APRETUDE:

The most **COMPREHENSIVE** and **INCLUSIVE** participant populations in PrEP pivotal clinical trials[1,2]

Designed to include the key populations impacted by HIV-1.[1-4] Trials included cisgender men and transgender women who have sex with men and cisgender women, with the majority under age 30. In the US, trials included Black/African American and Latinx people.[1]

Apretude
cabotegravir 200 mg/mL
extended-release injectable suspension
for PrEP pre-exposure prophylaxis

INDICATION

APRETUDE is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF APRETUDE FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED HIV-1 INFECTION

Individuals must be tested for HIV-1 infection prior to initiating APRETUDE or oral cabotegravir, and with each subsequent injection of APRETUDE, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of APRETUDE by individuals with undiagnosed HIV-1 infection. Do not initiate APRETUDE for HIV-1 PrEP unless negative infection status is confirmed. Individuals who become infected with HIV-1 while receiving APRETUDE for PrEP must transition to a complete HIV-1 treatment regimen.

Please see additional Important Safety Information throughout. Please click for full Prescribing Information, including Boxed Warning, for APRETUDE.

PrEP=pre-exposure prophylaxis.

Pivotal trial design and endpoints

THE PrEP TRIALS SHOWN HAD VARYING TRIAL DESIGNS AND ENDPOINTS. PRODUCT COMPARISONS SHOULD NOT BE MADE BASED ON THESE DATA. TRIAL INFORMATION PRESENTED THROUGHOUT THIS BROCHURE IS NOT INTENDED TO MAKE ANY COMPARATIVE REPRESENTATION ABOUT PrEP AGENT EFFICACY OR SAFETY.

Pivotal trials refer to the clinical studies used to support initial FDA approval for these drugs for use as PrEP. This is not a comprehensive representation of all PrEP trials.

	APRETUDE (cabotegravir)		TRUVADA (emtricitabine/tenofovir disoproxil fumarate)		DESCOVY (emtricitabine/tenofovir alafenamide)
Study name	**HPTN 083**	**HPTN 084**	iPrEx	Partners PrEP	DISCOVER Trial
Primary endpoint	**Incidence of HIV-1 infection vs TDF/FTC**		Incidence of HIV-1 infection[5]	Seroconversion of HIV-negative partner[6]	Incidence of HIV-1 infection[7]
Comparator	**TDF/FTC**		Placebo[5]	TDF/FTC, TDF,* or placebo[5]	TDF/FTC[7]

*TDF is not approved for PrEP as a stand-alone agent.[8]
FDA=US Food and Drug Administration; HPTN=HIV Prevention Trials Network; TDF=tenofovir disoproxil fumarate; TDF/FTC=tenofovir disoproxil fumarate/emtricitabine.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- Do not use APRETUDE in individuals:
  - with unknown or positive HIV-1 status
  - with previous hypersensitivity reaction to cabotegravir
  - receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, and rifapentine

WARNINGS AND PRECAUTIONS

Comprehensive Management to Reduce the Risk of HIV-1 Infection:

- Use APRETUDE as part of a comprehensive prevention strategy, including adherence to the administration schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs). APRETUDE is not always effective in preventing HIV-1 acquisition. Risk for HIV-1 acquisition includes, but is not limited to, condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network. Inform, counsel, and support individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner[s] HIV-1 status, including viral suppression status; regular testing for STIs)

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Continue reading for a detailed comparison of the populations in each trial

These trials had different population breakdowns for...

1 Gender and Sexuality[1,2]

2 Race and Ethnicity[1,2]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Comprehensive Management to Reduce the Risk of HIV-1 Infection: (cont'd)

- Use APRETUDE only in individuals confirmed to be HIV-1 negative. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only APRETUDE, because APRETUDE alone does not constitute a complete regimen for HIV-1 treatment. Prior to initiating APRETUDE, ask seronegative individuals about recent (in past month) potential exposure events and evaluate for current or recent signs or symptoms consistent with acute HIV-1 infection (e.g., fever, fatigue, myalgia, skin rash). If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute HIV-1 infection
- When using APRETUDE, HIV-1 testing should be repeated prior to each injection and upon diagnosis of any other STIs
- Additional HIV testing to determine HIV status is needed if an HIV-1 test indicates possible HIV-1 infection or if symptoms consistent with acute HIV-1 infection develop following an exposure event. If HIV-1 infection is confirmed, then transition the individual to a complete HIV-1 treatment

