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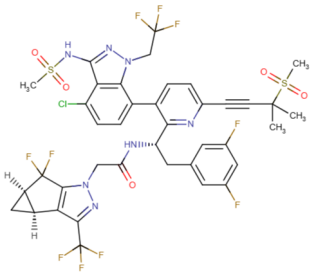


Lenacapavir Once-Yearly

Developer(s)

Gilead

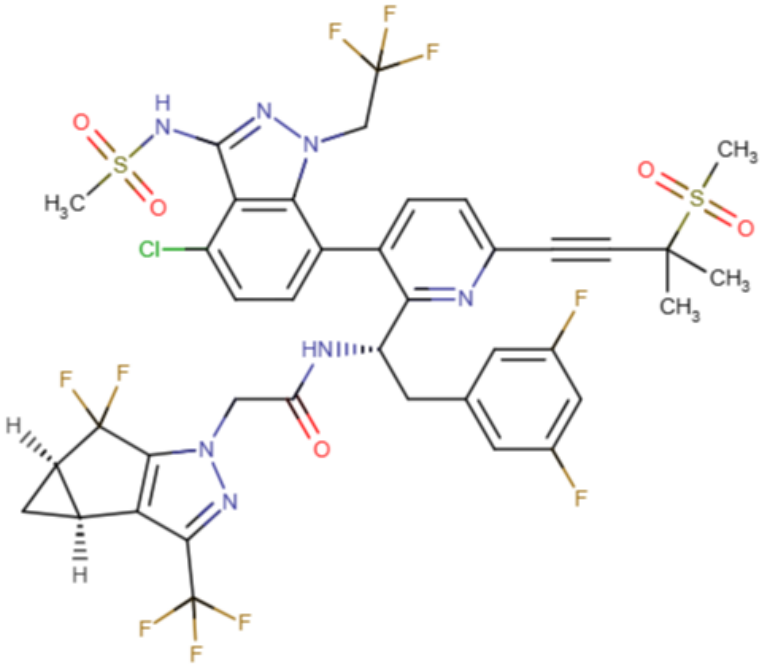
Originator

https://www.gilead.com/

United States

Gilead Sciences, Inc. is a multinational biopharmaceutical company that develops and manufactures innovative medicines for life-threatening diseases, including anti-viral therapeutics for HIV/AIDS, Hepatitis B, Hepatitis C and Covid-19. Headquartered in Foster City, California, Gilead was originally founded in 1987 and is currently listed on both the S&P 500 and the NASDAQ Biotechnology Index.

Drug structure



Lenacapavir Chemical Structure

Sourced From Drugbank

Drug information

Associated long-acting platforms

Aqueous Solution

Administration route

Intramuscular

Therapeutic area(s)

HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)
Prevention

Use of drug

Ease of administration

Administered by a community health worker
Administered by a nurse
Administered by a specialty health worker
Self-administered
To be determined

User acceptance

Not provided

Dosage

Available dose and strength

5000 mg - 2x5mL (although lower dosing might be sought with 2x3mL injections)

Frequency of administration

Once yearly

Maximum dose

Not provided

Recommended dosing regimen

Loading dose to be determined

Additional comments

Once-yearly intramuscular lenacapavir (5000 mg) provided higher Ctrough levels than the twice-yearly subcutaneous formulation. Future development suggests a lower optimal dose for the intramuscular option. A significant difference in the Phase I trial was the absence of oral loading doses for the once-yearly intramuscular formulation, which were required for the twice-yearly subcutaneous version due to its slow initial release. The intramuscular formulation also exhibited a faster initial increase in lenacapavir blood plasma concentration.

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB15673

Generic name

Lenacapavir Once-Yearly

Brand name

Not provided

Compound type

Small molecule

Summary

Once yearly lenacapavir (LEN) is an investigational intramuscular injectable formulation currently in clinical development for potential once-yearly HIV pre-exposure prophylaxis (PrEP). A phase I trial evaluating two once-yearly formulations found that a single 5000 mg intramuscular dose of lenacapavir resulted in sustained median plasma concentrations above those of the twice-yearly subcutaneous formulation (927 mg) for at least 56 weeks. Notably, the median concentrations at weeks 52 and 56 for the intramuscular formulations (50.7-65.6 ng/mL) were higher than the median concentration at week 26 (23.4 ng/mL) observed in PURPOSE 1 and 2. Once-yearly intramuscular lenacapavir may therefore further improve PrEP adherence, persistence, and scalability by offering reduced dosing frequency.

Approval status

Formulation is currently in early clinical development and not yet approved in any jurisdiction.

