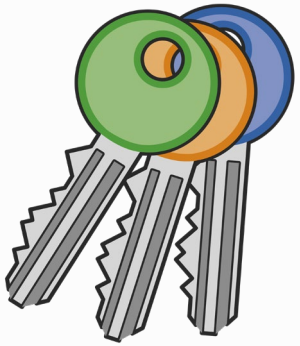
AETC AIDS Education & Training Center Program Southeast

Antiretroviral Therapy: Keys to Success



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Disclosure of Financial Relationships

- This speaker has the following financial relationship to disclose:
  - Bristol-Myers Squibb (spouse's employer)

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.

Objectives

- Discuss initial antiretroviral therapy (ART) options according to the most recent Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV
- List factors involved in selecting initial antiretroviral therapy (ART)
- Utilizing patient case scenarios, select initial regimens taking into account co-morbidities, drug-drug interactions, and patient preferences
- Identify resources to assist patients in maintaining access to ART

Objectives

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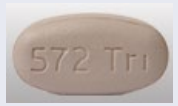
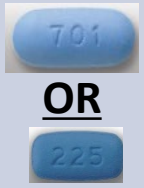
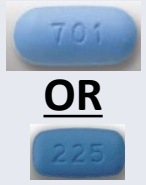
HIV Treatment Guidelines

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. February 24, 2021.

Unless otherwise noted, information in this presentation is adapted from these guidelines.

Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv

Recommended Initial Regimens for Most People with HIV

INSTI + 2 NRTIs	
	Bictegravir/tenofovir alafenamide/emtricitabine
	Dolutegravir/abacavir/lamivudine ***Only if HLA-B*5701 negative and no hepatitis B virus (HBV) coinfection***
 +  **OR**	Dolutegravir + tenofovir[1] + (emtricitabine or lamivudine)
 **OR**  +  **OR**	Raltegravir + tenofovir[1] + (emtricitabine or lamivudine)

1. Tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)

Recommended Initial Regimens for Most People with HIV (Continued)

INSTI + 1 NRTI	
	Dolutegravir/lamivudine ***Only if*** **- HIV RNA < 500,000 copies/mL** **- no HBV coinfection** **- genotype results shows no reverse transcriptase resistance**

Initial Regimens-
Certain Clinical Situations

INSTI + 2 NRTIs
Elvitegravir/cobicistat/tenofovir[1]/emtricitabine
Boosted PI + 2 NRTIs (In general, boosted darunavir preferred) **/r or /c indicates ritonavir or cobicistat for boosting**
Darunavir/c **or** darunavir/r + tenofovir[1] + (emtricitabine or lamivudine)
Atazanavir/c **or** atazanavir/r + tenofovir[1] + (emtricitabine or lamivudine)
Darunavir/c **or** darunavir/r + abacavir/lamivudine ***Only if HLA-B*5701 negative and no HBV coinfection***

