HIV Therapies in 2022

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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.

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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
- Utilizing patient case scenarios, select ART taking into account co-morbidities, drug-drug interactions, prior treatment, resistance, and patient preferences
- Describe strategies to optimize antiretroviral therapy in the setting of viral suppression including the role of the long-acting injection cabotegravir/rilpivirine

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HIV Therapy Evolution: 2000 to 2020

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HIV Therapy Evolution: 2021

January 22, 2021

Cabenuva Approved as First Long-Acting Injectable for HIV Treatment

Brian Park, PharmD

The Food and Drug Administration (FDA) has approved Cabenuva (cabotegravir and rilpivirine; ViiV Healthcare) injection for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

Cabenuva injection is administered once a month. Vocabria is an oral tablet formulation of cabotegravir.

https://www.empr.com/home/news/cabenuva-cabotegravir-rilpivirine-once-monthly-injection-hiv-1-infection/#

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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. January 20, 2022.

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

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

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

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Recommended Initial Regimens for Most People with HIV

INSTI + 2 NRTIs or INSTI + 1 NRTI

	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)
	Dolutegravir/lamivudine ***Only if* HIV RNA < 500,000 copies/mL, no HBV coinfection, genotype results shows no reverse transcriptase resistance**

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

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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

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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

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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

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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

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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.

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What regimen would you choose for Cynthia?

A. Bictegravir/TAF/FTC (Biktarvy)
B. Darunavir/cobicistat + TAF/FTC (Prezcobix + Descovy)
C. Dolutegravir + TAF/FTC (Tivicay + Descovy)
D. Dolutegravir + TDF/FTC (Tivicay + Truvada)
E. Raltegravir + TDF/FTC (Isentress + Truvada)

TAF=tenofovir alafenamide, TDF=tenofovir disoproxil fumarate, FTC=emtricitabine

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What to Start
Raltegravir Removed from "Recommended for Most PWH"

- Updated data show low overall prevalence of neural tube defects (NTD) with dolutegravir (DTG)
  - DTG back to "Preferred" category for conception & pregnancy
  - No longer an indication to choose raltegravir (RAL) over DTG
- RAL has a lower barrier to resistance than DTG and BIC
- RAL regimens have higher pill burden than other options

Tsepamo Study Outcomes	Conception	
	DTG	Non-DTG
Results as of April 2020	n = 3,591	n = 19,361
NTD prevalence (95% CI)	**0.19** (0.09-0.40)	**0.11** (0.07-0.17)

clinicalinfo.hiv.gov; Zash R et al. IAS 2020.

Wood B. November 2021 AIDS Clinical Conference: ART Update: New Guidelines & Medications [PowerPoint]. Northwest AIDS Education and Training Center; November 16, 2021. Available at http://aidsetc.org/. Accessed February 27, 2022.

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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. Now a preferred NRTI in pregnant women or women trying to conceive-see https://clinicalinfo.hiv.gov/en/table/table-5-situation-specific-recommendations-use-antiretroviral-drugs-pregnant-people-and
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.

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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

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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)

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

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

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INSTI Interactions

	Bictegravir (BIC)	Dolutegravir (DTG)	Elvitegravir/ cobicistat (EVG/c)	Raltegravir (RAL)	Cabotegravir (CAB) - ORAL
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 coinbine	Take oral CAB ≥ 4 hours before or ≥ 2 hours after antacids containing Al, Mg, Ca
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	Take CAB ≥ 2 hours before or ≥ 4 hours after supplements that contain polyvalent cations
H2-Receptor Antagonists	No dose adjustment necessary				
Proton Pump Inhibitors	No dose adjustment necessary				

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Patient Case Larry

- LM is a 45 year old man with HIV infection since 2018.
- He has been well-controlled on a regimen of bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy)
  - HIV VL < 20 and CD4 1331 (in Oct 2019 when last seen)
- He returns to clinic for follow-up after being incarcerated for 18 months. He reported being without ART for 1 week.
- He was provided Biktarvy through the test and treat program and labs were drawn.

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Patient Case Larry

- Labs:
  - Genotype: pansensitive
  - AST/ALT: WNL
  - eGFR 108 mL/min
  - HIV VL < 20 copies/mL CD4 1453 cells/mm^3
- Quantiferon TB Gold Plus: positive

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Patient Case Larry

- Patient is evaluated for TB disease (chest x-ray and sputum are negative)
- TB disease is ruled out and provider plans to start treatment for LTBI
- The TB practitioner would like to use a shorter course LTBI regimen and asks whether isoniazid/rifapentine once weekly for 3 months (3HP) can be used in this patient.

