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Coverage Policy Number **IP0124**

Vocabria

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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.

Overview

This policy supports medical necessity review for cabotegravir (Vocabria®).

The manufacturer will be supplying Vocabria (cabotegravir) directly to individuals. When applicable, the below medically necessity criteria will apply.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Cabotegravir (Vocabria) is considered medically necessary when ONE of the following is met:

1. **Human Immunodeficiency Virus (HIV) Treatment, Oral Lead-In to Assess the Tolerability of cabotegravir.** Individual meets **ALL** of the following criteria:
    A. 12 years of age, or older

B. Virologically suppressed (HIV-1 RNA < 50 copies/mL) at 12 and 6 months prior to start of therapy
C. Currently receiving antiretrovirals for the treatment of HIV-1 with a stable regimen (≥ 4 months)
D. Will receive a one month trial of Vocabria with Edurant to assess tolerability prior to starting Cabenuva.
E. According to the prescriber, individual meets ONE of the following:
    i. 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
F. Medication is prescribed by, or in consultation with, a physician who specializes in the treatment of HIV infection

2. **Human Immunodeficiency Virus (HIV) Treatment, Oral Therapy for Planned Missed Doses of Cabenuva.** Individual meets **ALL** of the following criteria:
    A. 12 years of age or older
    B. Virologically suppressed (HIV-1 RNA < 50 copies/mL)
    C. Received at least 1 maintenance dose of Cabenuva (400 mg/600 mg)
    D. Plans to miss up to two scheduled doses of Cabenuva by greater than 7 days, according to the prescriber
    E. The medication will be prescribed in combination with Edurant (rilpivirine tablets)
    F. Medication is prescribed by, or in consultation with, a physician who specializes in the treatment of HIV infection

3. **Pre-exposure Prophylaxis of Human Immunodeficiency Virus (HIV)-1 Infection, Oral Lead-In to Assess the Tolerability of cabotegravir.** Individual meets **ALL** of the following criteria:
    A. Weighs at least 35 kg
    B. If tolerated, Apretude will be started upon completion of approximately 1 month of therapy with Vocabria
    C. Medication is prescribed by, or in consultation with, a physician who specializes in the treatment of HIV infection

4. **Pre-exposure Prophylaxis of Human Immunodeficiency Virus (HIV)-1 Infection, Oral Therapy for Planned Missed Doses of Apretude (cabotegravir extended-release injectable suspension).** Individual meets **ALL** of the following criteria:
    A. Weighs at least 35 kg
    B. Plans to miss ONE scheduled dose of Apretude by greater than 7 days, according to the prescriber
    C. Medication is prescribed by, or in consultation with, a physician who specializes in the treatment of HIV infection.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Not applicable for continuation beyond initial approval duration.

Authorization Duration

Initial approval duration:
1. Human Immunodeficiency Virus (HIV), Oral Lead-In to Assess the Tolerability of cabotegravir: up to 1 month

2. Human Immunodeficiency Virus (HIV), Oral Therapy for Planned Missed Doses of Cabenuva: up to 2 months
3. Pre-exposure Prophylaxis of Human Immunodeficiency Virus (HIV)-1 Infection, Oral Lead-In to Assess the Tolerability of cabotegravir: up to 1 month
4. Pre-exposure Prophylaxis of Human Immunodeficiency Virus (HIV)-1 Infection, Oral Therapy for Planned Missed Doses of Apretude (cabotegravir extended-release injectable suspension): up to 2 months

Reauthorization approval duration: not applicable

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Human Immunodeficiency Virus Treatment in Antiretroviral Treatment-Naïve Individuals.** Vocabria is indicated in combination with Edurant (rilpivirine tablets) for the short-term treatment of HIV-1 infection in adults 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 either cabotegravir or rilpivirine.[1] 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.[2,3]

2. **Duration of Use for > 2 Consecutive Months.** The recommended duration of Vocabria therapy is 1 month for oral lead-in.[1] Vocabria is also indicated as a daily regimen to replace up to two planned missed injections of Cabenuva (administered once monthly) for up to two consecutive months or to replace one planned missed injection of Apretude (administered once every 2 months).

