

# Long-Acting Injectable Antiretroviral Agents for HIV

Policy Number: PHARMACY 337.2 T2  
Effective Date: July 1, 2021

[➔ Instructions for Use](#)

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## Related Policies

- [Acquired Rare Disease Drug Therapy Exception Process](#)
- [Drug Coverage Guidelines](#)
- [Provider Administered Drugs – Site of Care](#)
- [Review at Launch for New to Market Medications](#)

## Coverage Rationale

[➔ See Benefit Considerations](#)

Cabenuva (cabotegravir/rilpivirine) has been added to the Review at Launch program. Some members may not be eligible for coverage of this medication at this time. Refer to the policy titled [Review at Launch for New to Market Medications](#) for additional details.

This policy refers to the following long-acting injectable antiretroviral products:

- Cabenuva (cabotegravir/rilpivirine)

Cabenuva (cabotegravir/rilpivirine) is proven for the treatment of a human immunodeficiency virus type-1 (HIV-1) in patients who are virologically suppressed (HIV-1 RNA less than 50 copies per mL). Cabenuva is medically necessary when the following additional criteria are met:<sup>1-3</sup>

- For initial therapy, all of the following:
  - Diagnosis of HIV-1 infection; and
  - Patient has no prior virologic failures or baseline resistance to either cabotegravir or rilpivirine; and
  - Patient is currently on a stable antiretroviral regimen; and
  - Submission of medical records (e.g., chart notes, laboratory results) showing viral suppression (HIV-1 RNA less than 50 copies per mL) for at least 6 months prior to initiation of Cabenuva; and
  - Provider attests that patient demonstrates treatment readiness by both of the following:
    - Patient understands the risks of missed doses of Cabenuva
    - Patient has the ability to adhere to the required monthly injection appointments;
 and
  - Provider confirms that tolerability will be assessed using a 28-day oral lead-in of Vocabria (cabotegravir) and Edurant® (rilpivirine) tablets prior to the first injection of Cabenuva; and
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Initial authorization is for no more than 12 months.

- For continuation therapy, all of the following:
  - Patient has previously received treatment with Cabenuva; and
  - Physician confirms that the patient has achieved and maintained viral suppression (HIV-1 RNA less than 50 copies per mL) while on Cabenuva therapy; and
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Authorization is for no more than 12 months.

Cabenuva is unproven and not medically necessary for the treatment of:

- Human immunodeficiency virus type-1 (HIV-1) in patients who are not currently virally suppressed (HIV-1 RNA less than 50 copies per mL)

## Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

Required Clinical Information
<b>Cabenuva</b>
For initial therapy requests, medical notes or laboratory results documenting the following: <ul style="list-style-type: none"> <li>• Viral suppression (HIV-1 RNA less than 50 copies per mL) for at least 6 months prior to initiation of Cabenuva</li> </ul>

## Prior Authorization Requirements

- Prior to Oct. 1, 2021: Prior authorization is not required, however it is strongly recommended for Cabenuva. While no penalty will be imposed for failure to request a pre-service review, if one is not requested, a medical necessity review will be conducted post-service to determine coverage. It is the referring physician's responsibility to provide medical documentation to demonstrate clinical necessity for the medication. Refer to [Review at Launch for New to Market Medications](#).
- On or after Oct. 1, 2021: Prior authorization is required in all sites of service.

## Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

HCPCS Code	Description
C9077	Injection, cabotegravir and rilpivirine, 2 mg/3 mg
J3490	Unclassified drugs

Diagnosis Code	Description
B20	Human immunodeficiency virus [HIV] disease
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status

## Background

Cabenuva (cabotegravir/rilpivirine) is a 2-drug co-packaged product of extended-release injectable suspension formulations of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1

non-nucleoside reverse transcriptase inhibitor (NNRTI). Cabotegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration which is essential for the HIV replication cycle. Rilpivirine is a diarylpyrimidine NNRTI of HIV-1 and inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase (RT).<sup>1</sup>

## Benefit Considerations

Some Certificates of Coverage allow coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met; refer to the Administrative Policy titled [Acquired Rare Disease Drug Therapy Exception Process](#).

