LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

Developed by

medicines patent pool

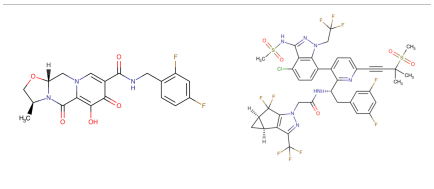
UNIVERSITY OF LIVERPOOL

CELT

Supported by

Unitaid
SAVE LIVES FASTER

leap



Cabotegravir and Lenacapavir

Developer(s)

ViiV Healthcare

Originator

https://viivhealthcare.com/

United Kingdom

ViiV Healthcare is a pharmaceutical company that specializes in the development of therapies for HIV infection. The company is headquartered in Brentford in the United Kingdom and was initially formed in November 2009 as a part of a joint venture between GlaxoSmithKline and Pfizer.

Gilead Sciences, Inc.

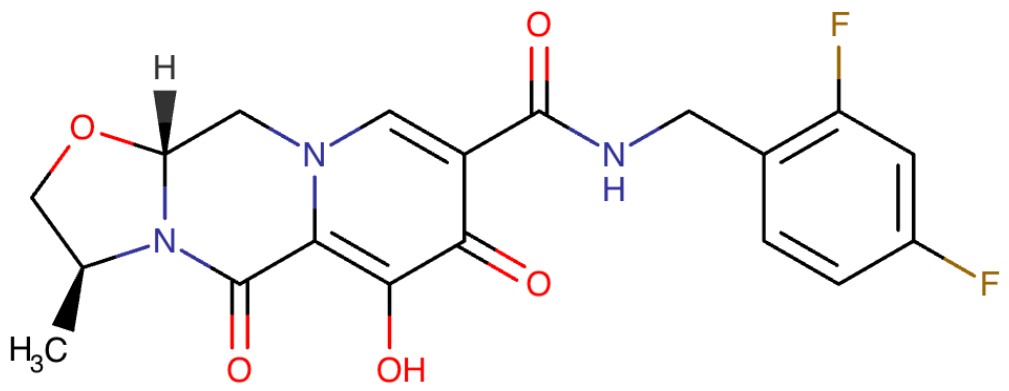
Originator

https://www.gilead.com/

United States

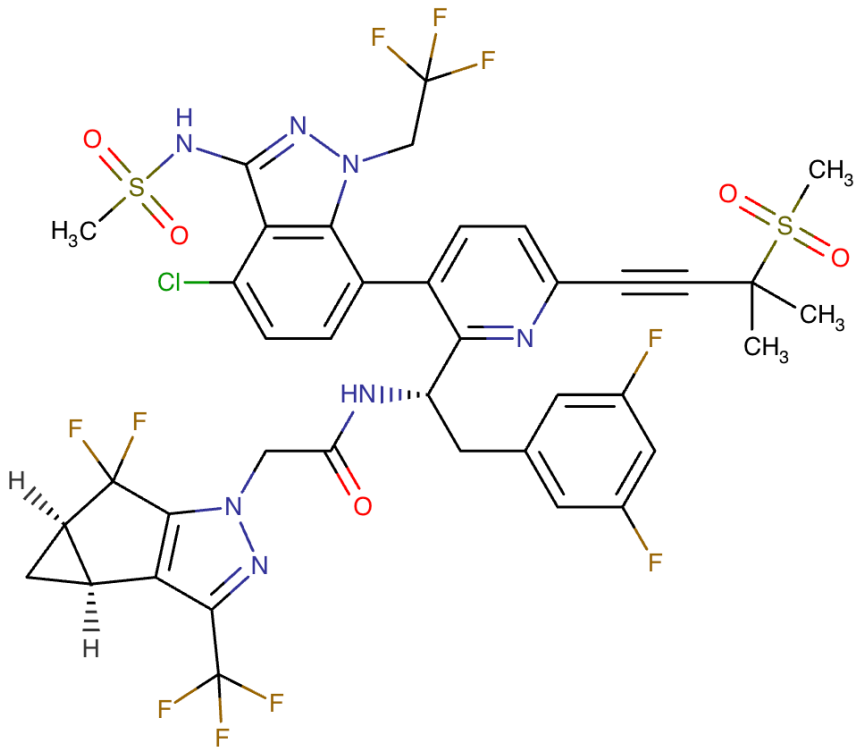
Gilead Sciences, Inc. is a multinational biopharmaceutical company that develops and manufactures innovative medicines for life-threatening diseases, including anti-viral therapeutics for HIV/AIDS, Hepatitis B, Hepatitis C and Covid-19. Headquartered in Foster City, California, Gilead was originally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

