HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VOCABRIA safely and effectively. See full prescribing information for VOCABRIA.

VOCABRIA (cabotegravir) tablets, for oral use
Initial U.S. Approval: 2021

----------RECENT MAJOR CHANGES ----------
Warnings and Precautions, Depressive Disorders (5.4) 12/2023

---------- INDICATIONS AND USAGE----------
HIV-1 Treatment: VOCABRIA is an HIV-1 integrase strand transfer inhibitor (INSTI) indicated in combination with EDURANT (rilpivirine) for short-term treatment of HIV-1 infection 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. (1.1)
HIV-1 Pre-Exposure Prophylaxis: VOCABRIA is indicated for short-term pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating VOCABRIA for HIV-1 PrEP. (1.2)
VOCABRIA may be used as:
- oral lead-in to assess the tolerability of cabotegravir prior to administration of CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) for HIV-1 treatment or APRETUDE (cabotegravir extended-release injectable suspension) for HIV-1 PrEP. (1.1, 1.2)
- oral therapy for patients who will miss planned injection dosing with CABENUVA for HIV-1 treatment or APRETUDE for HIV-1 PrEP. (1.1, 1.2)

----------DOSAGE AND ADMINISTRATION----------
- One tablet of VOCABRIA 30 mg taken orally once daily in combination with 1 tablet of EDURANT 25 mg taken orally once daily with a meal:
  - for approximately 1 month if oral lead-in is used for HIV-1 treatment. (2.1)
  - for up to 2 months to replace up to 2 consecutive missed monthly injections of CABENUVA (2.2)

  Refer to 2.1 for dosing recommendations for missed injections. (2.1)
- HIV-1 Screening: Screen all individuals for HIV-1 infection prior to initiating VOCABRIA and APRETUDE for HIV-1 PrEP and at least once every 3 months while taking APRETUDE. (2.2)
- One tablet of VOCABRIA 30 mg taken orally once daily for approximately 1 month if oral lead-in is used for HIV-1 PrEP. Refer to 2.2 for dosing recommendations for missed injections. (2.2)

---------- DOSAGE FORMS AND STRENGTHS----------
Tablets: 30 mg (3)

---------- CONTRAINDICATIONS ----------
- Previous hypersensitivity reaction to cabotegravir. (4)
- Coadministration with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, and rifapentine. (4)
- Positive HIV-1 status for HIV-1 PrEP. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- HIV-1 PrEP: Comprehensive management to reduce the risk of HIV-1 acquisition. (5.1)
- Hypersensitivity reactions have been reported in association with integrase inhibitors. Discontinue VOCABRIA immediately if signs or symptoms of hypersensitivity reactions develop. (5.2)
- Hepatotoxicity has been reported in patients receiving cabotegravir. Monitoring of liver chemistries is recommended when VOCABRIA is used for HIV-1 treatment. Clinical and laboratory monitoring should be considered when VOCABRIA is used for HIV-1 PrEP. Discontinue VOCABRIA if hepatotoxicity is suspected. (5.3)
- Depressive disorders have been reported with VOCABRIA when used with EDURANT for HIV-1 treatment. Prompt evaluation is recommended for depressive symptoms. (5.4)
- Risks Associated with Combination Treatment: Review the prescribing information for EDURANT for information on rilpivirine prior to initiation of VOCABRIA in combination with EDURANT. (5.6)

---------- ADVERSE REACTIONS ----------
- In patients with HIV-1, the most common adverse reactions observed in at least 3 participants receiving VOCABRIA were fatigue, headache, diarrhea, nausea, dizziness, abnormal dreams, anxiety, insomnia, abdominal discomfort, abdominal distension, and asthenia. (6.1)
- In individuals without HIV-1 receiving VOCABRIA, the most common adverse reactions reported in ≥1% were headache, diarrhea, nausea, dizziness, upper respiratory tract infection, somnolence, fatigue, abnormal dreams, and abdominal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact ViiV Healthcare at 1-877-844-8872 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS----------
- Refer to the full prescribing information for important drug interactions with VOCABRIA. (4, 5.5, 7)
- VOCABRIA in combination with EDURANT is a complete regimen for HIV-1 treatment. Coadministration with other antiretroviral medications for PrEP is not recommended. (7.1)
- Drugs that induce uridine diphosphate glucuronosyltransferase (UGT)1A1 may decrease the plasma concentrations of cabotegravir. (4, 7.2, 7.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Treatment of HIV-1 Infection

VOCABRIA is indicated in combination with EDURANT (rilpivirine) tablets for short-term treatment of HIV-1 infection 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 *[see Microbiology (12.4), Clinical Studies (14.1)]*:

- oral lead-in to assess the tolerability of cabotegravir prior to administration of cabotegravir extended-release injectable suspension, a component of CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension).
- oral therapy for patients who will miss planned injection dosing with CABENUVA.