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What do you tell the TB provider?

A. 3HP should not be used as it has not been studied in patients with HIV infection
B. 3HP should not be used in patients receiving ART
C. 3HP can be used as no interaction is expected with Biktarvy
D. 3HP can be used but ART regimen modification is necessary

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LTBI Treatment-June 2021 Update

- Selection of tuberculosis (TB)-preventive treatment for individuals with HIV and latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral (ARV) regimen as noted below.
  - With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII)**.
  - With once-weekly isoniazid plus rifapentine for 3 months:
    - Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used **(AII)**.
    - Dolutegravir (DTG) 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII)**. This 3-month regimen **is not recommended** for patients who require twice-daily DTG therapy (e.g., those with certain integrase strand transfer inhibitors [INSTI]-associated resistance substitutions or clinically suspected INSTI resistance) **(AIII)**.
  - With once-daily isoniazid and rifapentine for 1 month:
    - EFV 600 mg once daily (in combination with either ABC/3TC or TDF/FTC) can be used without dose adjustment **(AI)**.
  - If rifampin or rifapentine is used to treat LTBI, clinicians should review Tables 24a through 24e to assess the potential for drug-drug interactions among different ARV drugs and the rifamycins **(AII)**.

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https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/tuberculosishiv-coinfection?view=full

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Rifamycin Drug Interactions

- All rifamycins are inducers of cytochrome P450 drug metabolism and P-glycoprotein (P-gp)
  - Rifampin > rifabutin
  - Rifapentine depends on dose used (more interactions with daily doses used for TB disease)
- Inhibitors of CYP3A may ↑ rifabutin levels
- Inducers of CYP3A ↓ rifabutin levels

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Rifapentine (RPT) Interactions with ART

- RPT should not be used for treatment of TB disease in patient with HIV
- Use of RPT for LTBI in patients on ART has been limited by drug-drug interactions

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Patient Case Rhonda

- Patient is a 61 year old woman with HIV infection since 2011 who recently relocated from South Florida.
- Her HIV VL has been well-controlled on a regimen of bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy) since 2018.
- PMH: HIV, diabetes, hypertension, reflux
- Medications: lisinopril 20 mg daily, metformin XR 2000 mg daily, omeprazole 20 mg daily

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Patient Case Rhonda

- Most recent labs
  - HIV VL < 20, CD4 354
  - eGFR 48 (down from 72 one year prior)
- The provider would like to modify the regimen to one that does not contain tenofovir due to declining renal function.
- Additional labs are done:
  - Archive genotype: No significant mutations
  - HLA B*5701 negative

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What regimen would you choose for Rhonda?

A. Dolutegravir/abacavir/lamivudine (Triumeq)
B. Dolutegravir/rilpivirine (Juluca)
C. Dolutegravir/lamivudine (Dovato)
D. Dolutegravir + darunavir/cobicistat (Tivicay + Prezcobix)

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Patient Case Rhonda

- Rhonda's regimen is changed to dolutegravir/lamivudine.
- Labs repeated 4 weeks after regimen change show the following:
  - HIV VL 776 copies/mL
  - eGFR 59 (up from 48 six weeks prior)

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Are there any drug-drug interactions of concern with Rhonda's medications?

1. No, all of her medications can be used together without any adjustments
2. Yes, omeprazole can decrease dolutegravir levels and should be taken ≥ 12 hours after dolutegravir
3. Yes, omeprazole and metformin should not be combined with dolutegravir
4. Yes, metformin may require a dosage adjustment

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Metformin Interactions

BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
DTG	**DTG 50 mg Once Daily plus Metformin 500 mg Twice Daily:** • Metformin AUC ↑ 79% and C_{max} ↑ 66% **DTG 50 mg Twice Daily plus Metformin 500 mg Twice Daily:** • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	Start metformin at lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.
CAB (PO and IM), RAL	↔ metformin expected	No dose adjustment needed.

From Table 24. Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents. Department of Health and Human Services. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/.