Drug structure



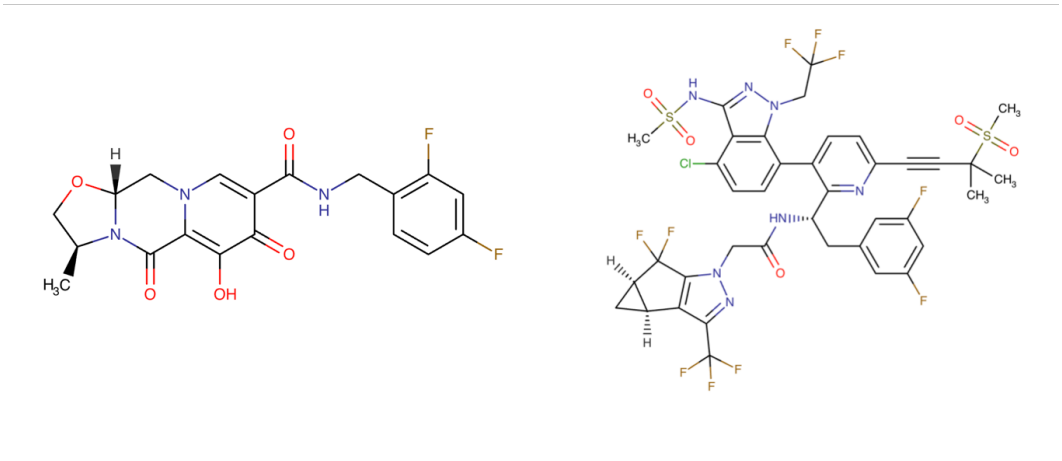
Cabotegravir Chemical Structure

Sourced From DrugBank



Lenacapavir Chemical Structure

Sourced From DrugBank



Cabotegravir and Lenacapavir Chemical Structure

Composite adapted from individual chemical structures sourced from DrugBank

Drug information

Associated long-acting platforms

Aqueous drug particle suspension, Aqueous solution

Administration route

Subcutaneous, Intramuscular

Therapeutic area(s)

HIV

Use case(s)

Treatment

Use of drug

Ease of administration

Administered by a community health worker
Administered by a nurse

User acceptance

Not provided

Dosage

Available dose and strength

Not provided

Frequency of administration

Not provided

Maximum dose

Not provided

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB11751
https://go.drugbank.com/drugs/DB15673

Generic name

Cabotegravir and Lenacapavir

Brand name

Apretude (CAB), Vocabria (CAB), Sunlenca (LEN)

Compound type

Small molecule

Summary

Cabotegravir and Lenacapavir (CAB/LEN) is an investigational drug combination in clinical development for the treatment of HIV-1. Currently, the only approved complete long-acting ART therapy regimen in both the U.S. and Europe is a combination of intramuscular CAB and rilpivirine (CAB/RPV). This regimen is approved for individuals with prior viral suppression on oral ART. LEN is a novel HIV-1 capsid inhibitor administered via subcutaneous injection every 26 weeks and has recently been approved for the treatment of multidrug-resistant (MDR) HIV. While it has been studied in both treatment-naïve (CALIBRATE study) and MDR individuals (CAPELLA), the use of LEN in combination with CAB LA for individuals with NNRTI resistance and/or oral ART adherence challenges is currently being evaluated.

Approval status

Given the limited number of available LA-ART medications, healthcare providers are increasingly prescribing injectable LEN through insurance programs and using it off-

label with LA CAB (+/- RPV) for select patients with adherence challenges and NNRTI resistance.