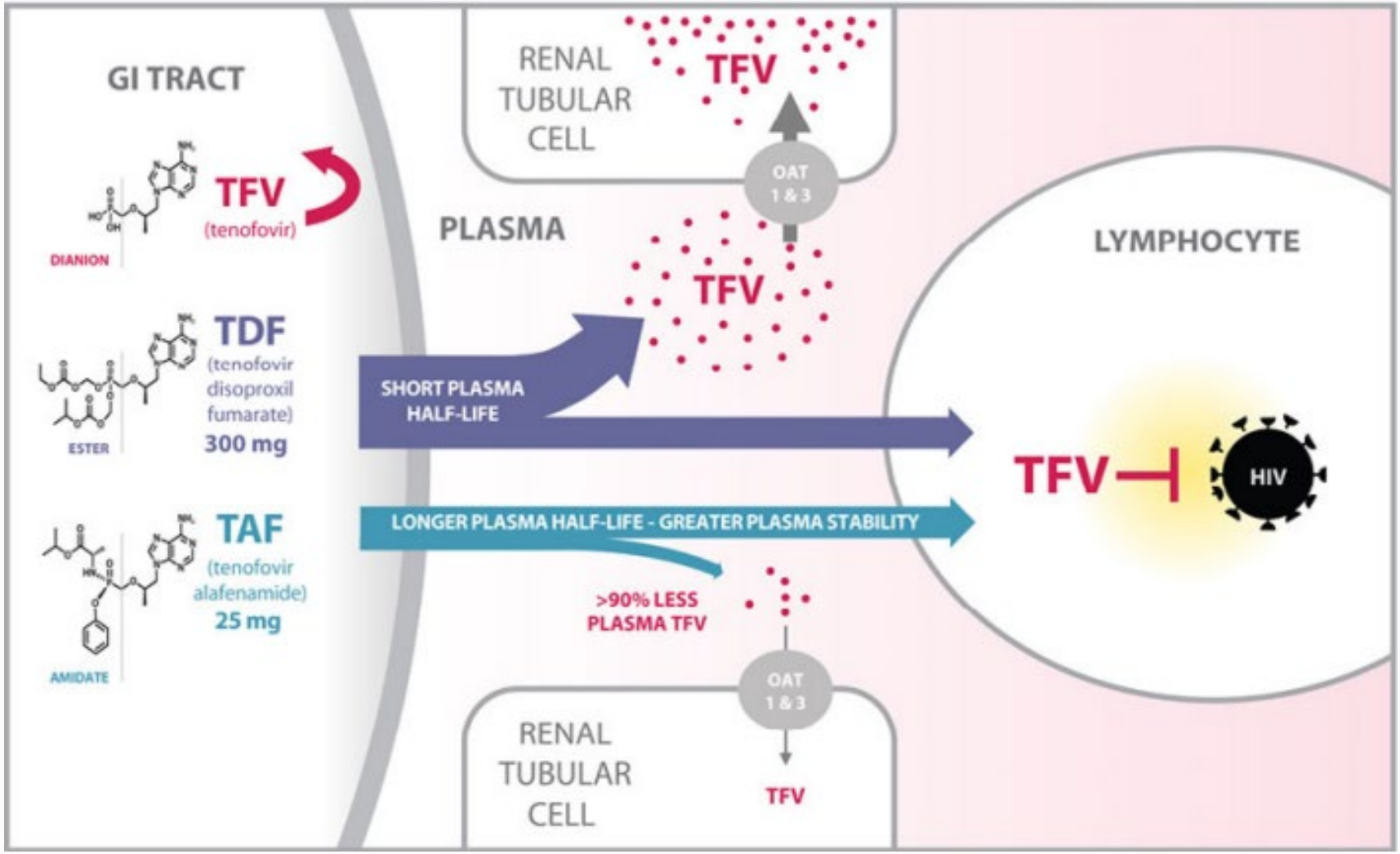
1. Tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)

Initial Regimens-
Certain Clinical Situations

NNRTI + 2 NRTIs
Doravirine + tenofovir[1] + (emtricitabine or lamivudine)
Efavirenz + tenofovir[1] + (emtricitabine or lamivudine)
Rilpivirine/tenofovir[1]/emtricitabine ***If HIV RNA < 100,000 and CD4 > 200***

1. Tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)

TAF vs. TDF: What is the Difference?



Antela, et al. HIV Medicine (2016), 17 (Suppl. 2), 4--16 Available at http://onlinelibrary.wiley.com/doi/10.1111/hiv.12401/pdf

TAF vs TDF

Drug	Use for Hep B	Use for PrEP	Use in Pregnancy	Increased lipids	Renal Effects	Weight Gain
TAF	Yes	Yes[1]	Yes[2]	More[3]	Less	More[4]
TDF	Yes	Yes	Yes	Less	More	Less

1. TAF/FTC (Descovy) is approved for use in PrEP in men or transgender women who have sex with men
2. Alternative NRTI in pregnant women or women trying to conceive(see https://clinicalinfo.hiv.gov/en/guidelines/perinatal/table-5-situation-specific-recommendations-use-antiretroviral-drugs-pregnant)
3. Higher LDL, HDL and triglycerides but no difference in total cholesterol/HDL ratio-clinical significance unknown
4. More common in women and Black or Hispanic patients.

