Health Technology Briefing
July 2024

Lenacapavir for preventing HIV infection

Company/Developer	Gilead Sciences Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33517	NICE ID: Not Available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Lenacapavir is in clinical development for the prevention of human immunodeficiency virus (HIV) in people who are at risk of HIV infection. HIV is a virus that damages the cells in the immune system and weakens the ability to fight everyday infections and disease. AIDS (acquired immune deficiency syndrome) is the name used to describe the potentially life-threatening infections and illnesses that happen when the immune system has been severely damaged by the HIV virus. There's currently no cure for HIV, but there are effective drug treatments that enable most people with the virus to live a long and healthy life. Pre-exposure prophylaxis (PrEP) is an antiviral therapy which when taken regularly significantly reduce the risk of the transmission of HIV during unprotected sex. Currently, the only preventative treatment available is two versions of oral medication which are taken daily or on an event-based schedule. Whilst these are highly effective at preventing HIV when taken as prescribed, they are associated with adherence issues due to the dosing schedule and the stigma around taking antiretrovirals, therefore, a long-acting form of PrEP medication is desirable.

Lenacapavir acts by interfering with the HIV's structure, thereby preventing the virus from multiplying, and reducing the amount of HIV in the body. Lenacapavir is designed to be administered twice yearly via subcutaneous injection. If licenced, twice yearly lenacapavir injections could offer an additional PrEP option to people with higher risk of HIV.

Proposed Indication

For HIV pre-exposure prophylaxis (PrEP) in people ≥16 years at risk for HIV infection.[1,2]

Technology

Description

Lenacapavir (GS-6207, Sunlenca) is a long-acting HIV-1 capsid inhibitor, with a multi-stage mechanism of action.[3] Lenacapavir belongs to a group of HIV drugs called capsid inhibitors. Capsid inhibitors interfere with HIV capsid, a protein shell that protects HIV's genetic material and enzymes needed for replication. Capsid inhibitors can disrupt HIV capsid during multiple stages of the viral life cycle. This prevents HIV from multiplying and can reduce the amount of HIV in the body.[4]

Lenacapavir is in clinical development for PrEP of HIV-1 in people at risk for HIV infection. In the phase III clinical trial (PURPOSE 2, NCT04925752), participants received a subcutaneous (SC) injection of 927mg lenacapavir administered every 26 weeks, alongside currently used PrEP emtricitabine/tenofovir disoproxil fumarate (F/TDF), and an oral tablet of 600mg lenacapavir on days 1 and 2.[1]

Key Innovation

Lenacapavir is a potential long-acting injectable HIV-1 capsid inhibitor in development for the prevention of HIV-1 infection. Unlike many antivirals that target a single stage of viral replication, lenacapavir inhibits HIV-1 at multiple stages of its lifecycle and, to date, shows no known cross-resistance to other existing drug classes.[5] Currently two types of oral medication are licensed for PrEP in the UK.[6] However, oral treatments require strict adherence to a daily or event based dosing schedules to be fully effective. This creates a need for longer acting treatments.[7,8] Evidence suggests a preference for long acting PrEP over daily oral PrEP among men in the USA.[9] Studies also highlight the stigma associated with taking preventative PrEP, as individuals are concerned about being perceived as HIV positive or facing rejection from partners.[7] Longer acting, injectable PrEP methods could help achieve the government's action plan of ending HIV transmissions by 2030 as provision of a wider choice of PrEP methods may improve uptake, acceptability, and adherence.[10]

Lenacapavir is currently approved, in combination with other antiretrovirals, for HIV treatment in persons with multidrug-resistant HIV-1 infection.[11] SC lenacapavir in combination with an optimised background regimen, including the use of other antiretroviral agents, in participants with multidrug-resistant HIV-1 has been shown to result in a high rate of virological suppression and meaningful increases in CD4 cell counts.[12] Similarly, a macaque model study has demonstrated proof of concept that lenacapavir can offer effective long-lasting HIV prophylaxis as a monotherapy.[13] If approved, lenacapavir would be the only injectable HIV-1 PrEP treatment option administered twice yearly.

Regulatory & Development Status

Lenacapavir in combination with other antiretrovirals has Marketing Authorisation in the EU/UK for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen, for oral loading prior to administration of long-acting lenacapavir injection.[12,14,15]

Lenacapavir is also in phase II and III clinical development for the treatment of HIV-1 infection.[16]

Patient Group

Disease Area and Clinical Need

HIV is a virus that damages the cells in your immune system and weakens your ability to fight everyday infections and disease. AIDS (acquired immune deficiency syndrome) is the name used to describe a number of potentially life-threatening infections and illnesses that happen when your immune system has been severely damaged by the HIV virus. In the UK, most cases of HIV are caused by having unprotected vaginal or anal sex. A person with HIV can pass the virus on to others even if they do not have any symptoms. HIV is transmitted through certain body fluids, such as blood, semen, vaginal fluids, breast milk, and anal lining, therefore, people who inject drugs and share equipment are also at higher risk.[17] There's currently no cure for HIV, but there are effective drug treatments that enable most people with the virus to live a long and healthy life. With an early diagnosis and effective treatments, most people with HIV will not develop any AIDS-related illnesses and will live a near-normal lifespan. Most people experience a short flu-like illness two to six weeks after HIV infection, which lasts for a week or two. After these symptoms disappear, HIV may not cause any symptoms for many years, although the virus continues to damage the immune system.[12]