Regulatory authorities

Unknown

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Cabotegravir is commercially manufactured by the innovator (ViiV Healthcare) and three generic manufacturers have received a licence through the Medicines Patent Pool to manufacture generic versions by 2026/2027. Lenacapavir is commercially manufactured by Gilead Sciences Inc.

Tentative equipment list for manufacturing

Cabotegravir: Conventional wet-bead milling (ball mill), depyrogenated glass vials. Lenacapavir: Equipment: Stainless steel pharmaceutical reactors, glass-lined reactors, rotary evaporator (rotovap), flash chromatography columns, stainless steel autoclave, cooling bath, silica gel chromatography columns, vacuum distillation apparatus, simulated moving bed chromatography system, Chiralpak columns.

Manufacturing

Cabotegravir is subject to a gamma-irradiation pre-sterilization step prior to a conventional wet-bead milling manufacturing procedure. The Cabotegravir milling process is initiated alongside pharmaceutical excipients (polyethylene glycol 3350, water for injection, polysorbate 20 and mannitol) for an overall 200nm drug particle size. Storage of injectable lenacapavir in borosilicate vials is contraindicated due to issues with chemical compatibility. Instead, it is recommended that vials are made from aluminosilicate glass.

Specific analytical instrument required for characterization of formulation

Cabotegravir: PANalytical X’Pert PRO diffractometer equipped with a theta/theta coupled goniometer (or equivalent x-ray powder diffractor) to determine drug particle size, Mettler TGA/DSC 1 instrument for thermal analysis, HPLC to evaluate drug content, impurities and dissolution, HPLC UV-Vis Detector for drug identification. Lenacapavir: Proton nuclear magnetic resonance (1H NMR), High-performance liquid chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC).

Clinical trials

CALENDULA

Identifier

NCT06657885

Link

https://clinicaltrials.gov/study/NCT06657885

Phase

Phase II

Status

Not yet recruiting

Sponsor

Institut de Médecine et d'Epidémiologie Appliquée - Fondation Internationale Léon M'Ba

More details

This study is a Phase II, prospective, single-arm, multicenter, non-randomized pilot study designed to evaluate the antiretroviral efficacy of lenacapavir in combination with cabotegravir injection over 48 weeks of follow-up in participants who meet the study inclusion criteria. Efficacy is defined as the absence of virologic failure at S48. Virologic success is defined as maintaining or achieving CV \< 50 copies/mL without interruption of long-acting dual therapy with cabotegravir/lenacapavir at the end of 48 weeks. The study will be conducted at several sites in France in adults 18 years of age and older. Minors and persons under legal guardianship will not be included in the

study. Long-acting treatments are evolving thanks to new "long-acting" molecules. These molecules ensure prolong

Purpose

CAbotégravir LENacapavir DUal Long Acting

Interventions

Intervention 1
Drug: Cabotegravir (Initiation) Oral Tablet
Dosage: 30 mg

Intervention 2
Drug: Cabotegravir (Maintenance) Intramuscular Injection
Dosage: N/A (Every 8 weeks)

Intervention 3
Drug: Lenacapavir (Initiation) Subcutaneous injection
Dosage: Two injections of 463.5mg/1.5mL in distinct abdominal sites

Intervention 4
Drug: Lenacapavir (Initiation)
Dosage: Two 300mg tablets

Intervention 5
Drug: Lenacapavir (Maintenance) Subcutaneous Injection
Dosage: Two injections of 463.5mg/1.5mL in distinct abdominal sites every 24 weeks

Countries

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2025-01-15

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-10-23

Estimated Primary Completion Date

2026-07-15

Estimated Completion Date

2026-09-15

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Inclusion: - Age ≥ 18 years - HIV-1 infection - Stable oral antiretroviral treatment for at least 6 months - Multi-treated patients who have received multiple lines of antiretroviral treatment - Undetectable patients with CV \< 50 copies/mL in the last 6 months (a single blip between 50 and 200 copies/mL in the last 6 months is allowed) and eligible to switch to the lenacapavir/cabotegravir strategy on the basis of a collegial decision by clinicians, virologists and pharmacologists following a multidisciplinary meeting due to the presence of resistance mutations, including to NNRTIs, oral drug intolerance or drug-drug interactions - Detectable, virologically uncontrolled HIV viral load ≥ 200 c/mL in the last 12 months who is eligible to switch to the lenacapavir/cabotegravir strategy

