and manage the care of adults with HIV-2.
- Identify the similarities and differences in treatment for individuals with HIV-1 and HIV-2.
- Recommend preferred antiretroviral (ARV) regimens for treatment and identify ARVs to avoid.
- Encourage clinicians to use the services of the NYSDOH *Wadsworth Center*, the NYS public health laboratory, for testing used in monitoring HIV-2.
- 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.

Guideline development: This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care provided to people who have HIV, hepatitis C virus, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the *Medical Care Criteria Committee* (Adult HIV and related guidelines) with developing evidence-based clinical recommendations for identifying and treating HIV-2. The resulting recommendations are based on an extensive review of the medical literature and reflect consensus among this panel of experts. Each recommendation is rated for strength and for quality of the evidence (see below). If recommendations are based on expert opinion, the rationale for the opinion is included.

AIDS Institute Clinical Guidelines Program: Recommendations Ratings (updated June 2019 [a])	
Strength of Recommendation Ratings	
A	Strong recommendation
B	Moderate recommendation
C	Optional
Quality of Supporting Evidence Ratings	
1	Indicates that the evidence supporting a recommendation is derived from published results of at least one randomized trial with clinical outcomes or validated laboratory endpoints.
*	Indicates that the evidence supporting a recommendation is strong because it is: 1) based on a self-evident conclusion(s); 2) conclusive, published, in vitro data; or 3) well-established, accepted practice that cannot be tested because ethics would preclude a clinical trial.
2	Indicates that the evidence supporting a recommendation is derived from published results of at least one well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.

AIDS Institute Clinical Guidelines Program: Recommendations Ratings (updated June 2019 [a])	
2†	Indicates that the evidence supporting a recommendation has been extrapolated from published results of well-designed studies (including non-randomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
3	Indicates that a recommendation is based on the expert opinion of the committee members. The rationale for the recommendation is provided in the guideline text.
a. With the June 2019 update, the ratings for quality of supporting evidence were expanded to add the * rating and the 2† rating.	

HIV-2 Overview

The HIV-2 virus was first isolated in West Africa in the mid-1980s among individuals living with AIDS [Clavel, et al. 1986]. HIV-2 infection is endemic in West Africa, with the highest prevalence in Cape Verde, the Ivory Coast, Gambia, Guinea-Bissau, Mali, Mauritania, Nigeria, and Sierra Leone [Gottlieb, et al. 2018]. Although rare, HIV-2 infection has also been reported in several countries in Europe, South America, and Asia, and in the United States [Gottlieb 2018]. As of June 2010, 166 cases of HIV-2 had been reported in the United States and 46% of those were from New York City [CDC 2011]. The majority of individuals with HIV-2 are from West Africa or have had sexual contact or shared injection drug equipment with someone from this region [Torian, et al. 2010].

HIV-2 infection is associated with slower disease progression than HIV-1 infection because of lower plasma viral load levels of HIV-2 [Simon, et al. 1993; Popper, et al. 1999; Gottlieb, et al. 2002; MacNeil, et al. 2007; van der Loeff, et al. 2010]. With lower levels of virus, HIV-2 is transmitted less efficiently than HIV-1 through sexual behavior and from mother to child [Adjorlolo-Johnson, et al. 1994; O'Donovan, et al. 2000; Burgard, et al. 2010]. Similar to HIV-1, HIV-2 disease progression correlates with increasing plasma HIV-2 viral load [Gottlieb, et al. 2002]. Although HIV-2 is less virulent than HIV-1, individuals with HIV-2 manifest clinical signs, symptoms, and opportunistic infections (OIs) similar to those seen with HIV-1. In addition, the majority of individuals with HIV-2, if untreated, will eventually progress to AIDS and death [Esbjornsson, et al. 2018].