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A deeper dive into study characteristics

COMPREHENSIVE

Among these 5 trials, HPTN 084 was the only trial conducted exclusively in cisgender women

	APRETUDE (cabotegravir)		TRUVADA (emtricitabine/tenofovir disoproxil fumarate)		DESCOVY (emtricitabine/tenofovir alafenamide)
Study name	**HPTN 083***	**HPTN 084**	iPrEx	Partners PrEP	DISCOVER Trial
N value	**4566**	**3224**	2499[5]	4758[5]	5335[7]
n values	**APRETUDE: 2281** **TDF/FTC: 2285**	**APRETUDE: 1614** **TDF/FTC: 1610**	TRUVADA: 1251[5] Placebo: 1248[5]	TRUVADA: 1583[5] TDF†: 1589[5] Placebo: 1586[5]	DESCOVY: 2670[7] TDF/FTC: 2665[7]
Participants studied	**MSM and TGW who have sex with men**	**Cisgender women aged 18-45 years[2]**	MSM and TGW who have sex with men[5]	Adult heterosexual couples[6,10]	MSM and TGW who have sex with men[7]
Trial locations	**43 sites around the world, including the US[1]**	**20 sites around sub-Saharan Africa[2]**	Peru, Ecuador, South Africa, Brazil, Thailand, and the US[9]	Kenya, Uganda[5]	US, Canada, United Kingdom, and Europe[11]

*In HPTN 083, trial sites were encouraged to target the most at-risk populations (<30 years, Black MSM) with a recruitment goal of 50% in the US sites. The study also aimed to enroll 10% TGW.[12]
†TDF is not approved for PrEP as a stand-alone agent.[8]
MSM=men who have sex with men; TGW=transgender women.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Comprehensive Management to Reduce the Risk of HIV-1 Infection: (cont'd)

- Counsel HIV-1 uninfected individuals to strictly adhere to the recommended dosing and testing schedule for APRETUDE

Potential Risk of Resistance with APRETUDE:

- There is a potential risk of developing resistance to APRETUDE if an individual acquires HIV-1 either before, while taking, or following discontinuation of APRETUDE. To minimize this risk, it is essential to clinically reassess individuals for risk of HIV-1 acquisition and to test before each injection to confirm HIV-1–negative status. Individuals who are confirmed to have HIV-1 infection must transition to a complete HIV-1 treatment. If individuals at continuing risk of HIV-1 acquisition discontinue APRETUDE, alternative forms of PrEP should be considered and initiated within 2 months of the final injection of APRETUDE

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A deeper dive into study characteristics (cont'd)

DIVERSE

Participants in the APRETUDE trials were closely aligned with the populations at risk for new HIV diagnoses[1-4]

	APRETUDE (cabotegravir)		TRUVADA (emtricitabine/tenofovir disoproxil fumarate)		DESCOVY (emtricitabine/tenofovir alafenamide)
Study name	**HPTN 083**	**HPTN 084**	iPrEx	Partners PrEP	DISCOVER Trial
N value	**4566**	**3224**	2499[5]	4758[5]	5335[7]
Race and ethnicity (%)	**Black: 50[1]* Non-Black: 50[1]* Latinx: 18[1]* (US sites only)**	**Black African: 97[2]**	Hispanic/Latinx: 72[5] White: 18[5] Black: 9[5] Asian: 5[5]	Not reported (conducted in Kenya and Uganda)[5]	White: 84[7] Hispanic/Latinx: 24[7] Black/Mixed Black: 9[7] Asian: 4[7]
Gender and sexuality (%)	**MSM: 87[1] TGW who have sex with men: 13[1] Preferred not to answer: 0.1[1]**	**Cisgender women: >99**	Assigned cis male sex at birth, identify as transgender: 12[9,13] Assigned cis male sex at birth, identify as female: 1[9,13] Assigned cis male sex at birth, identify as male: 87[9,13]	Among the sero-discordant couples, 62% of the negative partners were male and 38% were female[6]	Cisgender men: 99[7] TGW: 1[7]
Median age (years)	**26**	**25**	27[5]	33 (HIV-negative partner)[10]	34[7]

*US sites only.[1]

PARTICIPANTS IN THE APRETUDE STUDIES ARE AMONG THE MOST DIVERSE IN PrEP TRIALS TO DATE

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Long-Acting Properties and Potential Associated Risks with APRETUDE:

