

Long-Acting Injectable Antiretroviral Agents for HIV

Policy Number: CS2021D0103B
Effective Date: October 1, 2021

[Instructions for Use](#)

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Commercial Policy
• Long-Acting Injectable Antiretroviral Agents for HIV

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Florida	Refer to the state’s Medicaid clinical policy
Indiana	None
Kentucky	None
Louisiana	None
North Carolina	None
Pennsylvania	Refer to the state’s Medicaid clinical policy
Washington	Refer to the state’s Medicaid clinical policy

Coverage Rationale

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

- 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:¹⁻³

- 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.

HCPSC Code*	Required Clinical Information
Cabenuva	
J0741	For initial therapy requests, medical notes or laboratory results documenting the following: <ul style="list-style-type: none"> ● Viral suppression (HIV-1 RNA less than 50 copies per mL) for at least 6 months prior to initiation of Cabenuva

*For code description, see the [Applicable Codes](#) section.

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 federal, state, or contractual requirements 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 and Guidelines may apply.

HCPSC Code	Description
J0741	Injection, cabotegravir and rilpivirine, 2 mg/3 mg

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).¹

Clinical Evidence

The efficacy of Cabenuva has been evaluated in two Phase 3 randomized, multicenter, active-controlled, parallel-arm, open-label, non-inferiority trials:²⁻³

- Trial 201584 (FLAIR, [NCT02938520]), (n = 629): HIV-1-infected, antiretroviral treatment (ART)-naïve 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.¹

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.² 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

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
10/01/2021	<p>Coverage Rationale</p> <ul style="list-style-type: none"> Removed reference link to the Medical Benefit Drug Policy titled <i>Review at Launch for New to Market Medications</i> <p>Documentation Requirements</p> <ul style="list-style-type: none"> Updated list of CPT codes with associated documentation requirements to reflect quarterly edits: <ul style="list-style-type: none"> Removed C9077 Replaced J3490 with J0741 <p>Applicable Codes</p> <ul style="list-style-type: none"> Updated list of applicable HCPCS codes to reflect quarterly edits: <ul style="list-style-type: none"> Removed C9077 Replaced J3490 with J0741 <p>Supporting Information</p> <ul style="list-style-type: none"> Archived previous policy version CS2021D0103A

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.