There are many similarities in the management of patients with HIV-1 and those with HIV-2, including prophylaxis for and treatment of OIs and timing of antiretroviral therapy (ART) initiation. As noted in the section on treatment, below, ART should be recommended for all patients diagnosed with HIV-2 [Ba, et al. 2018]. As with HIV-1, the patient should make the final decision of whether and when to initiate ART.

A key difference in the clinical management of HIV-2 compared with HIV-1 is that resistance testing is not commercially available in the United States and guidance in interpreting mutations is not readily available for HIV-2. Another important difference in management is that the nonnucleoside reverse transcriptase inhibitor (NNRTI) class of ARV medications is not effective against HIV-2. Furthermore, unlike in HIV-1, there are no randomized clinical trials of ARV treatment for HIV-2 that indicate the optimal time to initiate treatment or the preferred initial regimen. Therefore, treatment recommendations for HIV-2 are in large part derived from clinical studies conducted in HIV-1. Because HIV-1 and HIV-2 share the same pathogenic process, extrapolating to HIV-2 from HIV-1 is a clinically valid approach.

Diagnosis of HIV-2

RECOMMENDATIONS: DIAGNOSIS OF HIV-2

- To diagnose HIV-2 infection, clinicians should follow the steps in the Centers for Disease Control and Prevention/Association of Public Health Laboratories (CDC/APHL) *HIV Diagnostic Testing Algorithm* and the recommendations in the NYSDOH AI guideline *HIV Testing*. (A1)
 - See the NYSDOH guideline *HIV Testing > Steps in the HIV Diagnostic Testing Algorithm* and *HIV-2 RNA Tests for Diagnostic Use*
- In individuals who are confirmed to have HIV-2 antibodies, clinicians should perform a clinical evaluation for HIV-2 infection that is similar in scope to the evaluation of patients with HIV-1. (A1) HIV-2 antibodies are confirmed by a reactive result to an HIV-1/2 or HIV-1/2 antigen/antibody (Ag/Ab) immunoassay and a positive result for HIV-2 Abs on a Food and Drug Administration (FDA)-approved supplemental HIV-1/2 Ab differentiation assay.
 - See the NYSDOH guideline *HIV Testing > HIV-2 RNA Tests for Diagnostic Use*

Before the 4th-generation HIV-1/2 Ag/Ab and HIV-1/2 Ab differentiation immunoassays for HIV testing became widely available, clinicians suspected chronic HIV-2 infection in certain clinical scenarios, such as a declining CD4 cell count in an HIV-1–seropositive, untreated individual with an undetectable HIV-1 plasma viral load, or an opportunistic infection in an individual from West Africa who is not HIV-1 seropositive.

Currently, all HIV testing performed according to the CDC/APHL algorithm begins with a FDA-approved 4th-generation HIV-1/2 Ag/Ab combination immunoassay [CDC 2018], which detects HIV-1 p24 antigen and HIV-1 and HIV-2 antibodies but not HIV-2 antigen. If the combination immunoassay is reactive, a supplemental HIV-1/2 Ab differentiation assay is performed. There are 4 scenarios, described below, in which clinicians should consider HIV-2 infection.

