UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Human Immunodeficiency Virus – Sunlenca Prior Authorization Policy
- Sunlenca® (lenacapavir subcutaneous injection – Gilead)

REVIEW DATE: 01/04/2023; selected revision 04/12/2023

OVERVIEW
Sunlenca, a human immunodeficiency virus type 1 (HIV-1) capsid inhibitor, is indicated in combination with other antiretroviral(s) for the treatment of HIV-1 infection in heavily treatment-experienced adults with **multidrug resistant HIV-1 infection** failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.[1] Of note, Sunlenca is also available as tablets which are not addressed in this policy.

Clinical Efficacy
The efficacy of Sunlenca was evaluated in one Phase II/III, randomized, double-blind, placebo-controlled, multicenter, pivotal study in patients with multidrug resistant HIV-1.[2] Eligible patients had documented resistance to two or more agents from three of four main antiretroviral classes (nucleoside reverse transcriptase inhibitor [NRTI], non-nucleoside reverse transcriptase inhibitor [NNRTI], protease inhibitor, and integrase strand-transfer inhibitor [INSTI]) and two or fewer active antiretrovirals from the four main classes that could be effectively combined for optimized background therapy.

Dosing
Initial treatment with Sunlenca has two scheduling options. Option 1: Two subcutaneous (SC) injections (927mg) and two tablets (600 mg) on Day 1, then two tablets (600 mg) on Day 2. Option 2: Two tablets (600 mg) on Days 1 and 2, one tablet (300 mg) on Day 8, and two SC injections (927 mg) on Day 15. For either option, maintenance treatment begins 26 weeks (± 2 weeks) after the initial dosing regimen is completed and continues as two SC injections (927 mg) once every 6 months (Q6M). Injections are given by a healthcare provider. Missed dose. During the maintenance period, if > 28 weeks have elapsed since the last injection and if clinically appropriate to continue Sunlenca treatment, restart the initiation dosage regimen from Day 1 using either Option 1 or Option 2.

Guidelines
Sunlenca is not addressed as an approved agent in guidelines.[4,5] According to the Department of Health and Human Services Guidelines for the use of antiretroviral s in adults and adolescents with HIV (January 20, 2022), in patients with multidrug resistance without fully active antiretroviral options, consensus on optimal management is lacking.[4] Virologic suppression remains the goal of treatment; however, if it cannot be achieved, the goals are to preserve immune function, prevention clinical progression, and minimize the development of further resistance that may compromise future regimens. The Guidelines note that that even partial virologic suppression of HIV-1 RNA to > 0.5 $\log_{10}$ copies/mL from baseline correlates with clinical benefit. There is evidence that continuing antiretroviral therapy even in the presence of viremia and the absence of CD4+ count increases reduces the risk of disease progression. Additional data suggest that even modest reductions in HIV-1 RNA levels continue to confer immunologic and clinical benefits. In general, adding a single, fully active antiretroviral to the regimen is not recommended because of the risk of rapid development of resistance. Patients with ongoing detectable viremia who lack sufficient treatment options to construct a fully suppressive regimen are noted to be candidates for Trogarzo® (ibalizumab-uiyk intravenous injection) and/or Rukobia™ (fostemsavir extended-release tablets). Sunlenca is only mentioned as an agent in clinical trials, but not approved.

The International Antiviral Society-USA (December 2022) provides some guidance on patients with viral failure; Sunlenca is mentioned in patients with INSTI resistance as a product under FDA review.[5] Management of INSTI resistance can be difficult and guidance from an expert in HIV drug resistance is recommended for selection of the optimal regimen. If INSTI resistance is relatively limited, and a new regimen is to include an INSTI, dolutegravir should be administered twice daily. The regimen should also include at least one, and preferably two other fully active drugs, optimally from drug classes not previously used. Therapies may include Rukobia, Sunlenca (currently under FDA review), Selzentry® (maraviroc tablets, generic and oral solution), Trogarzo, or Fuzeon® (enfuviritide SC injection).