TAF vs. TDF-Use in Renal Dysfunction and Hemodialysis (HD)

Drug	CrCL (mL/min)	Dose
TAF	< 15 and not on HD[1]	**Not recommended**
	< 15 and on HD[2]	One tablet once daily
TDF	30-49	300 mg every 48 hours
	10-29	300 mg twice weekly (every 72-96 hours)
	< 10 and not on HD	No recommendation
	On HD[2]	300 mg every 7 days[3]

1. Recommendations vary depending on co-formulation used. See https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/antiretroviral-dosing-recommendations-patients-renal-or-hepatic
2. Dose after HD if given on HD day(s)
3. Assumes three HD sessions of 4 hours duration each

Patient Case Ricky

- Ricky is a 28 year old man who was recently discharged from the hospital where he was diagnosed with HIV/AIDS and disseminated *Mycobacterium avium* complex infection
- He comes to the clinic to initiate ART
- He states he has no preference with respect to food requirements or the need for a single tablet regimen but would prefer a once daily regimen

Patient Case Ricky

- Labs:
  - Genotype: pansensitive
  - AST/ALT: WNL
  - eGFR 103 mL/min
  - VL 182,000 copies/mL CD4 43 cells/mm^3
- Allergies: NKDA
- Medications: rifabutin 300 mg po once daily, azithromycin 500 mg po once daily, ethambutol 1000 mg po once daily, trimethoprim/sulfamethoxazole 1 DS tab po once daily

Why is a TAF-containing regimen not recommended for Ricky?

A. TAF may not be as effective as TDF in patients with high viral loads
B. Due to drug-drug interactions, TAF levels would be expected to be increased
C. Due to drug-drug interactions, TAF levels would be expected to be decreased
D. I'm not sure, I thought TAF could be used in all patients

TAF Drug Interactions

- Strong P-glycoprotein (P-gp) inducers are expected to ↓ TAF concentrations
  - Rifamycins (i.e., rifampin, rifabutin)
  - St. John's Wort
  - Carbamazepine
  - Oxcarbazepine
  - Phenytoin
  - Phenobarbital

Objectives

- Discuss initial antiretroviral therapy (ART) options according to the most recent Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV
- List the factors involved in selecting initial antiretroviral therapy (ART)
- Utilizing patient case scenarios, select initial regimens taking into account co-morbidities, drug-drug interactions, and patient preferences
- Identify resources to assist patients in maintaining access to ART

Factors in Regimen Selection

- Viral load and CD4 cell count
- HIV resistance
- HLA-B*5701 status
- Co-morbid conditions
- Co-infections
- Pregnancy or pregnancy potential
- Potential adverse effects
- Potential drug-drug interactions
- Patient preferences
- Access/cost

Specific Comorbid Conditions

- Comorbid Conditions
  - E.g., Cardiovascular disease, hyperlipidemia, obesity, renal disease, osteoporosis or decreased bone density, psychiatric illness
- Coinfections: hepatitis C virus (HCV), hepatitis B virus (HBV), tuberculosis (TB)

Regimen/Drug Factors

- Potential adverse effects
- Potential drug-drug interactions
- Convenience (e.g., pill burden, dosing frequency, food requirements)
- Regimen's genetic barrier to resistance (i.e., how easy is it for the virus to become resistant to the medicines in the event of missed doses)
- Cost

Conversations About Patient Preferences and Barriers to Adherence

- Dosing frequency, pill burden, food requirements, size of pills, potential side effects
- What is the patient's typical day like?
- What time would be most convenient to take medications?
  - It is best to tailor the regimen to predictable and routine daily events
    - How will schedule differ on weekends?
    - What will happen if they travel?
- Will the cost of medications impact access?

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Patient Case Cynthia

- Cynthia is a 28 year old woman recently diagnosed with HIV infection who presents to the clinic to start ART through a rapid start program
- Baseline labs: drawn at visit, not yet available.
- PMH: treated for chlamydia x 2
- Social history: unmarried, never smoked, does not drink alcohol, has 1 child (3 years old) and is interested in having more. Her only birth control method is condoms.

What regimen would you choose for Cynthia?