## Clinical Evidence

The efficacy of Cabenuva has been evaluated in two Phase 3 randomized, multicenter, activecontrolled, parallel-arm, openlabel, non-inferiority trials:<sup>2-3</sup>

- Trial 201584 (FLAIR, [NCT02938520]), (n = 629): HIV-1-infected, antiretroviral treatment (ART)- naive subjects received a dolutegravir INSTI-containing regimen for 20 weeks (either dolutegravir/abacavir/lamivudine or dolutegravir plus 2 other NRTIs if subjects were HLA-B\*5701 positive). Subjects who were virologically suppressed (HIV-1 RNA less than 50 copies/mL, n = 566) were then randomized (1:1) to receive either a cabotegravir plus rilpivirine regimen or remain on the current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly injections with Cabenuva for an additional 44 weeks.
- Trial 201585 (ATLAS, [NCT02951052]), (n = 616): HIV-1-infected, ART-experienced, virologically-suppressed (for at least 6 months; median prior treatment duration was 4.3 years) subjects (HIV-1 RNA less than 50 copies/mL) were randomized and received either a cabotegravir plus rilpivirine regimen or remained on their current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly injections with Cabenuva for an additional 44 weeks.

The primary analysis was conducted after all subjects completed their Week 48 visit or discontinued the trial prematurely. The primary endpoint of FLAIR and ATLAS was the proportion of subjects with plasma HIV-1 RNA greater than or equal to 50 copies/mL at Week 48. In both FLAIR and ATLAS 2% of subjects met the primary endpoint as compared to 2% and 1% in the comparator arms respectively. Subjects in both the FLAIR and ATLAS trials were virologically suppressed prior to Day 1 or at study entry, respectively, and no clinically relevant change from baseline in CD4+ cell counts was observed.<sup>1</sup>

In February 2021, the United States Department of Health and Human Services updated their guidelines for the use of antiretroviral agents in adults and adolescents with HIV with specific recommendations for use of Cabenuva.<sup>2</sup> The guidelines panel made the following recommendation: “Cabenuva can be used as an optimization strategy for people with HIV currently on oral ART with documented viral suppression for at least 3 months (although optimal duration is not defined)”. In the ATLAS trial, participants had viral suppression for at least 6 months on standard oral ART prior to randomization. A key consideration noted by the guidelines panel includes “experienced participants enrolled in completed clinical trials for Cabenuva were selected based on their history of good adherence and engagement in care, as documented by sustained viral suppression at baseline. Therefore, these therapies are currently recommended for participants who are similarly engaged in care.”

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Cabenuva, a 2-drug co-packaged product of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand

transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI), is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

## References

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealth Group National Pharmacy & Therapeutics Committee. [2021D00103A]

1. Cabenuva [package insert]. Research Triangle Park, NC: ViiV Healthcare. January 2021.
2. Swindells S, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression (ATLAS). N Engl J Med. 2020 March 382:1112-1123.
3. Orkin C, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection (FLAIR). N Engl J Med. 2020 March 382:1124-1135.
4. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Updated February 24, 2021. Available at: <https://aidsinfo.nih.gov/guidelines>. Accessed April 2, 2021.

## Policy History/Revision Information

Date	Summary of Changes
07/01/2021	<p><b>Applicable Codes</b></p> <ul style="list-style-type: none"> <li>Updated list of applicable HCPCS codes to reflect quarterly edits; replaced C9399 with C9077</li> </ul> <p><b>Supporting Information</b></p> <ul style="list-style-type: none"> <li>Archived previous policy version PHARMACY 337.1 T2</li> </ul>

## Instructions for Use

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

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