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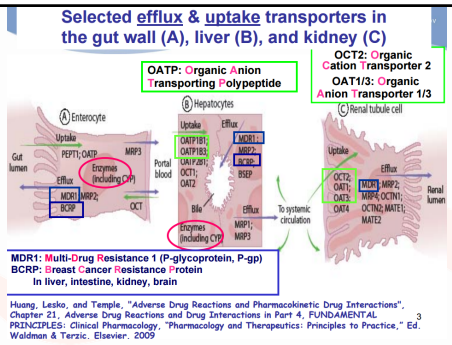
Selected efflux & uptake transporters in the gut wall (A), liver (B), and kidney (C)



Huang, Lesko, and Temple, "Adverse Drug Reactions and Pharmacokinetic Drug Interactions", Chapter 21, Adverse Drug Reactions and Drug Interactions in Part 4, FUNDAMENTAL PRINCIPLES: Clinical Pharmacology, "Pharmacology and Therapeutics: Principles to Practice," Ed. Waldman & Terzic. Elsevier. 2009

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Transported Mediated Drug-Drug Interactions.
http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/UCM207267.pdf

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Patient Case Rhonda

- Upon further review of prior records, the provider noted that the patient had been on prior regimens as follows:
  - Efavirenz/tenofovir disoproxil fumarate/emtricitabine 2012-2015 (genotype in 2015 showed M184V and K103N mutations)
  - Darunavir/ritonavir + tenofovir alafenamide/emtricitabine 2015-2018 (always suppressed on this regimen)

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Proviral HIV DNA Genotype: Obtaining Resistance Data

- DNA (archive) genotype[1,2]
  - Sequence mutations in cell-associated proviral DNA
  - Can be assessed at any HIV-1 RNA level, including undetectable
  - Less sensitive than cumulative RNA genotypes
- Concordance between DNA and RNA genotypes varies by study and ARV class (26%-84%)[2,3]
- Study 1824: switch to EVG/COBI/FTC/TAF among virologically suppressed patients with M184V/I mutation on RNA assay[4]
  - M184V/I detected with DNA assay in only 48% (40/84) of screened patients

1. Delaugerre. HIV Med. 2012;13:517. 2. Wirden. J Antimicrob Chemother. 2011;66:709.
3. Derache. PLoS One. 2015;10:e0117430. 4. Margot. IAS 2019. Abstr MOPEB249.

Slide credit: clinicaloptions.com

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DHHS Guidelines: Recommendations on Proviral DNA Genotyping

- Proviral DNA genotyping ***can be considered*** for individuals with suppressed HIV-1 RNA, particularly if complex or semicomplex preexisting resistance is suspected

> ***"… for individuals who have experienced multiple prior failures, a prolonged history of prior ARV regimens, and/or for whom genotypic resistance test results are not available, it may be appropriate to utilize proviral DNA genotypic testing"***

- Interpret results with caution
  - ***Presence*** of mutations ***rules in resistance/rules out susceptibility***
  - ***Absence*** of mutations ***does not necessarily rule out resistance/does not ensure susceptibility***

DHHS guidelines for the use of antiretroviral agents in adults and adolescents living with HIV.

Slide credit: clinicaloptions.com

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Patient Case Michael

- 45 year old man with HIV infection since 2020.
- His virus has been well-controlled on a regimen of bictegravir/tenofovir alafenamide/emtricitabine for 2 years
- Most recent labs:
  - HIV VL < 20, CD4 972
  - eGFR 104
- He is interested in the long-acting injectable HIV regimen

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Patient Case Michael

- PMH:
  - Reflux, schizophrenia, bipolar disorder, benign prostatic hyperplasia, insomnia
- Current meds:
  - Ziprasidone, lithium carbonate, zolpidem, pantoprazole, tamsulosin

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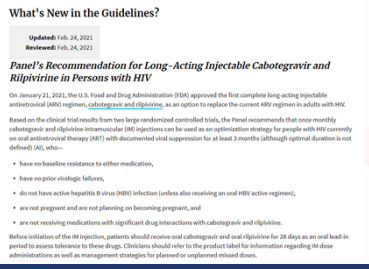
Cabotegravir/rilpivirine (Cabenuva)



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.

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Cabotegravir/rilpivirine Monthly

Drug	Oral Lead-in (at Least 28 Days) Month 1	Intramuscular (Gluteal) Initiation Injections (One-Time Dosing) At Month 2 (on the Last Day of Oral Lead-in Dosing)	Intramuscular (Gluteal) Continuation Injections (Once-Monthly Dosing) Month 3 Onwards
Cabotegravir	30 mg once daily with a meal	600 mg (3 mL)	400 mg (2 mL)
Rilpivirine	25 mg once daily with a meal	900 mg (3 mL)	600 mg (2 mL)

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Cabenuva. Package Insert. ViiV Healthcare. February 2022.