3. **Co-administration with Antiretrovirals for Human Immunodeficiency Virus Treatment other than Edurant.** Because Vocabria in combination with Edurant (rilpivirine tablets) is a complete regimen, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.[1]

Background

OVERVIEW
Vocabria, a human immunodeficiency virus type-1 (HIV-1) integrase strand-transfer inhibitor, is indicated for the following uses:

- **Short-term treatment of HIV-1 infection** in combination with Edurant® (rilpivirine tablets) for the in adults and adolescents 12 years of age and older and weighing at least 35 kg 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 either cabotegravir or rilpivirine, for use as:[1]
    - **Oral lead-in** to assess the tolerability of cabotegravir prior to administration of Cabenuva® (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension, co-packaged).
    - **Oral therapy for patients who will miss planned injection dosing with Cabenuva**.

- **Short-term pre-exposure prophylaxis (PrEP) of HIV-1 infection** in at-risk adults and adolescents and weighing at least 35 kg for short-term PrEP to reduce the risk of sexually acquired HIV-1 infection. Patients must have a negative HIV-1 test prior to initiating Vocabria for HIV-1 PrEP. Vocabria may be used as:
    - **Oral lead-in** to assess tolerability of Apretude (cabotegravir extended-release injectable suspension).

- **Oral therapy for patients who will miss planned injection dosing with Apretude.**

Short-term treatment of HIV-1 infection
For oral lead-in, the recommended dose is Vocabria 30 mg once daily (QD) in combination with Edurant 25 mg QD at approximately the same time each day with a meal for approximately 1 month (28 days).[1] The last oral dose should be taken on the same day monthly injections with Cabenuva are started.

If a patient plans to miss scheduled monthly injections of Cabenuva by more than 7 days, daily oral therapy is taken to replace up to two consecutive monthly injection visits.[1] The first dose of Vocabria 30 mg with Edurant 25 mg should be taken approximately 1 month after the last maintenance injection dose of Cabenuva and continued until the day injection dosing is restarted.[1,6]

Short-term PrEP of HIV-1 infection
For oral lead-in, which is optional for PrEP, the recommended dose is Vocabria 30 mg for approximately 1 month (28 days).[1] Following the oral lead-in, start injection of Apretude on the last day of oral lead-in or within 3 days.

If the patient plans to miss a scheduled injection of Apretude by more than 7 days, daily oral therapy is taken to replace one every 2-month injection visit.[1] The first dose of Vocabria 30 mg should be taken approximately 2 months after the last injection dose of Apretude. Restart Apretude on the day oral dosing completes or within 3 days.

HIV Treatment Guidelines
The Department of Health and Human Services (DHHS) Guidelines for the Use of Antiviral Agents in Adults and Adolescents with HIV (August 16, 2021) recognize Cabenuva as a long-acting ARV regimen that is an optimization option for patients who are engaged with their health care, virologically suppressed on oral therapy for 3 to 6 months, and who agree to make the frequent clinic visits needed.[4] The available data with Cabenuva are noted to support monthly IM injections to replace an existing oral ARV regimen in people with HIV-1 with sustained viral suppression for 3 to 6 months (optimal duration is not defined), who have good adherence and engagement in care, no baseline resistance to either medication, no prior virologic failures; who do not have active or occult hepatitis B virus (HBV) infection (unless the patient also is receiving an HBV active regimen); who are not pregnant or planning on becoming pregnant; and who are not receiving medications with significant drug interactions with oral (during lead-in or bridging therapy) or Cabenuva.

The DHHS guidelines do not recommend Cabenuva as initial therapy for people with HIV-1 because of the lack of data supporting the efficacy of this combination in ARV-naïve patients.[4] Patients desiring to use Cabenuva early in their treatment history should first attain viral suppression on a recommended regimen, then transition to a month of oral Vocabria + Edurant with maintenance of suppression before transitioning to Cabenuva.