- **HIV-1/HIV-2 differentiation assay is reactive for HIV-2 antibody:** The individual is considered HIV-2 antibody positive, and a clinical evaluation for HIV-2 infection should be performed (see *Monitoring ART in Individuals With HIV-2* in this guideline).
- **HIV-1/HIV-2 differentiation assay is reactive for HIV-1 and HIV-2 antibody:** The individual is considered HIV positive, undifferentiated, and HIV-1 RNA and HIV-2 RNA or DNA testing should be performed to confirm or exclude HIV-1/HIV-2 coinfection. A minority of individuals with HIV-2 are coinfecting with HIV-1. Qualitative and quantitative HIV-2 viral load testing is available by contacting the Bloodborne Viruses Laboratory at the Wadsworth Center (see *Box 1: Wadsworth Center Bloodborne Viruses Laboratory Services*, below).
- **HIV-1/HIV-2 differentiation assay is nonreactive or indeterminate for HIV-1 and/or HIV-2 antibody:** Plasma HIV-1 RNA testing should be performed to confirm or exclude acute HIV-1 infection [CDC 2018].
 - If the Ab differentiation assay is nonreactive or HIV-1 indeterminate and HIV-1 RNA is not detected, the individual is considered negative for HIV-1 and HIV-2.
 - If the antibody differentiation assay is either HIV-2 indeterminate or HIV indeterminate and HIV-1 RNA is not detected, then HIV-2 RNA testing may be used to confirm HIV-2 infection. However, because HIV-2 RNA levels can be low or undetectable in a person with HIV-2 infection, the absence of HIV-2 RNA does not exclude HIV-2 infection. Therefore, in a person at high risk for HIV-2 infection who has undetectable HIV-2 RNA, clinicians should consider testing for HIV-2 DNA or repeating the HIV testing algorithm in 2 to 4 weeks, starting with the HIV-1/2 Ag/Ab combination immunoassay. If results remain unclear, clinicians may consider obtaining other HIV-2–specific tests through public health or commercial laboratories or the CDC.
- Nonreactive 4th-generation HIV-1/2 Ag/Ab immunoassay and suspected recent exposure to HIV-2 (e.g., exposure from a sex partner from an HIV-2 endemic area): HIV-2 RNA testing may be required or the HIV testing algorithm may be repeated, beginning with the 4th-generation HIV-1/2 Ag/Ab immunoassay, 4 weeks (and not later than 12 weeks) after the first test.

Box 1: Wadsworth Center Bloodborne Viruses Laboratory Services

The *Wadsworth Center* offers HIV-2 viral load testing, free of charge, for patients and healthcare providers in New York State. To submit a specimen for HIV-2 viral load testing, please contact the Bloodborne Viruses Laboratory at (518) 474-2163. Specific services include:

- Quantitative detection of HIV-2 RNA in plasma samples for baseline and subsequent monitoring of response to ART in patients with confirmed HIV-2 infection.
- HIV-2 RNA viral load testing during pregnancy. Contact the lab at (518) 474-2163 early in the patient’s pregnancy to discuss the protocol and timing for testing.
- HIV testing for all newborns exposed to HIV (HIV-1 and HIV-2) in New York State, free of charge.
 - If a sample is reactive for HIV-2 antibodies, the Pediatric HIV Testing Service will perform a reverse transcription polymerase chain reaction (RT-PCR) test for qualitative detection of HIV-2 RNA.

Note: HIV-2 phenotypic and genotypic resistance testing is not offered at Wadsworth or commercially available in the United States.

Treatment of HIV-2

Updated September 2020

RECOMMENDATIONS: TREATMENT OF HIV-2

- Clinicians should recommend ART for all individuals diagnosed with HIV-2. (A2⁺)
- Clinicians should not prescribe any NNRTI for treatment of HIV-2 infection. (A*)
- Clinicians should recommend a single-tablet regimen (STR) that includes 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI) as the initial treatment for adults with HIV-2 who are not pregnant and not planning to become pregnant, including those with acute HIV-2 infection (see *Table 1: ART Regimens for Initial Treatment of Nonpregnant Adults with HIV-2*). (A2)
- For individuals with HIV-1/HIV-2 coinfection, clinicians should:
 - Perform *HIV-1 drug resistance testing* to guide the choice of an initial regimen or to modify a regimen if virologic failure develops. (A2)
 - Recommend an ART regimen that will suppress both viruses effectively. (A*)