1.2 HIV-1 Pre-Exposure Prophylaxis

VOCABRIA is indicated for short-term pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating VOCABRIA for HIV-1 PrEP. VOCABRIA may be used as *[see Dosage and Administration (2.2), Contraindications (4), Warnings and Precautions (5.1), Clinical Studies (14.2)]*:

- oral lead-in to assess the tolerability of cabotegravir prior to administration of APRETUDE (cabotegravir extended-release injectable suspension).
- oral PrEP for patients who will miss planned injection dosing with APRETUDE.

2 DOSAGE AND ADMINISTRATION

2.1 Treatment of HIV-1 Infection in Adults and Adolescents 12 Years of Age and Older and Weighing at Least 35 kg

Oral Lead-In Dosing to Assess Tolerability of Cabotegravir

Consult the prescribing information for CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) before initiating VOCABRIA to ensure therapy with CABENUVA is appropriate. See full prescribing information for CABENUVA.

Oral lead-in may be used to assess the tolerability of cabotegravir prior to the initiation of CABENUVA. The recommended oral lead-in daily dose is one 30-mg tablet of VOCABRIA

with one 25-mg tablet of EDURANT for approximately 1 month (at least 28 days). The last oral dose should be taken on the same day injections with CABENUVA are started.

Take VOCABRIA once daily with EDURANT at approximately the same time each day with a meal *[see Clinical Pharmacology (12.3)]*.

Because VOCABRIA is indicated in combination with EDURANT tablets, the prescribing information for EDURANT should also be consulted.

Recommended Oral Dosing to Replace Planned Missed Injections of CABENUVA

Planned Missed Injections for Patients on the Monthly Dosing Schedule: If a patient plans to miss a monthly scheduled injection of CABENUVA by more than 7 days, take daily oral therapy for up to 2 months to replace missed injection visits. For oral therapy with VOCABRIA and EDURANT, the recommended oral daily dose is one 30-mg tablet of VOCABRIA and one 25-mg tablet of EDURANT. Take VOCABRIA with EDURANT at approximately the same time each day with a meal.

The first dose of oral therapy should be taken 1 month (+/-7 days) after the last injection dose of CABENUVA and continued until the day injection dosing is restarted. For oral therapy with VOCABRIA and EDURANT of durations greater than 2 months, an alternative oral regimen is recommended. See full prescribing information for CABENUVA to resume monthly injection dosing.

Planned Missed Injections for Patients on the Every-2-Month Dosing Schedule: If a patient plans to miss a scheduled every-2-month injection of CABENUVA by more than 7 days, take daily oral therapy for up to 2 months to replace 1 missed scheduled every-2-month injection. For oral therapy with VOCABRIA and EDURANT of durations greater than 2 months, the recommended oral daily dose is one 30-mg tablet of VOCABRIA and one 25-mg tablet of EDURANT. Take VOCABRIA with EDURANT at approximately the same time each day with a meal.

The first dose of oral therapy should be taken approximately 2 months after the last injection dose of CABENUVA and continued until the day injection dosing is restarted. For oral therapy with VOCABRIA and EDURANT of durations greater than 2 months, an alternative oral regimen is recommended. See full prescribing information for CABENUVA to resume every-2-month injection dosing.

2.2 HIV-1 Pre-Exposure Prophylaxis in Adults and Adolescents Weighing at Least 35 kg

HIV-1 Screening for Individuals for HIV-1 Pre-Exposure Prophylaxis

Individuals must be tested for HIV-1 infection prior to initiating VOCABRIA and APRETUDE for HIV-1 PrEP, and with each subsequent injection of APRETUDE, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. If an antigen/antibody-specific test is used and provides negative results, then such negative results

should be confirmed using an RNA-specific assay, even if the results of the RNA-assay are available after VOCABRIA or APRETUDE administration *[see Contraindications (4), Warnings and Precautions (5.1)]*.

Oral Lead-In Dosing to Assess Tolerability of Cabotegravir for HIV-1 Pre-Exposure Prophylaxis

Consult the prescribing information for APRETUDE before initiating VOCABRIA to ensure use of APRETUDE is appropriate. See full prescribing information for APRETUDE.

Oral lead-in may be used to assess the tolerability of cabotegravir prior to the initiation of APRETUDE. The recommended oral daily dose is one 30-mg tablet of VOCABRIA for approximately 1 month (at least 28 days). Following oral lead-in, start initiation injection of APRETUDE on the last day of oral lead-in or within 3 days.

Oral Dosing to Replace a Planned Missed Injection of APRETUDE (One Every-2-Month Injection)

If an individual plans to miss a scheduled injection of APRETUDE by more than 7 days, take daily oral VOCABRIA to replace one every-2-month injection visit. The recommended oral daily dose is one 30-mg tablet of VOCABRIA. The first dose of oral VOCABRIA should be taken approximately 2 months after the last injection dose of APRETUDE. Restart injection with APRETUDE on the day oral dosing completes or within 3 days. See full prescribing information for APRETUDE to resume every-2-month injection dosing.

3 DOSAGE FORMS AND STRENGTHS

Tablets: 30 mg.

