Weekly Oral HIV Treatment Matches Daily Pills

The once-weekly islatravir/lenacapavir combination pill kept viral load suppressed in people switching from daily treatment.

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A once-weekly single-tablet regimen containing islatravir and lenacapavir maintained viral suppression in people with HIV who switched from a standard oral combination, according to an announcement from Gilead Sciences and Merck. If approved, this would be the first oral treatment that does not require daily pills.

Modern antiretroviral therapy is highly effective and generally well tolerated, so the choice of a regimen often comes down to ease of use, and regimens that can be taken less frequently are the future of HIV treatment. While long-acting injectables are the answer for some people, others find it inconvenient to schedule injection appointments—or they simply don't want shots.

"Long-acting oral therapies represent a new wave of transformational innovation in HIV drug development, with the potential to reshape the landscape of care," Gilead senior vice president of clinical development Jared Baeten, MD, PhD, said in the news release. "Innovative oral HIV treatment options that allow for less frequent dosing may make a meaningful difference in the lives of people living with the virus, potentially offering more flexibility and discretion."

Lenacapavir is Gilead's first-in-class HIV capsid inhibitor. A twice-yearly injectable formulation, sold as Sunlenca, was approved in 2022 for people with multidrug-resistant HIV. Injectable lenacapavir alone, sold as Yeztugo, was approved for pre-exposure prophylaxis (PrEP) last June. Lenacapavir is also available in a pill, which is used as part of an initial loading dose before injections.

Merck's islatravir is a nucleoside reverse transcriptase translocation inhibitor, which interferes with the HIV enzyme in a different way from familiar nucleoside/nucleotide reverse transcriptase inhibitors. A once-daily pill combining islatravir and Merck's NNRTI doravirine, sold as Idvynso, was approved in April.

Phase II clinical trial results, published in Annals of Internal Medicine last year, showed that most people who switched from Gilead's Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine) to separate islatravir and lenacapavir pills taken once weekly maintained an undetectable viral load (below 50) at 48 weeks. Follow-up data presented at the 2025 European AIDS Conference showed

that islatravir plus lenacapavir pills maintained viral suppression for two years.

This set the stage for the Phase III ISLEND-1 and ISLEND-2 trials, testing a fixed-dose combination pill containing 2 milligrams of islatravir and 300 mg of lenacapavir. This week, Gilead and Merck announced top-line findings from these trials, showing that the islatravir/lenacapavir single-tablet regimen is safe and effective.

In the double-blind ISLEND-1 trial (NCT06630286), participants with viral suppression on Biktarvy were randomly assigned to switch to the islatravir/lenacapavir combo pill or stay on their current regimen. At 48 weeks, a similar proportion of people maintained an undetectable viral load in both groups, showing that islatravir/lenacapavir was statistically non-inferior to Biktarvy and meeting the trial's primary endpoint.

In the open-label ISLEND-2 trial (NCT06630299), people with viral suppression on various standard-of-care daily oral combinations were randomized to switch to islatravir/lenacapavir or stay on their current treatment. Here, too, the new single-tablet regimen was found to be non-inferior to standard therapy, meeting the study's primary endpoint.

In both trials, the safety profile of islatravir/lenacapavir was generally comparable to that of the comparison regimens, with no new safety concerns identified, according to the announcement.

Importantly, people taking islatravir/lenacapavir did not experience decreases in their white blood cell counts. Development of islatravir hit a snag in 2021 when some people in earlier trials saw a decline in their CD4 T-cell or total lymphocyte counts, but Merck scientists determined that the doses used in those studies were too high. This side effect has not been seen at lower doses like the 2 mg in the new combo pill.

This week's announcement did not include details about the study populations, virological outcomes or tolerability, which will be presented at a future scientific conference. Gilead and Merck said they plan to submit the ISLEND data to the Food and Drug Administration and regulatory authorities in other countries.

"These results underscore the shared focus and commitment that we and our collaborators at Gilead have on continuing research to help people living with HIV," said Merck chief medical officer Eliav Barr, MD. "By advancing this investigational novel once-weekly oral regimen of islatravir and lenacapavir, we aim to bring forward a new long-acting oral option that, if approved, would represent the first of its kind with less frequent dosing and further expand options for people living with HIV."

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