In 2019, it was estimated that there are 105,200 people living with HIV in the UK. In 2022, 1,249,511 HIV negative people attended specialist sexual health services in England compared to 1,183,155 in 2021 (excluding people accessing reproductive care only). Overall, 9.7% (121,547) people were defined as having a PrEP need in 2022, compared to 7.5% (88,216) in 2021.[18] In England, 2022-23, there were 3,005 finished consultant episodes (FCE) and 1,563 admissions for Indication (ICD-10 codes B20-24) which resulted in 21,818 FCE bed days and 582 day cases.[19]

Recommended Treatment Options

NICE currently recommends a fixed-dose combination of emtricitabine with tenofovir disoproxil to prevent HIV infection in groups at high risk.[20]

Clinical Trial Information

Trial	**PURPOSE 2**; NCT04925752; A Phase 3, Double-Blind, Multicenter, Randomized Study to Evaluate the Efficacy and Safety of Subcutaneous Twice Yearly Long-Acting Lenacapavir for HIV Pre-Exposure Prophylaxis in Cisgender Men, Transgender Women, Transgender Men, and Gender Nonbinary People ≥ 16 Years of Age Who Have Sex With Male Partners and Are at Risk for HIV Infection **Phase III** – Active, not recruiting **Location(s):** USA and other countries **Primary completion date:** January 2025
Trial Design	Randomised, parallel assignment, double blind
Population	N=3295 (actual); cisgender male, transgender male, transgender female, and gender non-binary people who have condomless receptive anal sex with partners assigned male at birth and are at risk for HIV infection; aged 16 years and older.
Intervention(s)	Participants will receive the following for at least 52 weeks: - Oral lenacapavir tablet 600mg on days 1 and 2 - SC injection of lenacapavir 927mg every 26 weeks - Oral placebo-to-match emtricitabine/tenofovir disoproxil fumarate once daily.

Comparator(s)	Participants will receive the following for at least 52 weeks: - Matched placebo to oral and subcutaneous lenacapavir - Emtricitabine/tenofovir disoproxil fumarate 200/300 mg once daily.
Outcome(s)	Primary outcomes: - Incidence phase: background HIV incidence per 100-person-years - Randomised phase: number of participants with diagnosis of HIV-1 infection See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**PURPOSE 1**; **NCT04994509**; A Phase 3, Double-Blinded, Multicenter, Randomized Study to Evaluate Safety and Efficacy of Twice Yearly Long-Acting Subcutaneous Lenacapavir, and Daily Oral Emtricitabine/Tenofovir Alafenamide for Pre-Exposure Prophylaxis in Adolescent Girls and Young Women at Risk of HIV Infection **Phase III** – Active, not recruiting **Location(s):** South Africa, Uganda **Primary completion date:** January 2024
Trial Design	Randomised, parallel assignment, double blind.
Population	N=5368 (actual); adolescent girls and young women at risk of HIV infection; aged 16 to 25 years.
Intervention(s)	Participants will receive the following for at least 52 weeks: - Oral lenacapavir tablet 600mg on days 1 and 2 - SC injection of lenacapavir 927mg every 26 weeks - Oral placebo-to-match emtricitabine/tenofovir disoproxil fumarate or emtricitabine/tenofovir alafenamide once daily.
Comparator(s)	Participants will receive the following for at least 52 weeks: - Matched placebo to oral and subcutaneous lenacapavir. - Emtricitabine/tenofovir disoproxil fumarate 200/300 mg or emtricitabine/tenofovir alafenamide 200/25 mg once daily.
Outcome(s)	Primary outcomes: - Incidence phase: background HIV incidence per 100-person-years. - Randomised phase: HIV incidence reported per 100-person-years of follow-up. See trial record for full list of other outcomes.
Results (efficacy)	Interim analysis of its pivotal, Phase 3 PURPOSE 1 trial indicating that the company's twice-yearly injectable HIV-1 capsid inhibitor, lenacapavir, demonstrated 100% efficacy for the investigational use of HIV prevention in cisgender women. There were 0 incident cases of HIV infection among 2,134 women in the lenacapavir group (incidence 0.00 per 100 person-years). There were 16 incident cases among 1,068 women in the Truvada group (incidence 1.69 per 100 person-years).[21]

Results (safety)	Interim analysis also revealed lenacapavir was generally well-tolerated and no significant or new safety concerns were identified.[21]

Estimated Cost

The cost of lenacapavir is not yet known.

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Reducing sexually transmitted infections (NG221). June 2022.
- NICE clinical guideline. Sexually transmitted infections: condom distribution schemes (NG68). April 2017.
- NICE clinical guideline. HIV testing: increasing uptake among people who may have undiagnosed HIV (NG60). December 2016.
- NICE quality standard. Sexual health (QS178). February 2019.
- NICE quality standard. HIV testing: encouraging uptake (QS157). September 2017.
- NICE public health guideline. Contraceptive services for under 25s (PH51). March 2014.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy Proposition: Pre-exposure prophylaxis (PrEP) to prevent the acquisition of HIV in adults (F03X06). Draft for public consultation. 2016.
- NHS England. Clinical Commissioning Policy. Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents. 2016
- NHS England. Clinical Commissioning Policy: Treatment as prevention (TasP) in HIV infected adults. F03/P/c. 2015.
- NHS England. 2013/14 NHS Standard Contract for Specialised Human Immunodeficiency Virus Services (Adults). B06/S/a.

Other Guidance

- British HIV Association (BHIVA) and British Association for Sexual Health and HIV (BASHH). Guidelines on the use of HIV pre-exposure prophylaxis (PrEP). 2018.[22]
- European AIDS Clinical Society (EACS). Pre-exposure Prophylaxis (PrEP).[23]

Additional Information

Gilead did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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