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);.[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 the timing of the last update).[5]

PrEP Guidelines
Apretude has been incorporated into the US Public Health Service PrEP for the prevention of HIV infection in the US clinical practice guidelines (December 2021).[7] The update was published just prior to the FDA approval of Apretude. The guidelines recommend that all sexually active adult and adolescent patients receive information

about PrEP.[1] Table 1 provides a summary of the recommendations for daily oral PrEP and Apretude (every 2 months).

Table 1. US Public Health Service PrEP Recommendations (December 2021).[7]

	Recommendation for PrEP	Evidence Rating
Apretude[a]	For adults and adolescents who report sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition.	IA
FTC/TDF	For adult and adolescent (≥ 35 kg) **men and women**: • **Sexually active individuals** who report sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition; OR • **IDU** and report injection practices that place them at substantial ongoing risk of HIV exposure and acquisition.	1A
Descovy	For adult and adolescent (≥ 35 kg) **cis-gender men**[*] and **transgender women[†]:** • **Sexually active individuals** who report sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition. Descovy PrEP has **not been studied in cis-gender women[‡]** and is **not recommended** for HIV prevention for women or other individuals at risk through receptive vaginal sex (IA).	IA (cis-gender men) IIB (transgender women)

PrEP – Pre-exposure prophylaxis; [a] Conditioned on FDA-approval at the time of guideline publication; HIV – Human immunodeficiency virus; FTC/TDF – Emtricitabine/tenofovir disoproxil fumarate; IDU – Injection drug user(s); [*] Individuals assigned male sex at birth whose gender identity is male; [†] Individuals assigned male sex at birth whose gender identity is female; [‡] Individuals assigned female sex at birth whose gender identity is female.

The Guidelines also make the following points related to monitoring for PrEP.[7] Prior to prescribing PrEP, acute and chronic HIV infection must be excluded by symptom history and HIV testing must be performed immediately before any PrEP regimen is started (IA). HIV infection should be assessed every 2 months for patients receiving Apretude so that individuals with incident infection do not continue taking PrEP. PrEP regimens are inadequate therapy for established HIV infection, and their use in individuals with early HIV may create resistance to one or more of the medications (IA). Renal function should be assessed by estimated creatinine clearance (eCrCl) at baseline for PrEP patients taking daily emtricitabine/tenofovir disoproxil fumarate (FTC/TDF; Truvada®, generic) or Descovy® (emtricitabine/tenofovir alafenamide tablets), and monitored periodically so that patients in whom clinically significantly renal dysfunction is developing do not continue to take it (IIA). When PrEP is prescribed, clinicians should provide access to support for medication adherence and continuation in follow-up PrEP care (IIA) and additional proven effective risk-reduction services, as indicated by reported HIV exposure-prone behaviors, to enable the use of PrEP in combination with other effective prevention methods to reduce risk for sexual acquisition of STIs or bloodborne bacterial and viral infections though IDU (IIIA).

Recommendations specific to prescribing Apretude for PrEP are made.[7] Apretude may be especially appropriate for patients with significant renal disease, those who have difficulty with adherent use of oral PrEP and those who prefer injections every 2 months to an oral PrEP dosing schedule. Apretude should not be administered to an individual with a history of hypersensitivity reaction to cabotegravir. The recommended dosing in the guidelines is Apretude 600 mg into the gluteal muscle every 2 months; Vocabria 30 mg daily for 4-weeks as lead-in is optional. The oral lead-in may be used in patients who are especially worried about AEs to relieve anxiety about using Apretude. In patients who have been taking daily oral PrEP (i.e., Descovy or FTC/TDF), Apretude can be initiated as soon as an HIV-1 RNA test result confirms that they remain HIV negative (ideally within 1 week of the initiation visit).

References

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