- Residual concentrations of cabotegravir may remain in the systemic circulation of individuals for prolonged periods (up to 12 months or longer). Take the prolonged-release characteristics of cabotegravir into consideration and carefully select individuals who agree to the required every-2-month injection dosing schedule because non-adherence or missed doses could lead to HIV-1 acquisition and development of resistance

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IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity Reactions:

- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with APRETUDE
- Discontinue APRETUDE immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated

Hepatotoxicity:

- Hepatotoxicity has been reported in a limited number of individuals receiving cabotegravir with or without known pre-existing hepatic disease or identifiable risk factors
- Clinical and laboratory monitoring should be considered and APRETUDE should be discontinued if hepatotoxicity is suspected and individuals managed as clinically indicated

Depressive Disorders:

- Depressive disorders (including depression, depressed mood, major depression, persistent depressive disorder, suicidal ideation or attempt) have been reported with APRETUDE
- Promptly evaluate patients with depressive symptoms

Risk of Reduced Drug Concentration of APRETUDE Due to Drug Interactions:

- The concomitant use of APRETUDE and other drugs may result in reduced drug concentration of APRETUDE
- Refer to the full Prescribing Information for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations. Consider the potential for drug interactions prior to and during use of, and after discontinuation of APRETUDE; review concomitant medications during use of APRETUDE

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥1%, all grades) with APRETUDE were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection.

DRUG INTERACTIONS

- Refer to the full Prescribing Information for important drug interactions with APRETUDE
- Drugs that induce UGT1A1 may significantly decrease the plasma concentrations of cabotegravir

USE IN SPECIFIC POPULATIONS

- **Lactation:** Assess the benefit-risk of using APRETUDE to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation
- **Pediatrics:** Not recommended in individuals weighing less than 35 kg

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References: 1. Landovitz RJ, Donnell D, Clement ME, et al; HPTN 083 Study Team. Cabotegravir for HIV prevention in cisgender men and transgender women. *N Engl J Med.* 2021;385(7):595-608. doi:10.1056/NEJMoa2101016 **2.** Delany-Moretlwe S, Hughes JP, Bock P, et al; HPTN 084 study group. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. *Lancet.* 2022;399(10337):1779-1789. doi:10.1016/S0140-6736(22)00538-4 **3.** HIV diagnoses. Centers for Disease Control and Prevention. Updated October 28, 2022. Accessed January 4, 2023. https://www.cdc.gov/hiv/statistics/overview/in-us/diagnoses.html **4.** *In Danger: Global AIDS Update 2022.* Joint United Nations Programme on HIV/AIDS (UNAIDS); 2022. Accessed January 5, 2023. https://www.unaids.org/en/resources/documents/2022/in-danger-global-aids-update **5.** Truvada. Prescribing information. Gilead Sciences, Inc.; 2020. **6.** Baeten JM, Donnell D, Ndase P, et al; Partners PrEP Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med.* 2012;367(5):399-410. doi:10.1056/NEJMoa1108524 **7.** Descovy. Prescribing information. Gilead Sciences, Inc.; 2022. **8.** Viread. Prescribing information. Gilead Sciences, Inc.; 2019. **9.** Grant RM, Lama JR, Anderson PL, et al; iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med.* 2010;363(27):2587-2599. doi:10.1056/NEJMoa1011205 **10.** Mujugira A, Baeten JM, Donnell D, et al; Partners PrEP Study Team. Characteristics of HIV-1 serodiscordant couples enrolled in a clinical trial of antiretroviral pre-exposure prophylaxis for HIV-1 prevention. *PLoS One.* 2011;6(10):e25828. doi:10.1371/journal.pone.0025828 **11.** Mayer KH, Molina J-M, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomized, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet.* 2020;396(10246): 239-254. doi:10.1016/S0140-6736(20)31065-5 **12.** HIV Prevention Trials Network. HPTN 083: A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), for Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men (protocol version 4.0; February 10, 2021). Accessed January 26, 2023. https://www.hptn.org/research/studies/hptn083#views-field-field-public-files **13.** Deutsch MB, Glidden DV, Sevelius J, et al; iPrEx investigators. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. *Lancet HIV.* 2015;2(12): e512-e519. doi:10.1016/S2352-3018(15)00206-4

What could APRETUDE mean for your patients? See the data

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