Table 1: ART Regimens for Initial Treatment of Nonpregnant Adults With HIV-2*

PREFERRED Regimens	
Single-Tablet Regimens	Comments
Abacavir/lamivudine/dolutegravir (ABC/3TC/DTG; Triumeq)	<ul style="list-style-type: none"> • Initiate only in patients confirmed to be negative for HLA-B*5701. • Initiate only in patients with creatinine clearance (CrCl) ≥50 mL/min. • Consider underlying risk of coronary heart disease. • Documented DTG resistance after initiation in treatment-naïve patients is rare. • Clinicians should refer to the DHHS <i>Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States</i> when choosing an initial regimen for individuals of childbearing potential. • In patients with HIV/HBV coinfection, this regimen should be used in conjunction with other anti-HBV drugs.
Tenofovir alafenamide/emtricitabine/bictegravir (TAF 25 mg/FTC/BIC; Biktarvy)	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥30 mL/min. • Contains 25 mg of TAF, unboosted.

Table 1: ART Regimens for Initial Treatment of Nonpregnant Adults With HIV-2*

ALTERNATIVE Regimens	
Single-Tablet Regimens	Comments
Tenofovir alafenamide/emtricitabine/cobicistat/darunavir (TAF 10 mg/FTC/COBI/DRV; Symtuza)	<ul style="list-style-type: none"> Initiate only in patients with CrCl \geq30 mL/min. Carefully consider drug-drug interactions with COBI [Eron, et al. 2018]. Contains 10 mg TAF, boosted.
Tenofovir alafenamide/emtricitabine/cobicistat/elvitegravir (TAF 10 mg/FTC/COBI/EVG; Genvoya)	<ul style="list-style-type: none"> Initiate only in patients with CrCl \geq30 mL/min. Carefully consider drug-drug interactions with COBI. Contains 10 mg of TAF, boosted with COBI.
Once-Daily Multi-Tablet Regimens	Comments
Abacavir/lamivudine <i>and</i> raltegravir (ABC/3TC <i>and</i> RAL HD; Epzicom <i>and</i> Isentress HD)	<ul style="list-style-type: none"> Initiate only in patients confirmed to be negative for HLA-B*5701 and negative for HBsAg. Consider underlying risk of coronary heart disease. ABC/3TC once daily, RAL HD 1200 mg once daily dosed as two 600 mg HD tablets.
Tenofovir alafenamide/emtricitabine <i>and</i> darunavir <i>and</i> ritonavir (TAF/FTC <i>and</i> DRV/RTV; Descovy <i>and</i> Prezista <i>and</i> Norvir)	<ul style="list-style-type: none"> Carefully consider drug-drug interactions with RTV. Initiate only in patients with CrCl \geq30 mL/min. Contains 25 mg TAF, boosted. Use with caution in individuals with stage 3 chronic kidney disease.
Tenofovir alafenamide/emtricitabine <i>and</i> darunavir/cobicistat (TAF/FTC <i>and</i> DRV/COBI; Descovy <i>and</i> Prezcoibix)	<ul style="list-style-type: none"> Carefully consider drug-drug interactions with COBI. Initiate only in patients with CrCl \geq30 mL/min. Contains 25 mg TAF, boosted. Use with caution in individuals with stage 3 chronic kidney disease.
Tenofovir alafenamide/emtricitabine <i>and</i> dolutegravir (TAF 25 mg/FTC <i>and</i> DTG; Descovy <i>and</i> Tivicay)	<ul style="list-style-type: none"> Initiate only in patients with CrCl \geq30 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 <i>Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States</i> when choosing an initial regimen for individuals of childbearing potential.
Tenofovir alafenamide/emtricitabine <i>and</i> raltegravir (TAF 25 mg/FTC <i>and</i> RAL HD; Descovy <i>and</i> Isentress HD)	<ul style="list-style-type: none"> Initiate only in patients with CrCl \geq30 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.
<p>*Listed alphabetically; see prescribing information for individual drugs. 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; and 4) Refer to Table 8: ARV Dose Adjustments for Renal and Hepatic Impairment in the NYSDOH AI guideline Selecting an Initial ART Regimen for adjustment based on renal or hepatic function.</p>	

All FDA-approved NRTIs effectively inhibit HIV-2 reverse transcriptase [Menendez-Arias and Alvarez 2014]. Three HIV protease inhibitors effectively inhibit HIV-2, but given the availability of darunavir, use of lopinavir and saquinavir should be limited. Atazanavir, fosamprenavir, tipranavir, and nelfinavir have no or greatly reduced in vitro inhibitory activity against HIV-2. As a class, NNRTIs are not active against HIV-2 [Menendez-Arias and Alvarez 2014].

