

Company

ViiV Healthcare

Drug or Device Name

Apretude (cabotegravir extended-release injectable suspension)

Category

Pharmaceutical

Compound/Technical Name

Cabotegravir extended-release injectable suspension

Trade Name

APRETUDE

Date of Approval

12/20/2021

Therapeutic Categories

Antivirals - Integrase strand transfer inhibitor (INSTI)

Indications

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.

Background

HIV continues to be a global health crisis with more than 37 million people currently living with HIV. In the U.S. alone, an estimated 1.2 million people are living with HIV, and almost 37,000 new HIV diagnoses are made each year. As we look toward the future, PrEP (or pre-exposure prophylaxis) has a central role to play in helping to reduce new HIV cases and the impact HIV has on millions of lives each year. PrEP is proven to prevent HIV acquisition and is an essential tool to help end the HIV epidemic. Yet, the unfortunate reality is that, as of 2019, the U.S. Department of Health & Human Services estimated that less than 25% of people in the US who could benefit from PrEP were currently taking it. Furthermore, despite the widespread availability of daily oral PrEP, the only significant decline in new HIV diagnoses has occurred in white men who have sex with men. Broad uptake of PrEP—especially among Black and Latinx communities who are disproportionately impacted in the US and have benefited the least from the advances in HIV prevention—has been limited by a range of factors including stigma, confusion about the populations for which PrEP is indicated, and challenges with adhering to a daily dosing regimen. APRETUDE (cabotegravir extended-release injectable suspension) is the first and only long-acting injectable option for HIV prevention. It has demonstrated superior efficacy for the prevention of HIV-1 infection compared to daily oral TDF/FTC tablets. APRETUDE also

significantly reduces the frequency of PrEP dosing – from 365 days to as few as six injections per year after the initiation period. FDA approval of APRETUDE offers a new approach to the prevention of HIV. For the first time, people who are vulnerable to acquiring HIV now have options beyond a daily pill.

Development

APRETUDE (cabotegravir extended-release injectable suspension) is an integrase strand transfer inhibitor (INSTI) that prevents the integration of viral RNA into host DNA and is a structural analogue of dolutegravir, which is used extensively as a component of antiviral treatment regimens for people living with HIV. Unlike other INSTIs, cabotegravir has a long biological half-life and physicochemical attributes that make it uniquely suited for development as a long-acting formulation. Early clinical trials demonstrated that cabotegravir remains in the body for up to a year or longer after a single injection, validating the concept. Proof of principle for the prevention of HIV infection was achieved through extensive collaboration with academic centers at Aaron Diamond AIDS Research Center, the U.S. Centers for Disease Control and Prevention, and the National Institute of Allergy and Infectious Diseases (NIAID). Through these collaborations, non-human primate (NHP) research demonstrated that periodic cabotegravir injections could prevent infection in both male and female NHP and provided insights on the duration of protection after the last injection. These results enabled Phase 2 studies in humans at low risk of acquiring HIV, which showed that cabotegravir was safe, well-tolerated, and confirmed the final dose schedule. Clinical demonstration of safety and efficacy in populations most at risk of acquiring HIV was performed in collaboration with the HIV Prevention Trials Network and NIAID. Two international Phase III studies of almost 8000 participants in North and South America, Asia, and Africa investigated if cabotegravir prevents HIV infection in at-risk cisgender men, transgender women, and cisgender women who have sex with men. The blinded, randomized portions of both trials were stopped early by an independent Data Safety Monitoring Board after cabotegravir long-acting for PrEP was shown to be superior to daily oral emtricitabine/tenofovir disoproxil fumarate (TDF/FTC) tablets in preventing the acquisition of HIV in study participants.

Innovation

While there have been significant advancements in antiviral treatments in recent years, it is now recognized that ending the global HIV epidemic will take a combination of both treatment and prevention. The innovation behind APRETUDE represents a ground-breaking step forward in new options for HIV prevention and PrEP. Prior to FDA approval of APRETUDE as the first and only PrEP injectable, existing options were limited to daily oral pills, which can pose a challenge for some users with issues of non-adherence and lack of persistent use. APRETUDE's every two-month injection schedule eliminates the need for a daily pill and may contribute to the mitigation of key issues related to adherence, stigma, and negotiation of HIV protection with sexual partners. It is an option that may meet the different needs, lifestyles, and circumstances of persons who are at risk of sexually acquiring HIV. For the first time ever, there are now choices in HIV PrEP; this is essential progress if we are to make inroads on ending HIV around the world. The superior efficacy observed versus daily TDF/FTC tablets also sets a new standard for future research. With proven efficacy of long-acting medicines for PrEP, APRETUDE paves the way for the research of even longer-acting medicines with profiles that may support longer dosing intervals and different routes of administration. Additionally, as continued efforts are being made to ensure clinical trials are diverse, APRETUDE established the blueprint by including some of the largest numbers of transgender women and Black MSM ever enrolled in an HIV prevention trial. As we look toward the rest of the world, cabotegravir extended-release injectable suspension is poised to bring PrEP options into communities around the world. APRETUDE's rollout in the US brings us one step closer to the shared global goal of ending the HIV epidemic.

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