



# Sunlenca Pills Can Bridge Gaps When Injections Are Missed

People who used once-weekly oral lenacapavir maintained viral suppression when injections were interrupted.

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People who used Sunlenca (lenacapavir) pills as a “bridging” strategy when injections were temporarily unavailable were able to maintain viral suppression with no safety concerns, according to study results presented at the [International AIDS Society Conference on HIV Science](#) (#IAS2023) in Brisbane, Australia.

“In people who are receiving subcutaneous lenacapavir, sometimes treatment has to be interrupted. We found that oral bridging with lenacapavir in those individuals—including those who have multidrug-resistant HIV—not only is feasible but is also effective,” said presenter Jean-Michel Molina, MD, of the University of Paris Cité. Given these findings, he advised, “People on a long-acting regimen should keep some oral drugs in case they cannot get their injection at the right time.”

Long-acting injectable antiretrovirals, like Sunlenca, which is administered every six months, can offer greater convenience than daily pills, potentially leading to better adherence. But when medications are taken less frequently, it is even more critical that every dose be taken on time and that none are missed. This could happen, for example, if a person is traveling and does not have access to a provider who can administer an injection on schedule.

Gilead Sciences’ Sunlenca, the first HIV capsid inhibitor, has a long half-life in the body, allowing it to be administered by subcutaneous injection just twice a year. It also comes in an oral formulation that is used as an initial loading dose before starting injections and can be used for temporary bridging if injections must be interrupted.

Sunlenca works differently than older antiretrovirals and remains active against HIV that has developed resistance to other drugs. In December 2022, the Food and Drug Administration (FDA) [approved Sunlenca](#) for treatment-experienced people with multidrug-resistant HIV who cannot otherwise construct a fully suppressive regimen.

The approval was supported by results from the Phase II/III CAPELLA trial, which is evaluating Sunlenca for highly treatment-experienced people. At study entry, participants had a median age

of 52 years, had been living with HIV for 24 years on average and had used a median of 11 drugs. A majority had advanced immune suppression with a CD4 count below 200. An initial cohort of 36 participants was randomly assigned to add either Sunlenca pills or placebo pills to their current failing regimen for 14 days, at which point everyone was offered Sunlenca injections administered every six months plus an optimized background regimen. Another 36 people in a nonrandomized cohort received Sunlenca shots plus an optimized background regimen from the outset, after an oral loading dose.

At the 2022 Conference on Retroviruses and Opportunistic Infections (CROI), [researchers reported](#) that after 52 weeks of treatment—meaning two Sunlenca injections—83% of people in the randomized cohort had a viral load below 50. This rose to 94% for those with two or more active drugs in their background regimen but fell to 67% for those with none.

Sunlenca also shows promise for first-line treatment, though it is not yet approved for this indication. The Phase II CALIBRATE trial enrolled 182 previously untreated people with a median age of 29 years. They were randomly assigned to receive one of two regimens containing Sunlenca injections every six months plus one other antiretroviral, an all-oral regimen containing Sunlenca pills plus two other antiretrovirals or a standard three-drug single-tablet regimen. [As reported in The Lancet HIV](#), viral suppression rates after a year of treatment were comparable across all four groups, ranging from 85% to 92%.

In December 2021, the FDA [put a clinical hold](#) on Sunlenca trials due to safety concerns about the glass vials used for the injectable formulation. [The hold was lifted](#) in May 2022, after Gilead switched to a different type of glass. During the hold, CAPELLA and CALIBRATE participants were unable to receive Sunlenca injections and instead took Sunlenca pills once weekly, giving researchers an unplanned opportunity to evaluate the oral bridging strategy.

Among the 72 participants in CAPELLA, 57 used oral bridging, as did 82 of the 105 CALIBRATE participants in the two injectable Sunlenca arms. (Some people did not need oral bridging because their next injection was not scheduled during the hold period.) The median time on oral Sunlenca was 18 weeks, but some took the pills for up to 30 weeks. According to pill counts, most people achieved at least 95% adherence during this time.

All of the CALIBRATE participants maintained viral suppression throughout the oral bridging period, as did most CAPELLA participants who had an undetectable viral load when they switched to the pills. Of the 11 people who had a detectable viral load at the time of the switch, three achieved viral suppression while taking the pills, and none saw a notable rise in viral load. CD4 counts remained stable or increased during this period.

However, one CAPELLA participant who had an undetectable viral load at the time of the switch missed two doses of oral Sunlenca and experienced viral rebound (above 50 copies). This person developed a lenacapavir resistance-associated mutation, but nonetheless regained viral suppression with no change to their background regimen after resuming Sunlenca injections. This could suggest that the resistance mutation impaired viral fitness, Molina said.

Sunlenca pills were generally safe and well tolerated. Overall, side effects during the oral bridging period were similar to those seen with Sunlenca shots but without injection site reactions. However, a few participants experienced treatment-related diarrhea.

In a related analysis, Gilead scientists assessed pharmacokinetics during the oral bridging period. In both CAPELLA and CALIBRATE participants, lenacapavir concentrations remained above target levels previously found to be effective (four times the in vitro 95% effective concentration) until injections were resumed.

Taken together, these studies show that Sunlenca pills are a good substitute if people must miss an injection. Commenting on the findings, Anton Pozniak, MD, of Chelsea and Westminster Hospital in London, suggested that it would be a good idea for people who use long-acting injectables to keep a supply of the oral version on hand “because life’s not perfect.”

This strategy is already used for people who know they will miss a scheduled dose of [Cabenuva \(injectable cabotegravir and rilpivirine\)](#), which is administered every month or every other month and is currently the longest-acting complete antiretroviral regimen. In that case, two separate pills (branded as Vocabria and Edurant) are taken once daily until injections resume. Sunlenca pills only need to be taken once weekly.

While Sunlenca is the longest-acting antiretroviral medication approved to date, there are no other drugs that can be taken with it at such a long interval. However, at this year’s CROI, [researchers reported](#) that Sunlenca injections plus two broadly neutralizing antibodies have the potential to be a combined for a complete twice-yearly regimen.

Click here to read the [efficacy abstract](#) and the [pharmacokinetics abstract](#).

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