→ KEY POINT

- If a protease inhibitor is being considered as part of an ART regimen for treatment of HIV-2, boosted darunavir is preferred.
- Atazanavir **should not be used** because of its lack of potency in vitro against HIV-2.

Based on limited clinical trial data using the INSTIs elvitegravir and raltegravir, and in vitro data, it is expected that a DTG- or BIC-based regimen with 2 NRTIs can be used to treat treatment-naïve patients with HIV-2. In one study of a single-tablet regimen (EVG/COBI/TDF/FTC), 93.3% of subjects had viral suppression at 48 weeks [Ba, et al. 2018]. A study of a multi-tablet regimen (TDF/FTC and RAL) demonstrated that 96% of participants with HIV-2 completing the 48-week follow-up had an HIV-2 viral load <40 copies/mL [Matheron, et al. 2018]. It is important to involve patients in the decision-making process regarding initiation of ART, and clinicians should work to remove barriers to treatment initiation, such as lack of access to combination therapy.

In treatment-experienced patients with HIV-2, the ARVs listed in Table 1 can be considered if their potency has not been compromised by prior treatment failure and the likely emergence of drug resistance/cross-resistance. There are no commercially available genotypic or phenotypic drug resistance assays for HIV-2 available in the United States that can be used to guide the selection of an alternative ART regimen in the setting of virologic failure.

Bictegravir is highly potent against HIV-2 in vitro [Tsiang, et al. 2016; Le Hingrat, et al. 2018; Smith, et al. 2019]; however, there are no published data on the use of TAF/FTC/BIC in patients with HIV-2. If no drug resistance testing is available, DTG and BIC should be used with caution in ART-experienced patients with HIV-2 who have virologic failure on a RAL- or EVG- based ART regimen. The chemokine receptor antagonist maraviroc (MVC) is active against HIV-2 strains that exclusively use CCR5 for viral entry [Borrego, et al. 2012]. However, its use in the treatment of HIV-2 is limited because there is no commercially available tropism assay for HIV-2 to predict susceptibility to MVC. The fusion inhibitor enfuvirtide has no in vitro activity against HIV-2 [Menendez-Arias and Alvarez 2014; FDA 2018]. The recently approved attachment inhibitor fostemsavir has no activity against HIV-2 [FDA 2020]. Ibalizumab, a humanized monoclonal IgG-4 antibody that prevents HIV cell entry by binding to the host CD4 receptor, has *in vitro* evidence of activity against HIV-2 with IC₅₀ levels comparable to those found in HIV-1 group M strains [Hingrat 2020]. However, the *in vivo* efficacy of an ibalizumab-based regimen in individuals with antiretroviral-resistant HIV-2 infection has not been established.

In the setting of HIV-1/HIV-2 coinfection, HIV-1 drug resistance testing should be performed to guide the choice of an initial regimen or to modify a regimen if virologic failure develops. If HIV-1 drug-resistant virus has been identified, ARV agents that are active only against HIV-1 (such as an NNRTI) can be used to treat individuals with HIV-1/HIV-2 coinfection, as long as a combination of anti-HIV-2 active agents is also used to fully suppress both viruses.