A. BIC/TAF/FTC (Biktarvy)

B. DRV/c + TAF/FTC (Prezcobix + Descovy)

C. DTG + TAF/FTC (Tivicay + Descovy)

D. DTG + TDF/FTC (Tivicay + Truvada)

INSTI Risk of Neural Tube Defects

- Very small increased risk of neural tube defects seen with DTG
- Advantages of DTG include once daily dosing, well-tolerated, rapid viral suppression
- Perinatal guidelines now list DTG as a preferred agent throughout pregnancy and in women trying to conceive
- Guidelines stress importance of patient counseling and informed decision making
- See https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new-guidelines

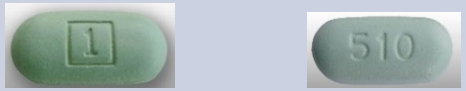
Patient Case James

- James is a 23 year old man recently diagnosed with HIV infection
- CD4 482 cells/mm^3, VL 29,852 copies/mL (no resistance detected)
- eGFR 98 mL/min, CBC and CMP: WNL
- No hepatitis B coinfection
- He states he would prefer a one pill once a day regimen and does not want a regimen that has to be taken with food

What regimen would you choose for James?

A. DTG/3TC (Dovato)
B. DTG/ABC/3TC (Triumeq)
C. BIC/TAF/FTC (Biktarvy)
D. RPV/TAF/FTC (Odefsey)
E. DRV/c/TAF/FTC (Symtuza)

ART with Food Requirements

Should be Taken With Food	
	Atazanavir (ATV, Reyataz)/r **OR** ATV/c (Evotaz)
	Darunavir/r (DRV, Prezista)/r **OR** DRV/c (Prezcobix) **OR** DRV/c/TAF/FTC (Symtuza)
	EVG/c/TDF/FTC (Stribild) **OR** EVG/c/TAF/FTC (Genvoya)

ART with Food Requirements

Should be Taken With a Full Meal	
   	Rilpivirine (Edurant) **OR** RPV/TDF/FTC (Complera) **OR** RPV/TAF/FTC (Odefsey) **OR** RPV/DTG (Juluca)
Should be Taken on an Empty Stomach	
 	EFV/FTCTDF (Atripla) **OR** EFV (Sustiva) **OR** EFV/3TC/TDF (Symfi)

Patient Case Alicia

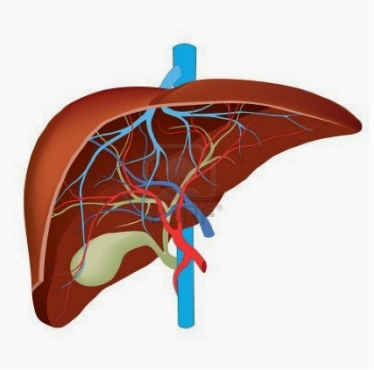
- Alicia is a 58 year old woman recently diagnosed with HIV infection who is being seen to initiate ART
- Baseline resistance test: no mutations detected
- CD4 375 cells/mm^3, VL 10,502 copies/mL
- eGFR 58 mL/min, AST 58, ALT 62
- Hepatitis screening
  - Hepatitis B infected, Hep B VL 1.2 million IU/mL
  - Hepatitis C uninfected
  - Hepatitis A nonimmune

Which regimen below would NOT be appropriate for Alicia?

A. DTG/3TC (Dovato)
B. TDF/FTC (Truvada) + DTG (Tivicay)
C. BIC/TAF/FTC (Biktarvy)
D. DRVc/TAF/FTC (Symtuza)
E. All of the above are appropriate options

Regimens for HBV Coinfected Patients

- It is important to use two drugs that are active against hepatitis B in people with HIV infection and HBV coinfection
  - Tenofovir (TAF or TDF)
  - Emtricitabine (FTC) or lamivudine (3TC)
- Poor adherence or lapses in therapy in people with HBV can lead to severe liver disease including failure and death



Patient Case Jessica

- Jessica is a 32 year old woman who was diagnosed with HIV infection in 2018.
- She is stable on a regimen of bictegravir/emtricitabine/tenofovir alfenamide (Biktarvy)
  - VL < 20 and CD4 789 cells/mm^3 on recent labs
- Concomitant medications: omeprazole 20 mg once daily, ethinyl estradiol/norgestimate (Sprintec) 1 tab daily, ferrous sulfate 325 mg twice daily (iron supplement)

Which medication is expected to interact with BIC/TAF/FTC (Biktarvy)?

