Apretude™ (cabotegravir) – New drug approval

- On December 20, 2021, the FDA announced the approval of ViiV Healthcare's Apretude (cabotegravir), in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired human immunodeficiency virus (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.
- According to the Centers for Disease Control and Prevention (CDC), about 25% of the 1.2 million people for whom PrEP is recommended were prescribed it, compared to only about 3% in 2015.
- Apretude is the first long-acting injectable PrEP option for reducing the risk of sexually acquired HIV-1.
    - Other drugs approved for PrEP include oral Truvada® (emtricitabine/tenofovir disoproxil fumarate) and oral Descovy® (emtricitabine/tenofovir alafenamide). Additionally, generics to Truvada are also available.
- Cabotegravir was previously approved, in combination with rilpivirine, under the brand name Cabenuva®. Cabenuva is approved for treatment of HIV-1 infection.
- The efficacy of Apretude was established in two randomized, double-blind, controlled studies. The first study, HPTN 083, was a non-inferiority trial in 4,566 HIV-1 uninfected men and transgender women who have sex with men and have evidence of high-risk behavior for HIV-1 infection. Patients received either Apretude or Truvada up to week 153. The primary endpoint was the rate of incident HIV-1 infections (corrected for early stopping).
    - The primary analysis demonstrated the superiority of Apretude vs. Truvada with a 66% reduction in the risk of acquiring HIV-1 infection (hazard ratio [HR] 0.34, 95% CI: 0.18, 0.62).
    - Following the primary analysis, extended retrospective virologic testing was performed to better characterize the timing of HIV-1 infections. As a result, 1 of the 13 HIV-1 incident infections in participants receiving Apretude was determined to be a prevalent infection which then yielded a 69% reduction in the risk of HIV-1 incidence infection. After readjudication of the endpoints, the incidence rate of HIV-1 per 100 person-years was 0.37 with Apretude vs. 1.22 with Truvada (HR 0.31, 95% CI: 0.16, 0.58; superiority p value = 0.0003).
- The second study, HPTN 084, was a superiority study in 3,224 HIV-1 uninfected cisgender women at risk of acquiring HIV-1. Patients received Apretude or Truvada up to week 153. The primary endpoint was the rate of incident HIV-1 infections (corrected for early stopping).
    - The primary analysis demonstrated the superiority of Apretude vs. Truvada with an 88% reduction in the risk of acquiring incident HIV-1 infection (HR 0.12, 95% CI: 0.05, 0.31).
    - Like the previous study, further testing revealed 1 of the infections on Apretude to be prevalent then yielding a 90% reduction in the risk of HIV-1 incident infection relative to Truvada. After readjudication of the endpoints, the incidence rate of HIV-1 per 100 person-years was 0.15 with Apretude vs. 1.85 with Truvada (HR 0.10, 95% CI: 0.04, 0.27; superiority p value < 0.0001).
- Apretude carries a boxed warning for risk of drug resistance with use of Apretude for HIV-1 PrEP in undiagnosed HIV-1 infection.

Continued . . .

- Apretude is contraindicated in individuals:
    - With unknown or positive HIV-1 status
    - With previous hypersensitivity rection to cabotegravir
    - Receiving coadministered drugs for which significant decreases in cabotegravir plasma concentrations may occur due to UGT1A1
- Additional warnings and precautions for Apretude include potential risk of resistance with Apretude, long-acting properties and potential associated risks with Apretude, hypersensitivity reactions, hepatotoxicity, depressive disorders, and risk of reduced drug concentration of Apretude due to drug interactions.
- The most common adverse reactions (≥ 1%) with Apretude use 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.
- Prior to initiating Apretude, oral lead-in dosing with cabotegravir tablets (Vocabria®) may be used for approximately 1 month with the recommended dosage to assess the tolerability of Apretude. Alternatively, a healthcare provider and individual may proceed directly to injection of Apretude without the use of an oral lead-in.
- If an oral lead-in is used, initiation injections should be administered on the last day of oral lead-in or within 3 days thereafter. The recommended initiation injection doses of Apretude in individuals is a single 600 mg intramuscular (IM) injection given 1 month apart for 2 consecutive months. Individuals may be given the second Apretude initiation injection up to 7 days before or after the date the individual is scheduled to receive the injections.
    - After the 2 initiation injection doses given consecutively 1 month apart, the recommended continuation injection dose of Apretude is a single 600 mg IM injection every 2 months. Individuals may be given Apretude up to 7 days before or after the date the individual is scheduled to receive the injections.
- Apretude must be administered by a healthcare provider by gluteal IM injection.
- 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.
- ViiV Healthcare plans to launch Apretude in early 2022. Apretude will be available as a 600 mg/3 mL injectable suspension in a single-dose vial.