Health status

Positive to : HIV
Negative to : HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

30

Allocation

Non-randomized

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 6 months
Once every 2 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous
Intramuscular

Use case

Treatment

Key results

Not provided

223616

Identifier

NCT06970223

Link

https://clinicaltrials.gov/study/NCT06970223

Phase

Phase I

Status

Recruiting

Sponsor

ViiV Healthcare

More details

This study will evaluate the tolerability and acceptability of injection site reactions (ISRs) of two long-acting (LA) injectables. Additional characteristics of the ISRs will be investigated and described as well as safety outcomes.

Purpose

A Study to Investigate if Long Acting Cabotegravir (CAB) and Lenacapavir (LEN) Injections Are Tolerable and Acceptable When Administered to Healthy Adults Without HIV

Interventions

Intervention 1

Cabotegravir long-acting

Intervention 2

Lenacapavir long-acting

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2025-04-22

Anticipated Date of Last Follow-up

2025-05-05

Estimated Primary Completion Date

2025-07-30

Estimated Completion Date

2026-07-07

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: Participants are eligible to be included in the study only if all the following criteria apply: 1. At the time of obtaining informed consent, 18 years of age. 2. Body weight 50 kg and BMI within the range 18 to 32 kg/m2 (inclusive). 3. Participants who are overtly healthy as determined by medical evaluation by a responsible and experienced physician, including medical history, physical examination, laboratory tests and cardiac monitoring. 4. A participant with a significant clinical abnormality or laboratory parameter(s) which is/are not specifically listed in the inclusion or exclusion criteria, outside the reference range for the population being studied may be included if the investigator determines and documents that the finding is unlikely to introduce additional

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

60

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Once every 2 months
Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous
Intramuscular

Use case

Treatment

Key results

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

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

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Patent info

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

Supporting material

Publications

Gandhi M, Hill L, Grochowski J, Nelson A, Koss CA, Mayorga-Munoz F, Oskarsson J, Shiels M, Avery A, Bamford L, Baron J, Short WR, Hileman CO. Case Series of People With HIV on the Long-Acting Combination of Lenacapavir and Cabotegravir: Call for a Trial. Open Forum Infect Dis. 2024 Apr 16;11(4):ofae125. DOI: 10.1093/ofid/ofae125. PMID: 38628952; PMCID: PMC11020301.

Background

Injectable cabotegravir (CAB)/rilpivirine (RPV) is the only combination long-acting (LA) antiretroviral regimen approved for HIV. RPV may not be effective among individuals with non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance, which has >10% prevalence in many countries. Lenacapavir (LEN) is an LA capsid inhibitor given every 6 months, but has not been studied in combination with other LA agents.

Methods

We assembled a case series from 4 US academic medical centers where patients with adherence challenges were prescribed LEN subcutaneously every 26 weeks/CAB (+/− RPV) intramuscularly every 4 or 8 weeks. Descriptive statistics, including viral load (VL) outcomes, were summarized.

Results

All patients (n = 34: 76% male; 24% cis/trans female; 41% Black; 38% Latino/a; median age [range], 47 [28–75] years; 29% and 71% on CAB every 4 or 8 weeks)

reported challenges adhering to oral ART. The reasons for using LEN/CAB with or without RPV were documented or suspected NNRTI mutations (n = 21, 59%), integrase mutations (n = 5, 15%), high VL (n = 6, 18%), or continued viremia on CAB/RPV alone (n = 4, 12%). Injection site reactions on LA LEN were reported in 44% (32% grade I, 12% grade 2). All patients but 2 (32/34; 94%) were suppressed (VL <75 copies/mL) after starting LEN at a median (range) of 8 (4–16) weeks, with 16/34 (47%) suppressed at baseline.

Conclusions

In this case series of 34 patients on LEN/CAB, high rates of virologic suppression (94%) were observed. Reasons for using LEN/CAB included adherence challenges and underlying resistance, mostly to NNRTIs. These data support a clinical trial of LEN/CAB among persons with NNRTI resistance.

Additional documents

No documents were uploaded

Useful links

There are no additional links

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