A. Omeprazole
B. Ethinyl estradiol/norgestimate
C. Ferrous sulfate
D. None of the above

INSTI Interactions

	Bictegravir (BIC)	Dolutegravir (DTG)	Elvitegravir/ cobicistat (EVG/c)	Raltegravir (RAL)
Antacids (e.g., Al, Mg, Ca)	• Take BIC ≥ 2 hours before or ≥ 6 hours after antacids containing Al or Mg • Take BIC with antacids containing Ca with food	Take DTG ≥ 2 hours before or ≥ 6 hours after antacids containing Al, Mg, Ca	Take EVG/c ≥ 2 hours before or ≥ 2 hours after antacids containing Al, Mg, Ca	**With calcium carbonate antacids:** • No dosage adjustment or separation needed with RAL 400 mg bid • Do not use once daily RAL HD formulation with calcium carbonate antacids **With Al and/or Mg containing antacids:** •Do not combine
Polyvalent cation (e.g., Al, Ca, Fe, Mg, Zn) containing medications including multivitamins, supplements, laxatives, sucralfate and buffered medications	**Supplements containing Ca or Fe:** • Take simultaneously with food or if fasting, take BIC ≥ 2 hours before **Other polyvalent cations (editor recommendation):** • Take BIC ≥ 2 hours before or ≥ 6 hours after	**Supplements containing Ca or Fe:** • Take simultaneously with food or if fasting, take DTG ≥ 2 hours before or ≥ 6 hours after **Other polyvalent cations:** • Take DTG ≥ 2 hours before or ≥ 6 hours after	Take EVG/c ≥ 2 hours before or ≥ 6 hours after polyvalent cation containing supplements	Take RAL ≥ 2 hours before or ≥ 6 hours after polyvalent cation containing supplements
H2-Receptor Antagonists	No dose adjustment necessary			
Proton Pump Inhibitors	No dose adjustment necessary			

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Patient Case Bill

- Bill is a 32 year old man with HIV infection who is seen at the clinic to restart ART
- He was previously well-controlled on bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy)
- He has private insurance through his job and was using a local pharmacy that told him his copay was $1000. He got frustrated and fell out of care for 1 year.

Patient Case Steven

- Patient came to your clinic to re-establish HIV care
- He stated that he has been well-controlled on efavirenz/emtricitabine/tenofovir disoproxil fumarate (Atripla) since 2009. HIV VL of < 20 and CD4 of 779 (25%)
  - Copay used to be less than $10 but as of the 1st of the year, the copay increased to $900 per month. He paid the copay when he could but started taking the medication every other day to stretch it out.
  - Client has Medicare but no longer has the low income subsidy

What resources could have been utilized to assist Bill and Steven in obtaining ART each month?

Copay Assistance Programs

Program	Website	Limitations
Pharmaceutical company programs	• https://www.gileadadvancingaccess.com/ • https://www.viivconnect.com/ • https://www.merck.com/patients/patient-financial-assistance/ • https://www.janssencarepath.com/	• Cannot be used in patients with federally funded insurance (e.g. Medicare, Medicaid, Tricare) • No income limitations
Good Days	• www.mygooddays.org	• Can be used in patients with federally-funded insurance • Income limitations
Patient Advocate Foundation	• www.copays.org/funds/hiv-aids-and-prevention/	• Can be used in patients with federally-funded insurance • Income limitations

Other Resources for Copays

- ADAP Premium Plus/copay assistance
- Ryan White medical case management

Patient Case-Anna

- Anna is a 48 year old woman who is seen in the clinic for follow-up of HIV infection.
- She is well-controlled on a regimen of emtricitabine/tenofovir alafenamide/darunavir/cobicistat (Symtuza). HIV VL < 20, CD4 1032 (48%)
- She is suffering from migraines and her provider has prescribed a new medication since sumatriptan is no longer working for her.