Monitoring ART in Individuals with HIV-2

RECOMMENDATIONS: MONITORING ART IN INDIVIDUALS WITH HIV-2

- For individuals who are newly diagnosed with HIV-2, clinicians should perform the same laboratory and diagnostic testing currently recommended for individuals with HIV-1, with the exception of drug resistance testing, which is not available. (A3)
 - Testing includes CD4 cell count, HIV-2 viral load, creatinine clearance, and status of coinfections such as hepatitis B and C viruses and tuberculosis (see NYSDOH AI guideline [Selecting an Initial ART Regimen > ART-Initiation Laboratory Testing](#)).
- Clinicians should use HIV-2 viral load testing and CD4 cell count to determine the effectiveness of an ART regimen in patients with HIV-2. (A2)
- If HIV-2 viral load testing is not available, clinicians should suspect treatment failure if individuals experience a sustained decrease in CD4 cell count or have clinical disease progression. (A2)
- If a clinical practice in New York State cannot obtain HIV-2 viral load testing from the Wadsworth Laboratory, clinicians should refer individuals with HIV-2 to a practice that has the ability to access HIV-2 viral load testing from the Wadsworth Laboratory. (A3)

There is no FDA-approved, HIV-2 quantitative viral load assay commercially available. However, an HIV-2 quantitative viral load test is available by contacting the Bloodborne Viruses Laboratory at the Wadsworth Center (see [Diagnosis of HIV-2 > Box 1: Wadsworth Center Bloodborne Viruses Laboratory Services](#) in this guideline). In New York State, HIV-2 viral load testing should be used to determine the effectiveness of an ART regimen in patients with HIV-2 [Ba, et al. 2018; Matheron, et al. 2018]. If clinicians outside of New York State do not have access to HIV-2 viral load testing, they should suspect treatment failure if an individual with HIV-2 has a sustained or progressive decline in CD4 cell count or experiences clinical disease progression on therapy. Data from a multi-cohort study indicate that patients with HIV-2 who were initiated on a first-line combination ART regimen had less robust CD4 cell count increases than individuals with HIV-1, even after adjustment for plasma viral load levels [Wittkop, et al. 2017]. In HIV-2, a muted CD4 cell count increase from baseline after treatment initiation may not necessarily imply that the regimen is ineffective. If patients with HIV-2 have either immunologic or virologic treatment failure, clinicians are strongly urged to refer them to or consult with experienced HIV-2 clinical management specialists.

In addition to monitoring ART, patients with HIV-2 require the same laboratory and diagnostic testing, use and appropriate discontinuation of prophylaxis for OIs, and use of immunizations as patients with HIV-1 (see NYSDOH AI guidelines [Primary Care Approach > Preventive Medicine](#) and [Immunizations for Adults with HIV](#)).

→ KEY POINT

- In New York State, the standard of care for individuals with HIV-2 is to initiate and maintain ART in order to achieve an undetectable HIV-2 viral load.

Pregnancy and HIV-2

☑ RECOMMENDATIONS: PREGNANCY AND HIV-2

- Clinicians should recommend ART for all pregnant individuals with HIV-2. (A2+)
 - Clinicians should recommend one of the ART regimens in Table 2. (A3)
 - Clinicians should not delay initiation of ART in pregnant individuals even if there is no or limited access to HIV-2 viral load testing. (A2+)
- In selecting an ART regimen for a pregnant individual with HIV-2, clinicians should **not** include:
 - Boosted atazanavir, because of its lack of efficacy against HIV-2. (A*)
 - Dolutegravir prior to 8 weeks. (A2+)
 - Efavirenz and rilpivirine, the NNRTIs recommended for treatment of HIV-1 during pregnancy, because of a lack of efficacy against HIV-2. (A*)

Note: For recommendations regarding administration of zidovudine for prophylaxis during labor and delivery, please see [Management During Labor and Delivery](#) in the NYSDOH AI guideline [Prevention of Mother-to-Child HIV Transmission](#), or see [AIDSinfo: Special Populations: HIV-2 Infection and Pregnancy](#) in the guideline [Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States](#).

