PRIOR AUTHORIZATION POLICY

POLICY: Human Immunodeficiency Virus – Cabenuva Prior Authorization Policy
- Cabenuva® (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension, co-packaged – ViiV/GlaxoSmithKline)

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OVERVIEW

Cabenuva, 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, is indicated as a complete regimen for the treatment of **HIV-1 infection** in adults to replace their current antiretroviral (ARV) regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen with no history of treatment failure and with no known or suspected resistance to cabotegravir or rilpivirine.[1]

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) should be used for approximately 1 month (at least 28 days) prior to the initiation of Cabenuva to assess the tolerability of cabotegravir and rilpivirine. On the last day of oral lead-in, the first dose of Cabenuva (600 mg/900 mg) is administered; monthly doses of Cabenuva (400 mg/600 mg) are administered starting at Month 3.

Table 1. Recommended Oral Lead-In and IM Injection Dosing Schedule in Adults.[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)

IM – Intramuscular.

If monthly Cabenuva doses are missed or delayed by > 7 days and oral therapy has not been taken in the interim, clinically reassess the patient to determine if resumption of Cabenuva remains appropriate. If Cabenuva will be continued, see Table 2 for dosing recommendations.

Table 2. Cabenuva Dosing Recommendation after Missed Injections.[*1]

Time Since Last Dose of Cabenuva	Recommendation
≤ 2 months	Resume with 400 mg (2 mL) cabotegravir and 600 mg (2 mL) rilpivirine IM monthly injections as soon as possible.
> 2 months	Re-initiate the patient with 600 mg (3 mL) cabotegravir and 900 mg (3 mL) rilpivirine IM injections then continue to follow the 400 mg (2 mL) cabotegravir and 600 mg (2 mL) rilpivirine IM monthly injection dosing schedule.

[*]Refer to oral dosing recommendations if a patient plans to miss a scheduled injection visit; IM – Intramuscular.

Clinical Efficacy

The use of Vocabria + Edurant as an oral lead-in and Cabenuva once monthly for maintenance therapy in adults with HIV-1 was evaluated in two published, Phase III, randomized, multicenter, active-controlled, parallel-arm, open-label, non-inferiority pivotal trials (FLAIR and ATLAS).[3,4] In FLAIR, patients were naïve to antiretroviral therapy and started on Triumeq® (abacavir/dolutegravir/lamivudine tablets) for 20 weeks then continued on Triumeq or were switched to the long-acting regimen of Vocabria/Cabenuva in accordance with the FDA-approved dosing regimen.[3] In ATLAS, patients who were virally suppressed on an oral antiretroviral regimen (excluding Triumeq) continued on their antiretroviral regimen or were switched to the long-acting regimen of Vocabria/Cabenuva in accordance with the FDA-approved dosing regimen.[4] In FLAIR (n = 566), at Week 48, the long-acting regimen was non-inferior to Triumeq; 2.1% and 2.5% of patients, respectively, did not maintain viral suppression.[3] In ATLAS (n = 618), at Week 48, the long-acting regimen was non-inferior to patients existing oral antiretrovirals: 1.6% and 1.0% of patients, respectively, did not maintain viral suppression.[4]

Guidelines

Cabenuva is addressed as an unapproved product in the International Antiviral Society-USA (IAS-USA) Panel Recommendations for Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults (2020); Cabenuva and Vocabria have not been addressed in the Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (last updated December 18, 2019).[4,5]

According to the IAS-USA, in the setting of viral suppression, switching from a three-drug regimen to a two-drug regimen is an appropriate strategy to manage toxic side effects, intolerance, adherence, or patient preference provided that both agents are fully active.[4] Recommended regimens include: dolutegravir/lamivudine (available as Dovato® [dolutegravir/lamivudine tablets] or Tivicay® [dolutegravir tablets] + lamivudine [Epivir®, generics]), dolutegravir/rilpivirine (available as Juluca® [dolutegravir/rilpivirine tablets] or Tivicay + Edurant), a boosted protease inhibitor (lopinavir, atazanavir [Reyataz®, generics], or darunavir [Prezista®, generics]) + lamivudine, or a long-acting injectable two-drug regimen of Cabenuva pending approval by regulatory bodies and availability. The DHHS guidelines provide identical examples of successful strategies for switching from three-drug to two-drug regimens in individuals with suppressed HIV (with the noted absence of Cabenuva likely due to the timing of the last update).[5]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Cabenuva. 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 Indications

1. **Human Immunodeficiency Virus (HIV).** Approve for the duration below if the patient meets ONE of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets all of the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has HIV type-1 (HIV-1) infection; AND
     - **iii.** Patient has HIV-1 RNA < 50 copies/mL (viral suppression) **[documentation required]**; AND
     - **iv.** Patient has completed, or will complete, and tolerated 1 month of therapy with Vocabria (cabotegravir tablets) + Edurant (rilpivirine tablets), according to the prescriber; AND
     - **v.** Prior to initiating Vocabria, the patient was treated with a stable regimen (≥ 4 months) of antiretrovirals for HIV-1 **[documentation required]**; AND
     - **vi.** According to the prescriber, the patient meets ONE of the following (a or b):
       - **a)** Patient has difficulty maintaining compliance with a daily antiretroviral regimen for HIV-1; OR
       - **b)** Patient has severe gastrointestinal issues that may limit absorption or tolerance of oral medications; AND
     - **vii.** The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection.
   - **B)** Patient is Currently Receiving Cabenuva. Approve for 1 year if the patient meets all of the following (i and ii):
     - **i.** Patient has HIV type-1 (HIV-1) infection; AND
     - **ii.** Patient has HIV-1 RNA < 50 copies/mL (viral suppression) **[documentation required]**.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Cabenuva is not recommended in the following situations:

1. **Pre-exposure Prophylaxis (PrEP).** Cabenuva is not indicated for the prevention of human immunodeficiency virus (HIV) in patients who are uninfected, but at risk of acquisition of HIV. Data from two unpublished trials have demonstrated the superiority of cabotegravir extended-release injectable suspension to Truvada® (tenofovir disoproxil fumarate/emtricitabine tablets, generics) for PrEP in cisgender men and transgender men who have sex with men as well as in cisgender women.[5] IAS-USA guidelines recommend cabotegravir extended-release injectable suspension for PrEP in cisgender men and transgender women who have sex with men; every 8 week maintenance dosing is recommended and oral lead-in with Vocabria is optional.[4] The other recommended regimens for PrEP are daily Truvada (all at-risk populations) or Descovy® (tenofovir alafenamide/emtricitabine tablets) [men who have sex with men with/at risk for kidney dysfunction, osteopenia, or osteoporosis]. Truvada and Descovy are FDA-approved for PrEP; neither Vocabria nor Cabenuva are FDA-approved for PrEP.

2. **Human Immunodeficiency Virus, Antiretroviral Treatment-Naïve Patients.** Cabenuva is indicated as a complete regimen for the treatment of HIV-1 infection in adults 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] In two pivotal trials, patients were either previously treated for 4 months (20 weeks) with Triumeq® (abacavir/dolutegravir/lamivudine tablets) or were on a stable antiretroviral regimen for ≥ 6 months.[2,3]

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

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 Healthcare/GlaxoSmithKline; January 2021.
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. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults. 2020 recommendations of the International Antiviral Society-USA Panel. *JAMA.* 2020;324(16):1651-1669.
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. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Updated December 18, 2019. Accessed April 28, 2021.