Patient Case-Anna

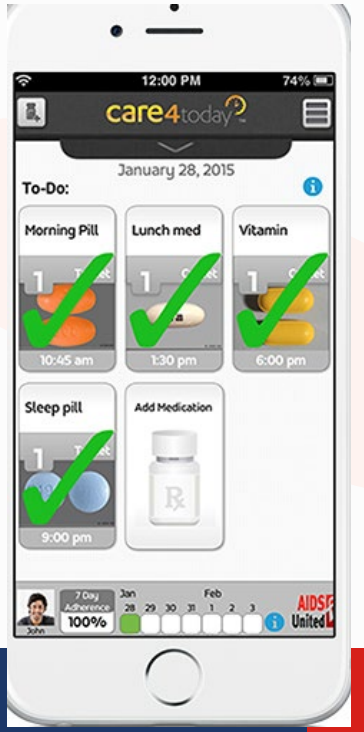
- Anna has no insurance and is currently on ADAP.
- She asks her Ryan White case manager for assistance in obtaining the medication since it is not on the ADAP formulary.
- You find out the medication is called galcanezumab-gnlm (Emgality) and costs over $800 per month.

Medication Resources

- GoodRX-provides discount cards for medications
  - https://www.goodrx.com/
- Pharmaceutical assistance programs
  - www.needymeds.org
- Ryan White medical case management
- Other area specific resources

Adherence Interventions

- Prescription and/or co-pay assistance programs
- Community resources to promote adherence (e.g., family, peer advocates)
- Pillboxes, planners, alarms, cell phone apps
- Referral to specialty pharmacy



Cabotegravir/rilpivirine (Cabenuva)

What's New in the Guidelines?

Updated: Feb. 24, 2021
Reviewed: Feb. 24, 2021

Panel's Recommendation for Long-Acting Injectable Cabotegravir and Rilpivirine in Persons with HIV

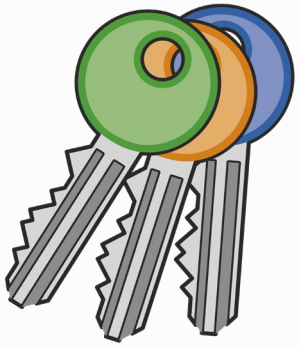
On January 21, 2021, the U.S. Food and Drug Administration (FDA) approved the first complete long-acting injectable antiretroviral (ARV) regimen, cabotegravir and rilpivirine, as an option to replace the current ARV regimen in adults with HIV.

Based on the clinical trial results from two large randomized controlled trials, the Panel recommends that once monthly cabotegravir and rilpivirine intramuscular (IM) injections can be used as an optimization strategy for people with HIV currently on oral antiretroviral therapy (ART) with documented viral suppression for at least 3 months (although optimal duration is not defined) (AI), who—

- have no baseline resistance to either medication,
- have no prior virologic failures,
- do not have active hepatitis B virus (HBV) infection (unless also receiving an oral HBV active regimen),
- are not pregnant and are not planning on becoming pregnant, and
- are not receiving medications with significant drug interactions with cabotegravir and rilpivirine.

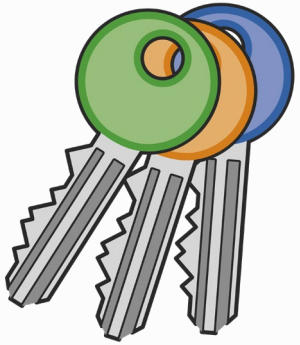
Before initiation of the IM injection, patients should receive oral cabotegravir and oral rilpivirine for 28 days as an oral lead-in period to assess tolerance to these drugs. Clinicians should refer to the product label for information regarding IM dose administrations as well as management strategies for planned or unplanned missed doses.