A combination of either TDF/FTC or ABC/3TC (if HLA-B*5701 is negative) plus either twice-daily RAL or twice-daily DRV/r is recommended during pregnancy. For individuals with HIV-2, viral load monitoring during pregnancy and prophylactic ART for the HIV-2–exposed infant should follow the recommendations for pregnancy and infant exposure in the setting of HIV-1 (see the NYSDOH AI guideline [Prevention of Mother-to-Child HIV Transmission](#)). During the early part of pregnancy, it is important that healthcare providers follow the Wadsworth Center protocol for accurate and timely submission of specimens and know the amount of time needed to return the results of HIV-2 viral load testing. For example, the Wadsworth Center Bloodborne Viruses Laboratory is not open on weekends, so if a patient's blood is drawn on a Thursday or Friday, the separated plasma should be stored at the drawing facility in a freezer and shipped on Monday, Tuesday, or Wednesday of the following week to ensure weekday delivery to the laboratory.

Serial HIV-2 diagnostic testing in HIV-2–exposed infants to confirm or exclude HIV-2 infection is available free of charge from the Wadsworth Center (see *Diagnosis of HIV-2 > Box 1: Wadsworth Center Bloodborne Viruses Laboratory Services* in this guideline). For diagnostic testing of infants exposed to HIV-2, whole blood collected in an EDTA tube (purple top, prevents blood clotting) must be received in the laboratory within 3 days of collection. Collection kits for pediatric HIV diagnostic testing may be requested from the Wadsworth Center Order Desk at (518) 474-4175.

Table 2: ART Regimens for Initial Treatment of Pregnant Adults With HIV-2*

<p>Abacavir/lamivudine (ABC/3TC; Epzicom) if HLA-B*5701 is negative and HBsAg is negative</p> <p>OR</p> <p>Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC; Truvada)</p>	<p>AND</p>	<p>Raltegravir twice daily (RAL; Isentress)</p> <p>OR</p> <p>Ritonavir-boosted darunavir twice daily (DRV/r; Prezista <i>and</i> Norvir)</p>
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*Listed alphabetically; for specific details, see NYSDOH AI guideline *Selecting an Initial ART Regimen > Specific Factors to Consider and Discuss with Patients* and drug package inserts.

Pre- and Post-Exposure Prophylaxis for HIV-2

RECOMMENDATION: PrEP AND PEP FOR HIV-2

- Clinicians should recommend TDF/FTC *and* RAL as post-exposure prophylaxis (PEP) after HIV-2 exposure (3TC may be substituted for FTC). (A2†)
 - DTG can be used instead of RAL in a PEP regimen if the exposed individual is not pregnant; if the individual is of childbearing potential, effective birth control should be in use (see *Use of Dolutegravir in Individuals of Childbearing Capacity*).
 - See the NYSDOH AI guidelines on *PEP for HIV Prevention*

As with HIV-1, TDF/FTC is active against HIV-2 [Menendez-Arias and Alvarez 2014] and could be used as a pre-exposure prophylaxis (PrEP) regimen to prevent infection with HIV-2. For more information on evaluating patients for PrEP see NYSDOH AI guideline *PrEP to Prevent HIV and Promote Sexual Health*.

All Recommendations

☑ ALL RECOMMENDATIONS: DIAGNOSIS AND MANAGEMENT OF HIV-2 IN ADULTS

Diagnosis of HIV-2

- To diagnose HIV-2 infection, clinicians should follow the steps in the Centers for Disease Control and Prevention/Association of Public Health Laboratories (CDC/APHL) *HIV Diagnostic Testing Algorithm* and the recommendations in the NYSDOH AI guideline *HIV Testing*. (A1)
 - See the NYSDOH guideline *HIV Testing > Steps in the HIV Diagnostic Testing Algorithm* and *HIV-2 RNA Tests for Diagnostic Use*
- In individuals who are confirmed to have HIV-2 antibodies, clinicians should perform a clinical evaluation for HIV-2 infection that is similar in scope to the evaluation of patients with HIV-1. (A1) HIV-2 antibodies are confirmed by a reactive result to an HIV-1/2 or HIV-1/2 antigen/antibody (Ag/Ab) immunoassay and a positive result for HIV-2 Abs on a Food and Drug Administration (FDA)-approved supplemental HIV-1/2 Ab differentiation assay.
 - See the NYSDOH guideline *HIV Testing > HIV-2 RNA Tests for Diagnostic Use*

