



Long-Acting HIV Treatment is Now Available

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Dear Colleague,

The U.S. Food and Drug Administration (FDA) has approved [monthly](#) or [bimonthly](#) injections of Cabenuva (cabotegravir and rilpivirine) as the first long-acting formulation of medicines to treat HIV. Other formulations are in the research and approval pipeline, including longer-acting injections, patches and implants for HIV treatment and prevention. The manufacturer has published updated [prescribing information](#) for Cabenuva, and the [U.S. Department of Health and Human Services](#) and [New York State Clinical Guidelines Program](#) have published prescribing guidelines. The New York City Department of Health and Mental Hygiene provides this summary to support the effective use of long-acting HIV medicines.

Approved use: The FDA approved Cabenuva as a complete treatment regimen for adults and adolescents with HIV who:

- Are already taking antiretroviral treatment
- Are virologically suppressed (viral load \leq 50 copies/mL)
- Have no history of treatment failure or known or suspected resistance to cabotegravir (CAB, an integrase strand-transfer inhibitor) or rilpivirine (RPV, a non-nucleoside reverse-transcriptase inhibitor)
- Weigh at least 35 kilograms

Clinical guidelines discourage prescribing injectable HIV treatment for people who are pregnant or breastfeeding.

Dosing: Each dose of Cabenuva involves separate intramuscular injections of long-acting cabotegravir (CAB-LA) and long-acting rilpivirine (RPV-LA). To assess tolerability of the medicines, the regimen may begin with an optional four weeks of lead-in oral dosing of 30 milligrams (mg) CAB and 25 mg RPV. Patients can receive either monthly or bimonthly dosing. For monthly dosing, patients receive twin initiation-dose injections of 600 mg CAB-LA and 900 mg RPV-LA and monthly maintenance-dose injections of 400 mg CAB-LA and 600 mg RPV-LA. [Bimonthly dosing](#) involves initial injections of 600 mg CAB-LA and 900 mg RPV-LA and identical injections one month after the initial dose and every two months thereafter.

Safety and effectiveness: The [ATLAS](#) and [FLAIR](#) clinical trials found that monthly injections of CAB-LA + RPV-LA were noninferior to the current oral treatment regimen of virally suppressed participants. [Pooled data](#) from 16 countries involved 1182 participants, and 28% of whom were assigned female sex at birth. Among those randomized to the CAB-LA + RPV-LA arms, 93% remained virally suppressed after 48 weeks; 2% had viral load $>$ 50 copies/mL; and 5% had no virologic data after discontinuing study participation, including 4% who withdrew due to adverse events. Treatment failure and evidence of drug-resistant virus were more common among participants in Russia with HIV-1 subtype A1, which is rare in the U.S.

[Side effects](#) observed in $\geq 2\%$ of participants included injection site reactions, fever, rash, fatigue, headache, body aches, nausea, dizziness and sleep disorders. The [ATLAS-2M](#) trial found that CAB-LA + RPV-LA is just as effective when injected every two months as when injected every month, and the FDA has approved this dosing schedule.

Long-lasting medicines: Injectable medicines linger in the body, which provides both benefit and a cause for concern. Long-acting HIV treatment may appeal to patients who do not want to take a daily pill or have difficulty consistently taking medicines. However, declining but persistent drug levels in people who miss injections can lead to the development of resistant virus, requiring providers and their public health partners to develop even more effective protocols to retain people in care.

Missed doses: Clinic staff must work closely with patients to help them avoid missed doses. If a patient plans to delay scheduled injections by more than seven days, prescribe daily oral cabotegravir and rilpivirine or another approved antiretroviral regimen to replace injections for up to two months. [Prescribing information](#) describes how to resume long-acting medicines if a patient misses injections and does not take oral replacement therapy. Monitoring early clinical experience [may help clarify](#) how effective Cabenuva remains after a person misses scheduled doses, which will help ensure that developed resistance and virologic failure remain rare. [U.S. guidelines](#) recommend providers evaluate whether people who miss doses beyond the seven-day window are appropriate candidates for continued injectable therapy.

Long-acting treatment for people with unsuppressed HIV: The FDA has not yet approved Cabenuva for people with unsuppressed HIV (viral load > 50 copies/mL) or a history of treatment failure, who may particularly benefit from an alternative to daily pill-taking. The [LATITUDE](#) study is evaluating the safety and effectiveness of injectable Cabenuva for people who have unsuppressed HIV or have fallen out of care.

Benefits and challenges for people with HIV: In the FLAIR and ATLAS trials, [98% of participants](#) who received CAB-LA + RPV-LA preferred the long-acting regimen. Studies on the acceptability of long-acting treatment among [Cabenuva trial participants](#) and [women taking daily HIV medicines](#) found that people with HIV appreciated the convenience of not having to take a daily pill but worried about managing more frequent clinic visits. Many anticipated emotional benefits from avoiding a daily reminder of living with HIV and situations in which they may have to disclose their HIV status. In the second study, most women preferred long-acting injections to daily pills; many perceived injections to be more effective and convenient, though some were reluctant to switch to a new regimen from one they knew was working.

Administering injections: New York State guidelines [describe how clinics can prepare](#) to provide injectable HIV treatment. As currently approved, a health care provider must administer Cabenuva monthly or bimonthly, requiring at least six patient visits a year, while many patients now see an HIV care provider twice a year for routine monitoring. Clinics [may face higher procurement costs](#) if they must pay for injections before administering them and must keep a stock on hand for patients who need immediate injections after missing scheduled doses. Cabenuva must be stored at 2 to 8 degrees C.

Access and cost: In New York State, Medicaid will reimburse for Cabenuva, and the New York State Department of Health [HIV Uninsured Care Program](#) covers the injections if prescribed through approved specialty pharmacies and shipped to the providing clinic, or if clinics procure their own inventory. The manufacturer ViiV Healthcare has listed [Cabenuva](#) for U.S. distribution at a [wholesale acquisition cost](#) higher than for most oral HIV medicines: \$5,940 for initiation-dose injections and \$3,960 for subsequent monthly doses. Private insurers may require prior authorization for people whose HIV is already controlled with less-expensive medicines, and patients could face higher out-of-pocket costs with Cabenuva than with their current oral HIV medicines. ViiV provides [financial assistance](#) to eligible patients with limited insurance coverage. As other formulations enter the market, the cost of long-acting HIV treatment is likely to decline, and access is likely to increase.

Equitable access to long-acting HIV medicines: Inform your patients that long-acting options for both HIV treatment and [pre-exposure prophylaxis \(PrEP\)](#) are now available, particularly patients from communities with the highest HIV burden. In 2019, 83% of new HIV diagnoses in [New York City](#) were among Black and Latino people, and HIV viral suppression was lower among Black, Latino, Native American, multiracial, transgender and younger people. [Ending the HIV epidemic](#) requires we work together to create broad access to the full array of effective HIV medicines and develop supports that ensure successful HIV outcomes for people experiencing poverty, racism, sexism, homophobia, transphobia, mental health issues or other social and structural barriers to care.

Sincerely,



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