Keys to Success



- Regimens are selected based on a variety of factors to optimize chances for treatment success
- Consider patient preferences in regimen selection
- Remember that patient circumstances change over time
- Let all patients know that there are resources to assist them in staying on ART and they should communicate any access issues to their provider or case manager immediately

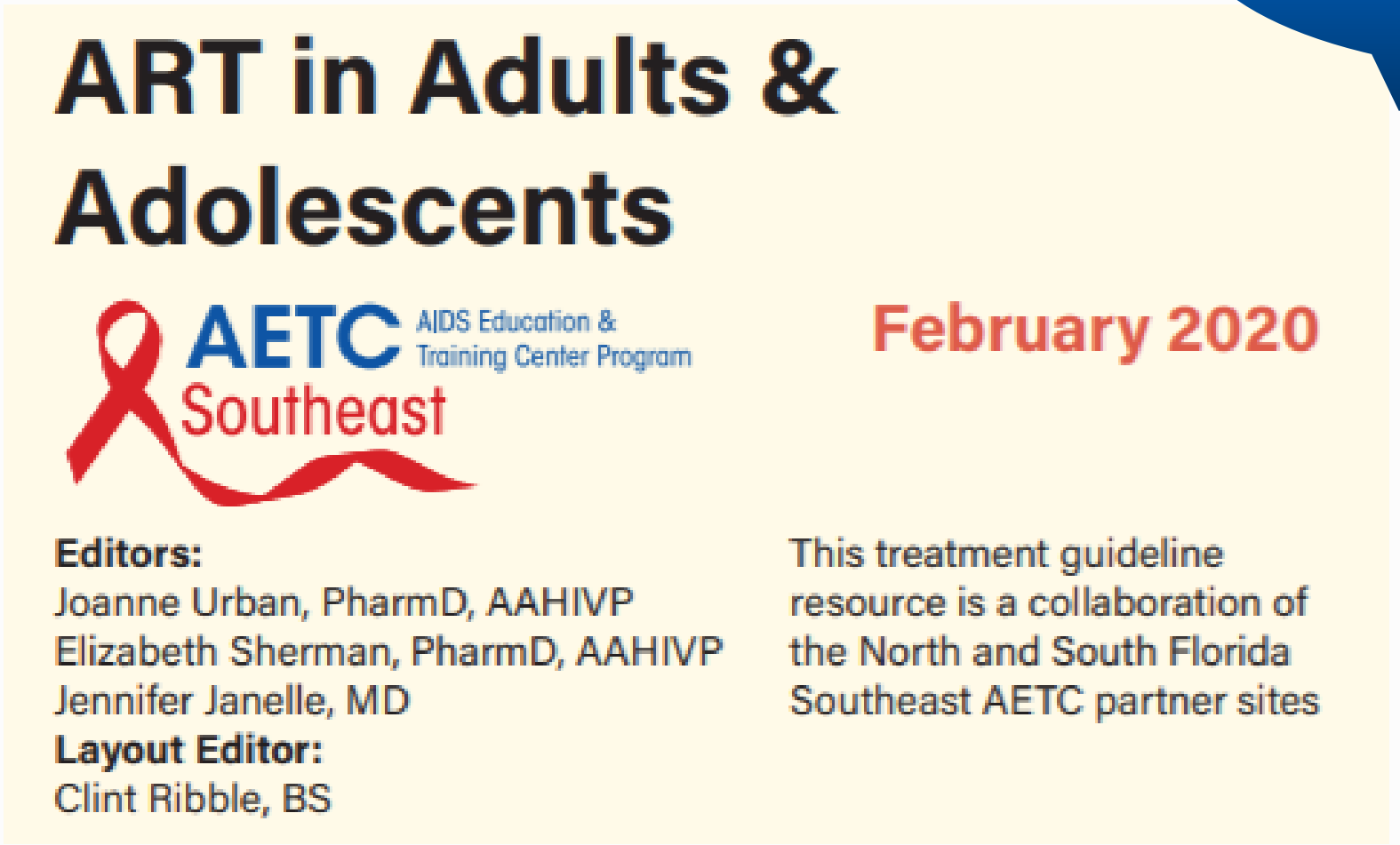
Keys to Success



- At every visit, assess any barriers to obtaining and taking medications
  - Pharmacy not filling prescriptions on time
  - Pharmacy providing partial antiretroviral regimen and/or filling medications on different dates throughout the month
  - Lack of transportation to pick up medications
  - Travel
  - Inability to afford copays and/or insurance premiums
  - Side effects
  - Forgetting to take medication or not taking the same time each day