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Cabotegravir/rilpivirine Every 2-Month

Drug	Oral Lead-in (at Least 28 Days) Month 1	Intramuscular (Gluteal) Injections[a] At Month 2, Month 3, and then Every 2 Months Onward (Starting at Month 5)
Cabotegravir	30 mg once daily with a meal	600 mg (3 mL)
Rilpivirine	25 mg once daily with a meal	900 mg (3 mL)

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Cabenuva. Package Insert. ViiV Healthcare. February 2022.

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Are there any drug-drug interaction concerns with cabotegravir/rilpivirine and Michael's other medications?

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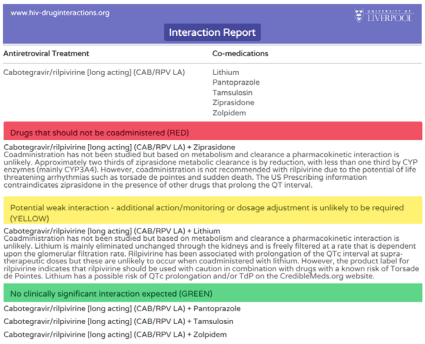
www.hiv-druginteractions.org

Interaction Report

Antiretroviral Treatment	Co-medications
Cabotegravir/rilpivirine [long acting] (CAB/RPV LA)	Lithium Pantoprazole Tamsulosin Ziprasidone Zolpidem

Drugs that should not be coadministered (RED)

Cabotegravir/rilpivirine [long acting] (CAB/RPV LA) + Ziprasidone
Coadministration has not been studied but based on metabolism and clearance a pharmacokinetic interaction is unlikely. Approximately two thirds of ziprasidone metabolic clearance is by reduction, with less than one third by CYP enzymes (mainly CYP3A4). However, coadministration is not recommended with rilpivirine due to the potential of life threatening arrhythmias such as torsade de pointes and sudden death. The US Prescribing information contraindicates ziprasidone in the presence of other drugs that prolong the QT interval.

Potential weak interaction - additional action/monitoring or dosage adjustment is unlikely to be required (YELLOW)

Cabotegravir/rilpivirine [long acting] (CAB/RPV LA) + Lithium
Coadministration has not been studied but based on metabolism and clearance a pharmacokinetic interaction is unlikely. Lithium is mainly eliminated unchanged through the kidneys and is freely filtered at a rate that is dependent upon the glomerular filtration rate. Rilpivirine has been associated with prolongation of the QTc interval at supra-therapeutic doses but these are unlikely to occur when coadministered with lithium. However, the product label for rilpivirine indicates that rilpivirine should be used with caution in combination with drugs with a known risk of Torsade de Pointes. Lithium has a possible risk of QTc prolongation and/or TdP on the CredibleMeds.org website.

No clinically significant interaction expected (GREEN)

Cabotegravir/rilpivirine [long acting] (CAB/RPV LA) + Pantoprazole

Cabotegravir/rilpivirine [long acting] (CAB/RPV LA) + Tamsulosin

Cabotegravir/rilpivirine [long acting] (CAB/RPV LA) + Zolpidem

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Oral Cabotegravir/rilpivirine Interactions with ARAs

ARA	Oral Rilpivirine Dosing Recommendation
Antacids (e.g., Al, Mg, Ca)	Take antacids ≥ 2 hours before or ≥ 4 hours after RPV
H2-Receptor Antagonists	Take H2-Receptor antagonists ≥ 12 hours before or ≥ 4 hours after RPV
Proton Pump Inhibitors	Do not combine-contraindicated

- No interaction between cabotegravir and H2-RAs or PPIs
- Take antacids ≥ 2 hours before or ≥ 4 hours after cabotegravir

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Cabotegravir/rilpivirine Drug Interactions

Table 8. Drug Interactions with CABENUVA

Concomitant Drug Class: Drug Name	Effect on Concentration	Clinical Comment
Anticonvulsants: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	↓Cabotegravir ↓Rilpivirine	Coadministration is contraindicated with CABENUVA due to potential for loss of virologic response and development of resistance *[see Contraindications (4)]*.
Antimycobacterials: Rifampin[a], Rifapentine	↓Cabotegravir ↓Rilpivirine	
Antimycobacterial: Rifabutin[a]	↓Cabotegravir ↔Rifabutin ↓Rilpivirine	
Glucocorticoid (systemic): Dexamethasone (more than a single-dose treatment)	↓Rilpivirine	
Herbal product: St John's wort (*Hypericum perforatum*)	↓Rilpivirine	

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Cabenuva. Package Insert. ViiV Healthcare. February 2022.

