Drug Coverage Policy

Effective Date..... 5/1/2025
Coverage Policy Number IP0123
Policy Title..... Cabenuva

Human Immunodeficiency Virus – Cabenuva

- Cabenuva® (cabotegravir extended-release intramuscular injection; rilpivirine extended-release intramuscular injection, co-packaged – ViiV/GlaxoSmithKline)

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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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.

OVERVIEW

*Cabenuva is a two-drug co-packaged product of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand-transfer inhibitor, and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor.[1] It is indicated as a complete regimen for the treatment of **HIV-1 infection** in patients ≥ 12 years of age and ≥ 35 kg to replace their current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to cabotegravir or rilpivirine.[1]*

Dosing
Cabenuva must be administered by a healthcare professional. Prior to starting Cabenuva, healthcare professionals should carefully select patients who agree to the required monthly injection dosing schedule and counsel patients about the importance of adherence to scheduled dosing visits to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance with missed doses.[1]

Oral lead-in with Vocabria® (cabotegravir tablets) + Edurant® (rilpivirine tablets) may be used for approximately 1 month (at least 28 days) prior to the initiation of Cabenuva to assess the tolerability of cabotegravir and rilpivirine. Cabenuva may be administered as a once-monthly injection or once every 2-month injection. Table 1 provides the recommended oral lead-in and monthly injection dosing schedule. Table 2 provides the recommended oral lead-in and every 2-month injection dosing schedule.

Table 1. Recommended Oral Lead-In and Monthly Intramuscular Injection Dosing Schedule.[1]

Vocabria + Edurant Lead-In (at Least 28 Days)	Cabenuva Initiation Injections (One-Time Dosing)	Cabenuva Continuation Injections (Once-Monthly Dosing)
Month 1	At Month 2 (On the Last Day of Oral Lead-In Dosing)	Month 3 Onwards
Vocabria (30 mg) QD with a meal	cabotegravir 600 mg (3 mL)	cabotegravir 400 mg (2 mL)
Edurant (25 mg) QD with a meal	rilpivirine 900 mg (3 mL)	rilpivirine 600 mg (2 mL)

QD – Once daily.

Table 2. Recommended Oral Lead-In and Every 2-Month Intramuscular Injection Dosing Schedule.[1]

Vocabria + Edurant Lead-In (at Least 28 Days)	Cabenuva Initiation Dosing	Cabenuva Continuation Injections (Once Every 2-Month Dosing)
Month 1	At Month 2 and Month 3	Month 5 Onwards
Vocabria (30 mg) QD with a meal	cabotegravir 600 mg (3 mL)	cabotegravir 600 mg (3 mL)
Edurant (25 mg) QD with a meal	rilpivirine 900 mg (3 mL)	rilpivirine 900 mg (3 mL)

QD – Once daily.

Guidelines
The Department of Health and Human Services (DHHS) Guidelines for the Use of Antiviral Agents in Adults and Adolescents with HIV (September 12, 2024) recommend Cabenuva (every month or every 2 months) to replace an existing oral antiretroviral regimen in patients with HIV who meet all of the following criteria: Sustained viral suppression on oral therapy for ≥ 3 months, no known

or suspected resistance to Cabenuva, no active hepatitis B virus infection (unless also receiving an agent for hepatitis B virus infection), not pregnant (or actively planning pregnancy), and not receiving medications with significant drug interactions with Cabenuva.[5] The Guidelines point out that the tablet formulation of cabotegravir (Vocabria®) is only available through the manufacturer, not in community pharmacies. Cabenuva is not recommended as initial therapy for people with HIV because of the lack of data supporting efficacy in this patient population. Patients who want to use Cabenuva early in their treatment history should first attain viral suppression on a recommended regimen prior to switching to Cabenuva.

Some people with HIV cannot reach or maintain viral suppression on oral antiretroviral therapy despite intensive adherence support.[5] Cabenuva has been used in this population with some success, although long-term efficacy data are limited. Based on very limited data, the Panel recommends the use of Cabenuva on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral antiretroviral therapy, who have no evidence of resistance to either component of Cabenuva, and with shared decision-making between providers and the patient. Importantly, the Panel recognizes the significant risk of developing resistance to non-nucleoside reverse transcriptase inhibitors, and particularly integrase strand transfer inhibitors if virologic failure occurs while on Cabenuva which could future treatment options and may also lead to HIV transmission.