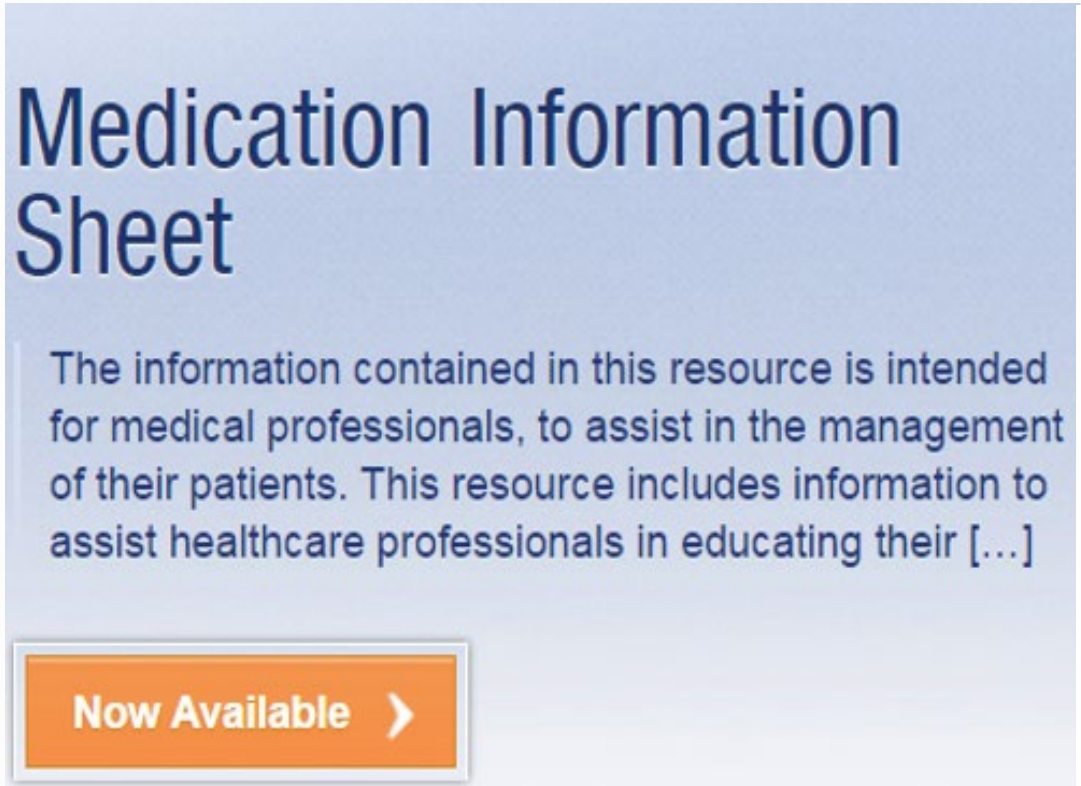
Antiretroviral Resources

Update in progress



http://www.seaetc.com/provider-resources/reference/

Antiretroviral Resources



Antiretroviral Patient Medication Information Sheets

Table of Contents

1. About this resource, Disclaimer, Photo Credits, Instructions
2. General information sheet - Provide this to all patients
3. Drug Specific Information Sheets - Provide sheet on each medication
   a. Nucleoside Reverse Transcriptase Inhibitors
      i. Abacavir (Ziagen®)
      ii. Emtricitabine (Emtriva®)
      iii. Lamivudine (Epivir®)
      iv. Tenofovir disoproxil fumarate (Viread®)
      v. Zidovudine (Retrovir®)
   b. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
      i. Efavirenz (Sustiva®)
      ii. Etravirine (Intelence®)
      iii. Nevirapine (Viramune®, Viramune XR®)
      iv. Rilpivirine (Edurant®)
   c. Protease Inhibitors (PIs)

http://aetc.medicine.ufl.edu/resources/drug-information-sheets /