Drug Coverage Policy

Effective Date.....9/15/2024
Coverage Policy Number IP0546
Policy Title.....Sunlenca

Human Immunodeficiency Virus – Sunlenca

- Sunlenca® (lenacapavir tablets and subcutaneous injection - Gilead)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Sunlenca, a human immunodeficiency virus type 1 (HIV-1) capsid inhibitor, is indicated in combination with other antiretroviral(s) for the treatment of **multidrug resistant HIV-1 infection** in heavily treatment-experienced adults failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.[1]

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 (927 mg) 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
According to the Department of Health and Human Services Guidelines for the use of antiretrovirals in adults and adolescents with HIV (December 6, 2023), in patients with multidrug resistance without fully active antiretroviral options, consensus on optimal management is lacking.[4] Maximal 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 Rukobia™ (fostemsavir extended-release tablets), Sunlenca, and/or Trogarzo® (ibalizumab-uiyk intravenous infusion). For people with multidrug-resistant HIV-2, Trogarzo and Sunlenca may be considered based on *in vitro* data. Optimal treatment strategies for individuals with HIV-2 are not defined.

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).

Medical Necessity Criteria

Sunlenca is considered medically necessary when the following are met:

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 (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 inhibitors 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 (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, improvement or stabilization of CD4 T-cell count.

   Dosing for Sunlenca Subcutaneous Injection. 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).

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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).[7,8]

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

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1961	Injection, lenacapavir, 1 mg

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, Berhe M, Crofoot G, et al. Lenacapavir administered every 26 days or daily in combination with oral daily antiretroviral therapy for initial treatment of HIV: a randomized open-label, active-controlled, phase 2 trial. *Lancet HIV*. 2023;10:e15-e23.
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: December 6, 2023. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new. Accessed December 19, 2023.
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.* 2023;329(1):63-84.
6. Smith RA, Raugi DN, Nixon RS, et al; on behalf of the University of Washington-Senegal HIV-2 Study Group. Antiviral activity of lenacapavir against HIV-2 isolates and drug resistant HIV-2 mutants. *J Infect Dis.* 2023 Dec 7. [Epub ahead of print].
7. Gilead Sciences. Pre-exposure prophylaxis study of lenacapavir and emtricitabine/tenofovir alafenamide in adolescent girls and young women at risk of HIV infection (PURPOSE 1). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2023 Dec 19]. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04994509. NLM Identifier: NCT049945091.
8. Gilead Sciences. Study of lenacapavir for HIV pre-exposure prophylaxis in people who are at risk for HIV infection (PURPOSE 2). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2023 Dec 19]. Available at: https://www.clinicaltrials.gov/study/NCT04925752. NLM Identifier: NCT04925752.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Updated the policy title to Human Immunodeficiency Virus – Sunlenca; previously it was Lenacapavir. **Human Immunodeficiency Virus (HIV)-1 Infection, Treatment:** Updated initial approval duration from 12 months to 6 months. Removed "History of multi-drug resistant Human Immunodeficiency Virus" and replaced with "According to the prescriber, the patient is failing a current antiretroviral regimen for HIV; AND According to the prescriber, the patient has resistance to two or more agents from at least THREE of the following antiviral classes: a)Nucleoside reverse transcriptase inhibitor; b)Non-nucleoside reverse transcriptase inhibitor; c)Protease inhibitor; d)Integrase strand transfer inhibitor". Examples of agents from each antiviral class were also included.	7/15/2024
Selected Revision	**Human Immunodeficiency Virus-1 Infection.** Patient is Currently Receiving Sunlenca: The note with examples of a response to a Sunlenca-containing regimen was updated to add improvement or stabilization in CD4 T-cell count.	9/15/2024

The policy effective date is in force until updated or retired.