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Sunlenca. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Sunlenca as well as the monitoring required for adverse events and long-term efficacy, approval requires Sunlenca to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sunlenca is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Human Immunodeficiency Virus (HIV)-1 Infection, Treatment.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following conditions (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, the patient is failing a current antiretroviral regimen for HIV; AND
     - **iii.** According to the prescriber, the patient has resistance to two or more agents from at least THREE of the following antiviral classes (a, b, c, d):
       - **a)** Nucleoside reverse transcriptase inhibitor;
         Note: Examples of nucleoside reverse transcriptase inhibitors include abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir disoproxil fumarate, tenofovir alafenamide, zidovudine.
       - **b)** Non-nucleoside reverse transcriptase inhibitor;
         Note: Examples of non-nucleoside reverse transcriptase inhibitor include delaviridine, efavirenz, etravirine, nevirapine, nevirapine XR, rilpivirine.
       - **c)** Protease inhibitor;
         Note: Examples of protease inhibitors include atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, tipranavir.
       - **d)** Integrase strand transfer inhibitor; AND

Note: Examples of integrase strand transfer inhibitors include raltegravir, dolutegravir, elvitegravir.

iv. The medication will be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND

v. The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection.

B) Patient is Currently Receiving Sunlenca. Approve for 1 year if the patient meets BOTH of the following conditions (i and ii):

i. The medication will continue to be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND

ii. Patient has responded to a Sunlenca-containing regimen, as determined by the prescriber. Note: Examples of a response are HIV RNA < 50 cells/mm^3, HIV-1 RNA ≥ 0.5 $\log_{10}$ reduction from baseline in viral load.

Dosing. Approve an initial dose of 927 mg subcutaneously one time, and maintenance dose of 927 mg subcutaneously every 6 months (± 2 weeks from the date of the last injection).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Sunlenca is not recommended in the following situations:

1. **Pre-Exposure Prophylaxis (PrEP) of Human Immunodeficiency Virus (HIV).** Sunlenca is not approved for this indication; however, it is under investigation in two Phase III, unpublished, and ongoing clinical trials for PrEP (PURPOSE 1 and PURPOSE 2).[2]

2. **Human Immunodeficiency Virus (HIV), Use in Treatment-Naïve Patients.** Sunlenca is not approved for this indication; however, it is under investigation in one Phase II, unpublished, and ongoing clinical trial in treatment-naïve adults with HIV-1 (CALIBRATE).[3]

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Sunlenca® tablets and subcutaneous injection [prescribing information]. Foster City, CA: Gilead; December 2022.
2. Segal-Maurer S, DeJesus E, Stelbrinka HJ; for the CAPELLA Study Investigators. Capsid inhibition with lenacapavir in multidrug-resistant HIV-1 infection. *N Engl J Med.* 2022; 1793-1803.
3. Gupta SK, Sims J, Brinson C, et al. Lenacapavir as part of a combination regimen in treatment-naïve people with HIV: Week 54 results [poster]. Presented at: CROI 2022; Virtual Event; February 12-16, 2022.
4. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Last Updated: September 21, 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed December 26, 2022.
5. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults 2022 recommendations of the International Antiviral Society–USA Panel. *JAMA.* [Epub ahead of Print Dec 1, 2022].

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/04/2023
Selected Revision	**Human Immunodeficiency Virus (HIV)-1 Infection, Treatment**: Dosing was updated to approve an initial dose of 927 mg subcutaneously one time and a maintenance dose of 927 mg every 6 months (± 2 weeks from the date of the last injection). Previously, two dosing options were provided: an initial dose of 927 mg subcutaneously one time (Day 1), and maintenance dose of 927 mg subcutaneously every 6 months (26 weeks) from the date of the last injection ± 2 weeks; OR an initial dose of 927 mg two times (Day 1 and Day 15), and maintenance dose of 927 mg subcutaneously every 6 months (26 weeks) from the date of the last injection ± 2 weeks.	04/12/2023