International Antiviral Society-USA Recommendations on Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults (2024) have similar recommendations to the DHHS guidelines for Cabenuva.[4] In individuals with no history of treatment failure and no known or suspected resistance to either agent, Cabenuva is an option. Cabenuva is not recommended for initial therapy in antiretroviral-naïve individuals. Cabenuva is recommended for patients who experience stigma or other adverse consequences of taking pills daily or in response to strong patient preference. For patients who are not able to take oral antiretroviral therapy and who have advanced HIV, Cabenuva with intensive case management and adherence support may be considered for individuals without viral suppression who meet the following criteria when no other treatment options are effective: Unable to take oral antiretroviral therapy consistently despite extensive efforts and clinical support, have high risk of HIV disease progression (CD4 cell count < 200 cells/mcL or acquired immunodeficiency syndrome-defining complications), and have virus susceptible to both components of Cabenuva.

Coverage Policy

POLICY STATEMENT
Prior Authorization is recommended for prescription benefit coverage of Cabenuva. 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 Cabenuva as well as the monitoring required for adverse events and long-term efficacy, approval requires Cabenuva to be prescribed by a physician who has consulted with or who specializes in the condition.

Documentation: Documentation is required where noted in the criteria. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

Cabenuva is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Human Immunodeficiency Virus (HIV)-1, Treatment.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient weighs ≥ 35 kg; AND
     - **iii.** Documentation provided that the patient has HIV-1 RNA < 50 copies/mL (viral suppression); AND
     - **iv.** Documentation provided that prior to initiating Cabenuva or 1 month lead-in with Vocabria (cabotegravir tablets), the patient was treated with a stable regimen (≥ 3 months) of antiretrovirals for HIV-1; AND
     - **v.** The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection; OR
   - **B)** Patient is Currently Receiving Cabenuva. Approve if documentation provided that the patient has HIV-1 RNA < 50 copies/mL (viral suppression).

   Dosing. Approve ONE of the following dosing regimens (A or B):
   - **A)** Once Monthly Dosing Regimen: Approve 600 mg/900 mg intramuscularly for one dose, then approve 400 mg/600 mg intramuscularly once-monthly thereafter (every 4 weeks); OR
   - **B)** Every 2 Months Dosing Regimen: Approve 600 mg/900 mg intramuscularly for two doses, 1 month apart, then approve 600 mg/900 mg intramuscularly once every 2 months thereafter (every 8 weeks).

Cabenuva for any other use is considered not medically necessary, 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)-1 Infection.** Cabenuva is not indicated for the prevention of HIV.

2. **Co-administration with Antiretrovirals for Human Immunodeficiency Virus (HIV) Treatment.** Because Cabenuva is a complete regimen, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.[1]

3. **Human Immunodeficiency Virus (HIV)-2 Infection.** Cabenuva is not indicated in patients with HIV-2 infection.[1] The Department of Health and Human Services guidelines further note that HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors, therefore, Cabenuva is not recommended for people with HIV-2.[5]

References

1. Cabenuva® injection [prescribing information]. Research Triangle Park, NJ: ViiV/GlaxoSmithKline; September 2024.
2. Orkin C, Arasteh K, Hernandez-Mora G, et al. Long-acting cabotegravir and rilpivirine after oral induction for HIV-1 infection. *N Engl J Med.* 2020; 382:1124-1135.
3. Swindells S, Andrade-Villaneuva JF, Richmond GJ, et al. Long-acting cabotegravir and rilpivirine for maintenance of HIV-1 suppression. *N Engl J Med.* 2020; 382; 12:1112-1123.
4. Rajesh RT, Landovitz RJ, and Sax P, et al. Antiretroviral drugs for treatment and prevention of HIV in adults: 2024 recommendations of the International Antiviral Society USA-Panel. *JAMA.* 2024 Dec 1 [Epub ahead of Print].
5. 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 12, 2024. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed on: February 4, 2025.
6. Orkin C, Bernal E, Tan DHS, et al. Initiation of long-acting cabotegravir plus rilpivirine as direct-to-injection or with an oral lead-in in adults with HIV-1 infection: Week 124 results of the open-label phase 3 FLAIR study. *Lancet HIV*. 2021;11: e668-e678.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Human Immunodeficiency Virus (HIV)-1, Treatment.** • **Added** criterion for minimum weight. • **Added** criterion for screening individual treated with a stable regimen for at least 3 months. • **Updated** criterion for continuation of treatment.	6/1/2024
Annual Revision	**Human Immunodeficiency Virus (HIV)-1, Treatment.** • **Added** documentation requirements (where noted) to medical necessity criteria.	5/1/2025

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