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Process for Obtaining Cabotegravir/rilpivirine

- Injectable medication comes from one of the designated specialty pharmacies.
  - Submit patient enrollment form to Viiv Connect (either electronically through portal or fax the form)
  - Submit prescription directly to one of the designated specialty pharmacies
- Oral lead-in medications provided by TheraCom Pharmacy

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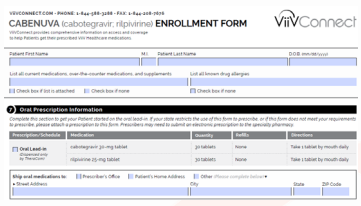
Cabenuva Patient Enrollment Form


VIIVCONNECT.COM · PHONE: 1-844-588-3288 · FAX: 1-844-208-0929

CABENUVA (cabotegravir, rilpivirine) ENROLLMENT FORM

ViiVConnect

Patient First Name | MI | Patient Last Name | DOB mm/dd/yyyy

List all current medications, over-the-counter medications, and supplements | List all known drug allergies

☐ Check box if list is attached ☐ Check box if none ☐ Check box if none

❷ Oral Prescription Information

Complete this section to get your Patient started on the oral lead-in. If your state restricts the use of this form to prescribe, or if this form does not meet your requirements to prescribe, please attach a prescription to this form. Prescribers may need to submit an electronic prescription to the specialty pharmacy.

Prescription / Schedule	Medication	Quantity	Refills	Directions
☐ Oral Lead-in (Dispensed by TheraCom)	cabotegravir 30-mg tablet	30 tablets	None	Take 1 tablet by mouth daily
	rilpivirine 25-mg tablet	30 tablets	None	Take 1 tablet by mouth daily

Ship oral medications to: ☐ Prescriber's Office ☐ Patient's Home Address ☐ Other (Please complete below)

• Street Address | City | State | ZIP Code

https://www.viivconnect.com/content/dam/cf-viiv/viiv-connect/master/pdf/CABENUVA_Enrollment_Form.pdf

AETC Southeast

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Coverage Determination

The information contained in this report was obtained verbally from the patient's insurer. Neither ViiVConnect nor ViiV Healthcare Company guarantee or provide any explicit or implicit warranty of coding, coverage, or reimbursement. Coding, coverage, and reimbursement policies may vary considerably by payer, patient, and setting of care. Actual coverage and reimbursement decisions are made by individual payers following the receipt of claims.

	Buy & Bill Acquisition	Specialty Pharmacy Acquisition: Medical Benefit	Specialty Pharmacy Acquisition: Pharmacy Benefit
Provider's Network Status:	In Network	In Network	
Coverage:	Covered	Not Covered	Not Covered
Coverage Outcome:	No Restrictions	Does Not Meet Medical Criteria	Specific Exclusion
Deductible:	$233.00		
Deductible Met:	$0.00		
Out-of-pocket Maximum:			
Out-of-pocket Maximum Met:			
Patient Cost-share:	20%		
Explanation Summary:	Benefits for Cabenuva, administration are covered with $233 deductible ($0 met) and once met the patient is responsible for 20% coinsurance.	Access for the Specialty Pharmacy under the Medical Benefit is not available for this Insurance Provider. It is Mandatory that the provider Buy & Bill	CABENUVA is not covered due to Specific Drug Exclusion. CABENUVA not listed on Formulary. There is currently no option for a Formulary Exception or Prior Authorization.

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Optimizing Therapy in Setting of Virologic Suppression

Management of the Treatment-Experienced Patient

Updated: Jun. 03, 2021
Reviewed: Jun. 03, 2021

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

Panel's Recommendations for Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/optimizing-antiretroviral-therapy-setting-virologic-suppression?view=full

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Optimizing Therapy in Setting of Virologic Suppression

- Adverse events, drug interactions, pill burden, pregnancy, cost, or desire to simplify may prompt a switch
- Review patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results
- A long-acting ARV regimen is an option for patients who are engaged with their health care, virologically suppressed on oral therapy for 3 to 6 months, and who agree to make the frequent clinic visits needed to receive the injectable drugs

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Optimizing Therapy in Setting of Virologic Suppression

- Remember to include drugs with HBV activity (e.g., lamivudine or emtricitabine with tenofovir) in patients with HBV/HIV coinfection
- Closely monitor patients to assess tolerability, viral suppression, adherence, and safety during the first 3 months after a regimen switch

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