Drug and Biologic Coverage Policy

Cabotegravir-Rilpivirine

Overview

This policy supports medical necessity review for cabotegravir-rilpivirine (Cabenuva™).

Medical Necessity Criteria

Cabotegravir-rilpivirine (Cabenuva) is considered medically necessary when the following are met:

1. **Human Immunodeficiency Virus (HIV)**. Individual meets ALL of the following criteria:
   A. Individual is ≥ 18 years of age
   B. Individual has HIV type-1 (HIV-1) infection
   C. Individual has HIV-1 RNA < 50 copies/mL (viral suppression) at 12 and 6 months prior to start of therapy
   D. Individual has completed, or will complete, and tolerated 1 month of therapy with Vocabria (cabotegravir tablets) + Edurant (rilpivirine tablets), according to the prescriber

Related Coverage Resources

HIV Products
HIV Products for Individual and Family Plans
Cabotegravir

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. 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.
E. Prior to initiating Vocabria, individual was treated with a stable regimen (≥ 4 months) of antiretrovirals for HIV-1

F. According to the prescriber, individual meets ONE of the following:
   i. Individual has difficulty maintaining compliance with a daily antiretroviral regimen for HIV-1
   ii. Individual has severe gastrointestinal issues that may limit absorption or tolerance of oral medications

G. The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection.

Reauthorization Criteria

Cabotegravir-rilpivirine (Cabenuva) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Cabotegravir-rilpivirine (Cabenuva) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Pre-exposure Prophylaxis (PrEP).** Cabenuva is not indicated for the prevention of human immunodeficiency virus (HIV) in individuals who are uninfected, but at risk of acquisition of HIV. Data from two uncontrolled 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. 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. The other recommended regimens for PrEP are daily Truvada (all at-risk populations) or Descovy® (tenofovir alafenamide/emtricitabine tablets) [MSM 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 Individuals.** 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. In two pivotal trials, individuals 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.

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.

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Background**

**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**

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

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**

<table>
<thead>
<tr>
<th>Time Since Last Dose of Cabenuva</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 months</td>
<td>Resume with 400 mg (2 mL) cabotegravir and 600 mg (2 mL) rilpivirine IM monthly injections as soon as possible.</td>
</tr>
<tr>
<td>&gt; 2 months</td>
<td>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.</td>
</tr>
</tbody>
</table>

*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). 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. 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. 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 (adjusted difference -0.4%; 95% confidence interval [CI]: -2.8, 2.1). 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 (adjusted difference 0.6%; 95% CI: -1.2, 2.5).

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). 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. 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).

References