CARECONTINUUM™

# UTILIZATION MANAGEMENT MEDICAL POLICY

**POLICY:** Human Immunodeficiency Virus – Cabenuva Utilization Management Medical Policy
- Cabenuva® (cabotegravir extended-release intramuscular injection; rilpivirine extended-release intramuscular injection, co-packaged – ViiV/GlaxoSmithKline)

**REVIEW DATE:** 02/05/2025

## 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.

## POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Cabenuva. 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. 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, initial approval requires Cabenuva to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Documentation:** Documentation is required for use of Cabenuva as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

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

**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.** Patient has HIV-1 RNA < 50 copies/mL (viral suppression) **[documentation required]**; AND
     - **iv.** 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 **[documentation required]**; 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 the patient has HIV-1 RNA < 50 copies/mL (viral suppression) **[documentation required]**.

   **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).

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cabenuva is not recommended in the following situations:

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]

4. 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. 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.

## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Annual Revision | No criteria changes. | 02/01/2023 |
| Selected Revision | **Human Immunodeficiency Virus Type-1 (HIV-1), Treatment:** Criteria requiring that, according to the prescriber, the patient either has difficulty maintaining compliance with a daily antiretroviral regimen for HIV-1 OR has severe gastrointestinal issues that may limit absorption or tolerance of oral medications was removed. | 12/06/2023 |
| Annual Revision | **Human Immunodeficiency Virus Type-1 (HIV-1), Treatment:** The criterion requiring that prior to initiating Cabenuva or 1 month lead-in with Vocabria (cabotegravir tablets), the patient was treated with a stable regimen (≥ 4 months) of antiretrovirals for HIV-1, was modified. The timeframe for the stable regimen was changed from ≥ 4 months to ≥ 3 months.<br>**Human Immunodeficiency Virus (HIV)-2 Infection.** This condition was added to the Conditions not Recommended for Approval. | 02/07/2024 |
| Annual Revision | No criteria changes. | 02/05/2025 |