Treatment of HIV-2

- Clinicians should recommend ART for all individuals diagnosed with HIV-2. (A2⁺)
- Clinicians should not prescribe any NNRTI for treatment of HIV-2 infection. (A*)
- Clinicians should recommend a single-tablet regimen (STR) that includes 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI) as the initial treatment for adults with HIV-2 who are not pregnant and not planning to become pregnant, including those with acute HIV-2 infection (see *Table 1: ART Regimens for Initial Treatment of Nonpregnant Adults with HIV-2*). (A2)
- For individuals with HIV-1/HIV-2 coinfection, clinicians should:
 - Perform *HIV-1 drug resistance testing* to guide the choice of an initial regimen or to modify a regimen if virologic failure develops. (A2)
 - Recommend an ART regimen that will suppress both viruses effectively. (A*)

Monitoring ART in Individuals with HIV-2

- For individuals who are newly diagnosed with HIV-2, clinicians should perform the same laboratory and diagnostic testing currently recommended for individuals with HIV-1, with the exception of drug resistance testing, which is not available. (A3)
 - Testing includes CD4 cell count, HIV-2 viral load, creatinine clearance, and status of coinfections such as hepatitis B and C viruses and tuberculosis (see NYSDOH AI guideline *Selecting an Initial ART Regimen > ART-Initiation Laboratory Testing*).
- Clinicians should use HIV-2 viral load testing and CD4 cell count to determine the effectiveness of an ART regimen in patients with HIV-2. (A2)
- If HIV-2 viral load testing is not available, clinicians should suspect treatment failure if individuals experience a sustained decrease in CD4 cell count or have clinical disease progression. (A2)
- If a clinical practice in New York State cannot obtain HIV-2 viral load testing from the Wadsworth Laboratory, clinicians should refer individuals with HIV-2 to a practice that has the ability to access HIV-2 viral load testing from the Wadsworth Laboratory. (A3)

Pregnancy and HIV-2

- Clinicians should recommend ART for all pregnant individuals with HIV-2. (A2⁺)
 - Clinicians should recommend one of the ART regimens in Table 2. (A3)
 - Clinicians should not delay initiation of ART in pregnant individuals even if there is no or limited access to HIV-2 viral load testing. (A2⁺)
- In selecting an ART regimen for a pregnant individual with HIV-2, clinicians should **not** include:
 - Boosted atazanavir, because of its lack of efficacy against HIV-2. (A*)

- Dolutegravir prior to 8 weeks. (A2†)
- Efavirenz and rilpivirine, the NNRTIs recommended for treatment of HIV-1 during pregnancy, because of a lack of efficacy against HIV-2. (A*)

Note: For recommendations regarding administration of zidovudine for prophylaxis during labor and delivery, please see *Management During Labor and Delivery* in the NYSDOH AI guideline *Prevention of Mother-to-Child HIV Transmission*, or see *AIDSinfo: Special Populations: HIV-2 Infection and Pregnancy* in the guideline *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States*.

PrEP and PEP for HIV-2

- Clinicians should recommend TDF/FTC and RAL as post-exposure prophylaxis (PEP) after HIV-2 exposure (3TC may be substituted for FTC). (A2†)
 - DTG can be used instead of RAL in a PEP regimen if the exposed individual is not pregnant; if the individual is of childbearing potential, effective birth control should be in use (see *Use of Dolutegravir in Individuals of Childbearing Capacity*).
 - See the NYSDOH AI guidelines on *PEP for HIV Prevention*

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