Regulatory authorities

Unknown

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Not provided

Clinical trials

Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study

Identifier

Not provided

Link

https://doi.org/10.1016/S0140-6736(25)00405-2

Phase

Phase I

Status

Not provided

Sponsor

Gilead Sciences Inc.

More details

Not provided

Purpose

Not provided

Interventions

Intervention 1

Once-yearly intramuscular lenacapavir formulation 1

Dosage: 5000 mg

Intervention 2

Once-yearly intramuscular lenacapavir formulation 2

Dosage: 5000 mg

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Not provided

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

40

Allocation

Not provided

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Not provided

Masking description

Not provided

Frequency of administration

Yearly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

PrEP

Key resources

Type	Title	Content	Link
Link	Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study		https://doi.org/10.1016/S014 6736(25)00405-2

Excipients

Proprietary excipients used

Not provided

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

Not provided

Residual solvents used

Not provided

Patent info

There are either no relevant patents or these were not yet submitted to LAPaL

Supporting material

Publications

Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study. Jogiraju, Vamshi et al. The Lancet, Volume 405, Issue 10485, 1147 - 1154

Background

Long-acting antiretrovirals can address barriers to HIV pre-exposure prophylaxis (PrEP), such as stigma and adherence. In two phase 3 trials, twice-yearly subcutaneous lenacapavir was safe and highly efficacious for PrEP in diverse populations. Furthering long-acting PrEP efforts, this study assessed the pharmacokinetics and safety of two once-yearly intramuscular lenacapavir formulations.

Methods

This phase 1, open-label study in participants aged 18–55 years without HIV evaluated the pharmacokinetics, safety, and tolerability of two lenacapavir free acid formulations administered by ventrogluteal intramuscular injection as a single 5000 mg dose (formulation 1 with 5% w/w ethanol, formulation 2 with 10% w/w ethanol). Pharmacokinetic samples were collected at prespecified timepoints up to 56 weeks. Lenacapavir plasma concentrations were measured with a validated liquid chromatography–tandem mass spectrometry method and summarised with non-compartmental analysis. Pharmacokinetic parameters evaluated included the area under the concentration–time curve for the once-yearly dosing interval calculated from days 1 to 365 (AUCdays 1–365), peak plasma concentration, time to reach peak plasma concentration, and trough concentration (Ctrough). Plasma concentration data from phase 3 studies of twice-yearly subcutaneous lenacapavir (PURPOSE 1 and PURPOSE 2) were pooled for comparison with once-yearly intramuscular lenacapavir

formulations. Safety and tolerability, including participant-reported pain scores, were assessed.

Findings

20 participants received lenacapavir formulation 1 and 20 received lenacapavir formulation 2. For estimation of pharmacokinetic parameters, sample size varied over time with at least 13 participants (formulation 1) and at least 19 participants (formulation 2) due to early discontinuations for reasons unrelated to the study drug. Following administration of intramuscular lenacapavir, concentrations increased rapidly, and median time to maximum concentration was 84·1 days (IQR 56·1–112·0) for formulation 1 and 69·9 days (55·3–105·5) for formulation 2. The highest median concentration of once-yearly intramuscular lenacapavir (247·0 ng/mL [IQR 184·0–346·0] for formulation 1, 336·0 ng/mL [233·5–474·3] for formulation 2) remained above the highest median twice-yearly subcutaneous lenacapavir concentration (67·3 ng/mL [46·8–91·4]). Median Ctrough at the end of 52 weeks for formulation 1 was 57·0 ng/mL (IQR 49·9–72·4) and for formulation 2 was 65·6 ng/mL (41·8–87·1), exceeding the median twice-yearly subcutaneous lenacapavir Ctrough of 23·4 ng/mL (15·7–34·3) at the end of 26 weeks. Median AUCdays 1–365 for formulation 1 was 1011·1 h*µg/mL (IQR 881·0–1490·2) and for formulation 2 was 1274·0 h*µg/mL (1177·3–1704·8). Adverse events were mostly grade 1 or 2. The most common was injection-site pain (16 [80%] participants given formulation 1, 15 [75%] given formulation 2), which was generally mild, resolved within 1 week, and was substantially reduced by pretreatment with ice.

Interpretation

Following administration of once-yearly intramuscular lenacapavir, median plasma concentrations exceeded those associated with efficacy in phase 3 studies of twice-yearly subcutaneous lenacapavir for PrEP for at least 56 weeks. Both formulations were safe and well tolerated. These data show the potential for biomedical HIV prevention with a once-yearly dosing interval.

Additional documents

No documents were uploaded

Useful links

- First Clinical Data for Gilead’s Investigational Once-Yearly Lenacapavir for HIV Prevention Presented at CROI 2025 and Published in The Lancet
- Pharmacokinetics and Safety of Once-Yearly Lenacapavir - CROI2025
- Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided