Lenacapavir (*Sunlenca*)

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Lenacapavir

**Oral Lenacapavir**

300 mg tablets

Take with or without food

**Subcutaneous Lenacapavir**

Each 1.5 mL vial = 463.5 mg

Administer as Subcutaneous Injection
Lenacapavir

- **Type of Medication**
  - HIV capsid inhibitor

- **Indication**
  - Treatment of HIV-1 in combination with other antiretroviral medications in heavily treatment-experienced adults with multidrug resistant HIV

- **Preparations**
  - Oral: 300 mg tablets
  - Subcutaneous injection: 463.5 mg/1.5 mL vial

- **Adverse Reactions**
  - Most common adverse effects are nausea and injection site reactions

- **Contraindications**
  - Contraindicated to give with strong CYP3A inducers

Source: Lenacapavir Prescribing Information.
# Lenacapavir Dosing Schedule

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Missed dose: If more than 28 weeks since last injection and clinically appropriate to continue lenacapavir, restart initiation from Day 1, using either Option 1 or Option 2
Lenacapavir Dosing: Initiation Option 1

**Initiation Option 1**

- **Day 1**: 600 mg
- **Day 2**: 600 mg
- **6 months**: 927 mg

**Maintenance**

- **Month 6**: 927 mg

**Dosing**

- Oral lenacapavir 300 mg
- Subcutaneous lenacapavir 463.5 mg
Lenacapavir Dosing: Initiation Option 2

**Initiation Option 2**

- **Day 1**: Oral lenacapavir 600 mg
- **Day 2**: Oral lenacapavir 600 mg
- **Day 8**: Oral lenacapavir 300 mg
- **Day 15**: Subcutaneous lenacapavir 463.5 mg

**Maintenance**

- 6 months: Oral lenacapavir 927 mg
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- 6 months: Oral lenacapavir 927 mg

Illustration: David H. Spach, MD
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Lenacapavir for Persons with Multidrug-Resistant HIV

CAPELLA
Lenacapavir in Multidrug Resistant HIV CAPELLA Study: Background

• **Background**
  – Phase 3, randomized, trial with oral and subcutaneous lenacapavir, a first-in-class capsid inhibitor, versus optimized background therapy (OBT)

• **Enrollment Criteria:**
  – Age ≥12 years
  – Virologic failure on current ART
  – HIV RNA >400 copies/mL for ≥8 wks
  – Documented HIV drug resistance to at least 2 HIV medications from at least 3 of the 4 main classes
  – At least one fully active agent available for HIV treatment

Lenacapavir in Multidrug Resistant HIV CAPELLA Study: Study Design

**Study Cohorts**

**Cohort 1 (Randomized, Stable Viremia)**
- First 36 participants with:
  - HIV RNA decrease <0.5 log between the screening and cohort-selection visits
  - HIV-1 RNA ≥ 400 copies/mL during screening

**Cohort 2 (Nonrandomized, Reduced Viremia)**
- Participants with:
  - HIV RNA decrease ≥0.5 log between the screening and cohort-selection visits
  - HIV-1 RNA <400 copies/mL during screening

**Day 1**
- Functional Monotherapy
  - *Oral Lenacapavir + failing therapy (n = 24)
  - Placebo + failing therapy (n = 12)

**Day 15**
- SC Lenacapavir Q6M + OBT for 52 weeks (n = 24)
- Oral Lenacapavir + OBT (n = 12)

**Week 52**
- Oral Lenacapavir + OBT (n = 36)
- SC Lenacapavir Q6M + OBT for 52 weeks (n = 36)
- Oral Lenacapavir + OBT (n = 12)

OBT = optimized background regimen

*Oral lenacapavir = 600 mg days 1 and 2, 300 mg day 8
^Oral lenacapavir = 600 mg days 15 and 16, 300 mg day 22
SC Lenacapavir = 927 mg every 6 months

Lenacapavir in Multidrug Resistant HIV CAPELLA Study: Results

Baseline to Day 15 Change in HIV RNA Level (Functional Monotherapy in Randomized Cohort)

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

Decrease in HIV RNA Level of ≥0.5 log at Day 15 (Functional Monotherapy in Randomized Cohort)

Lenacapavir in Multidrug Resistant HIV CAPELLA Study: Results

Virologic Responses at 26 Weeks

![Bar chart showing virologic responses at 26 weeks.](chart.png)

- **Cohort 1 (Randomized, Combined):**
  - HIV-1 RNA <50 copies/mL: 81 patients
  - HIV-1 RNA ≥50 copies/mL: 19 patients
  - No virologic data: 0 patients

- **Cohort 2 (Nonrandomized):**
  - HIV-1 RNA <50 copies/mL: 83 patients
  - HIV-1 RNA ≥50 copies/mL: 14 patients
  - No virologic data: 3 patients

Lenacapavir-related capsid substitutions developed in 8 participants

- 5 with M66I (alone)
- 1 with M66I + N74D
- 1 with Q67H + K70R
- 1 with K70H (alone)

Mutations and median change in lenacapavir susceptibility

- M66I: 234-fold decrease
- 1 with Q67H + K70R: 15-fold decrease
- 1 with K70H: 265-fold decrease
Conclusions: “In patients with multidrug-resistant HIV-1 infection, those who received lenacapavir had a greater reduction from baseline in viral load than those who received placebo.”

Lenacapavir in Treatment-Naïve Persons with HIV

CALIBRATE: Background

• **Background**
  - Phase 2 randomized, open-label trial in United States and Dominican Republic evaluating the efficacy of lenacapavir in various combinations as initial and maintenance antiretroviral therapy in persons with HIV

• **Enrollment Criteria:**
  - Age ≥18 years
  - Antiretroviral naïve
  - HIV RNA ≥200 copies/mL
  - CD4 count ≥200 cells/mm$^3$
  - Negative pregnancy test for women
  - Exclusions: hepatitis B, hepatitis C, or any active opportunistic infection

Lenacapavir in Treatment-Naïve Persons with HIV

CALIBRATE: Background

**Abbreviations:** LEN = lenacapavir; SC = subcutaneous; TAF-FTC = tenofovir alafenamide-emtricitabine; TAF = tenofovir alafenamide; BIC = bictegravir; BIC-TAF-FTC = bictegravir-tenofovir alafenamide-emtricitabine

*Groups 1 and 2: LEN Oral lead in = 600 mg days 1 and 2, 300 mg day 8; first dose LEN SC = 927 mg on day 15; requires HIV RNA <50 copies/mL on weeks 16 and 22 to change to 2-drug regimen

^Group 3: LEN oral 600 mg days 1 and 2, followed by 50 mg daily

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Lenacapavir in Treatment-Naïve Persons with HIV

CALIBRATE: Results

Lenacapavir in Treatment-Naïve Persons with HIV

CALIBRATE: Results

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results

**lenacapavir in treatment-naïve persons with HIV**

**calibrate: results**


**LEN SC + TAF-FTC to LEN SC + TAF**

**LEN SC + TAF-FTC to LEN SC + BIC**

**LEN PO + TAF-FTC**

**BIC-TAF-FTC**

**HIV RNA ≥50 copies/mL (%)**

- **Group 1:** 4
- **Group 2:** 4
- **Group 3:** 6
- **Group 4:** 0

Lenacapavir-related capsid substitutions developed in 2 of 157 participants

- Group 2 participant: Q67H + K70R
- Group 3 participant: Q67H

Interpretation: “Lenacapavir warrants further investigation as a potential antiretroviral used orally and as injection in combination with other antiretroviral drugs.”

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