March 2025

LENACAPAVIR

HIV PrEP

Gilead

DISEASE BURDEN

In 2023, 39.9 million people globally were living with HIV, 1.3 million people became newly infected, and 630,000 people died of HIV, most of which occurred in LMICs.

CLINICAL RELEVANCE

Lenacapavir, a novel long-acting capsid inhibitor for HIV prevention, is developed as a twice-yearly subcutaneous injection following an initial oral loading. Phase III trials (PURPOSE 1 & 2) showed high effectiveness with mild injection site reactions. Lenacapavir PrEP injections are also safe and effective in adolescents, expanding the product's potential impact. New intramuscular formulations with potential for a once-yearly administration for HIV prevention are investigated. A future shift to yearly dosing could improve adherence and accessibility, especially in resource-limited settings.

INTELLECTUAL PROPERTY LANDSCAPE

Lenacapavir primary patents have been filed or granted in several LMICs and are expected to expire between 2034 and 2037. Gilead also holds secondary patents that may provide exclusivity until 2038 in many LMICs. Gilead has signed bilateral licence agreements with six generic manufacturers, allowing for sales in 120 countries. LMICs beyond the licence territory would likely not have access to the generic products. It is unclear whether the new intramuscular yearly formulation is covered by the current patents and bilateral agreements.

SERVICE DELIVERY ENABLERS

Lenacapavir for PrEP does not require a companion drug. While long-acting injectable lenacapavir may warrant higher adherence, health system requirements for delivery might be higher compared to once-daily oral PrEP options that can be handed to clients for several months supply.

REGULATORY

Lenacapavir for PrEP is not approved by regulatory authorities yet. Submissions for approval were filed to EMA and USFDA. Bioequivalence studies are necessary for oral solid formulations. Biowaivers will not be an option for oral solid formulations. There is a possibility of biowaiver for the injectable product.

MANUFACTURING

Assuming the formulation is the same as the approved treatment: a spray-drying process is adopted for mandatory loading dose oral formulation. Injectable product is a standard solution, terminally sterilised. Standard excipients are used. The injectable formulation contains a specialised syringe along with vials. Shelf life is two years at room temperature for the tablets and the injectable product.

MARKET

Gilead has indicated that it will prioritise registration in 18 countries among those covered in the bilateral licensing agreements. Additionally, the company announced that it will supply all required lenacapavir at "no profit" until generic versions of lenacapavir are available. No price is announced yet.

EMA: The European Medicines Agency; HIV: Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **PrEP**: Pre-Exposure Prophylaxis ; **USFDA**: The United States Food and Drug Administration

LENACAPAVIR

HIV TREATMENT

Gilead

DISEASE BURDEN

In 2023, 39.9 million people globally were living with HIV, 1.3 million people became newly infected, and 630,000 people died of HIV, most of which occurred in LMICs.

CLINICAL RELEVANCE

Lenacapavir is approved as a sub-cutaneous injection every 6 months, for treating HIV-1 in heavily treatment-experienced (HTE) adults with failing regimens due to resistance or intolerance. Lenacapavir 6-monthly sub-cutaneous injections are also considered for combination with other agents to constitute fully injectable HIV treatment regimens. It is investigated in combination with synchronous administration of broadly neutralizing antibodies (bNAbs) and it is also considered in a regimen with cabotegravir. Ongoing phase III trials (ISLEND-1 & 2) are evaluating weekly oral treatment for virologically suppressed individuals, with a fixed-dose combination of islatravir and lenacapavir. Lenacapavir oral version is also investigated for use with once-daily bictegravir for HIV treatment.

INTELLECTUAL PROPERTY LANDSCAPE

Lenacapavir primary patents have been filed or granted in several LMICs and are expected to expire between 2034 and 2037. Gilead also holds secondary patents that may provide exclusivity until 2038 in many LMICs. Gilead has signed bilateral voluntary licence agreements with six generic manufacturers, allowing for sales in 120 countries. LMICs beyond the licence territory would likely not have access to the generic products.

SERVICE DELIVERY ENABLERS

Lenacapavir's possible companion drugs for a fully long-acting regimen are still under study. While long-acting injectable lenacapavir may have advantages in terms of adherence, health system requirements for delivery might be higher compared to once-daily oral treatment options such as TLD that can be handed to people needing the treatment with a multi-month dispensing. If successful, the oral weekly lenacapavir and islatravir candidate could support decentralised care while offering a valuable option for treatment.

REGULATORY

Lenacapavir for treatment is approved by several regulatory authorities. Bioequivalence studies are necessary for oral solid formulations. Biowaivers will not be an option for oral solid formulations. There is a possibility of biowaiver for injectable products.

MANUFACTURING

A spray drying process is adopted for the oral formulation. Injectable product is a standard solution, terminally sterilized. Standard excipients are used. The injectable formulation contains a specialised syringe along with vials. Shelf life is two years at room temperature for the tablets and the injectable product.

MARKET

While lenacapavir is currently approved for HIV treatment by some major regulatory authorities for HTE adults, it is not yet registered - and is therefore not available- in LMICs. Gilead signed royalty-free voluntary licensing agreements with six generic manufacturers to increase access to lenacapavir for HIV treatment in 120 countries. The agreements do not cover a broad treatment indication. A long-acting companion injectable allowing for a fully injectable regimen would considerably increase market size.

HIV: Human immunodeficiency virus; **HTE**: heavily treatment-experienced; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **TLD**: tenofovir, lamivudine and dolutegravir