4 CONTRAINDICATIONS

Treatment of HIV-1 Infection

VOCABRIA is contraindicated in patients:

- with previous hypersensitivity reaction to cabotegravir *[see Warnings and Precautions (5.2)]*.
- receiving the following coadministered drugs for which significant decreases in cabotegravir plasma concentrations may occur due to uridine diphosphate glucuronosyltransferase (UGT)1A1 enzyme induction, which may result in loss of virologic response *[see Drug Interactions (7.2, 7.3), Clinical Pharmacology (12.3)]*:
    - Anticonvulsants: Carbamazepine, oxcarbazepine, phenobarbital, phenytoin
    - Antimycobacterials: Rifampin, rifapentine

Prior to initiation of VOCABRIA, note that use of CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) with rifabutin is contraindicated.

Since VOCABRIA is taken in combination with EDURANT tablets, the prescribing information for EDURANT should be consulted for additional contraindications.

HIV-1 Pre-Exposure Prophylaxis

VOCABRIA is contraindicated in individuals:

- with unknown or positive HIV-1 status *[see Warnings and Precautions (5.1)]*.
- with previous hypersensitivity reaction to cabotegravir *[see Warnings and Precautions (5.2)]*.
- receiving the following coadministered drugs for which significant decreases in cabotegravir plasma concentrations may occur due to UGT1A1 enzyme induction, which may result in loss of efficacy *[see Drug Interactions (7.2, 7.3), Clinical Pharmacology (12.3)]*:
  - Anticonvulsants: Carbamazepine, oxcarbazepine, phenobarbital, phenytoin
  - Antimycobacterials: Rifampin, rifapentine

5 WARNINGS AND PRECAUTIONS

5.1 Comprehensive Management to Reduce the Risk of HIV-1 Infection When VOCABRIA is Used for HIV-1 Pre-Exposure Prophylaxis

Use of VOCABRIA for HIV-1 PrEP should be part of a comprehensive prevention strategy including adherence to the dosing schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs). VOCABRIA is not always effective in preventing HIV-1 acquisition *[see Clinical Studies (14.2)]*. The time from initiation of VOCABRIA for HIV-1 PrEP to maximal protection against HIV-1 infection is unknown.

Risk for HIV-1 acquisition includes behavioral, biological, or epidemiologic factors including, but not limited to, condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network.

Counsel individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner(s)' HIV-1 status, including viral suppression status; regular testing for STIs that can facilitate HIV-1 transmission). Inform individuals about and support their efforts in reducing sexual risk behavior.

VOCABRIA for HIV-1 PrEP to reduce the risk of acquiring HIV-1 should be used only in individuals confirmed to be HIV-1 negative *[see Contraindications (4)]*. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only VOCABRIA, because VOCABRIA alone does not constitute a complete regimen for HIV-1 treatment *[see Microbiology (12.4)]*; therefore, care should be taken to minimize the risk of initiating or continuing VOCABRIA before confirming the individual is HIV-1 negative.

- Prior to initiating VOCABRIA for HIV-1 PrEP, ask seronegative individuals about recent (in past month) potential exposure events (e.g., condomless sex or condom breaking during sex with a partner of unknown HIV-1 status or unknown viremic status, a recent STI), and evaluate for current or recent signs or symptoms consistent with acute HIV-1 infection (e.g., fever, fatigue, myalgia, skin rash).
- If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute or primary HIV-1 infection. Testing should be repeated prior to each injection of APRETUDE and upon diagnosis of any other STIs *[see Dosage and Administration (2.2)]*.
- If an HIV-1 test indicates possible HIV-1 infection, or if symptoms consistent with acute HIV-1 infection develop following an exposure event, additional HIV testing to determine HIV status is needed. If an individual has confirmed HIV-1 infection, then the individual must be transitioned to a complete HIV-1 treatment regimen.

Counsel individuals without HIV-1 to strictly adhere to the recommended dosing schedule for VOCABRIA in order to reduce the risk of HIV-1 acquisition and the potential development of resistance *[see Dosage and Administration (2.2), Microbiology (12.4)]*. Some individuals, such as adolescents, may benefit from frequent visits and counseling to support adherence to the dosing schedule *[see Use in Specific Populations (8.4), Microbiology (12.4), Clinical Studies (14.2)]*.

5.2 Hypersensitivity Reactions

Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with VOCABRIA *[see Adverse Reactions (6.1, 6.2)]*. Administration of oral lead-in dosing was used in clinical studies to help identify participants who may be at risk of a hypersensitivity reaction. Remain vigilant and discontinue VOCABRIA if a hypersensitivity reaction is suspected *[see Dosage and Administration (2.2), Contraindications (4), Adverse Reactions (6)]*.

Discontinue VOCABRIA immediately if signs or symptoms of hypersensitivity reactions develop (including, but not limited to, severe rash, or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, mucosal involvement [oral blisters or lesions], conjunctivitis, facial edema, hepatitis, eosinophilia, angioedema, difficulty breathing). Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated.

5.3 Hepatotoxicity

Hepatotoxicity has been reported in a limited number of patients receiving cabotegravir with or without known pre-existing hepatic disease or identifiable risk factors *[see Adverse Reactions (6.1)]*.

When VOCABRIA is Used for Treatment HIV-1 Infection

Patients with underlying liver disease or marked elevations in transaminases prior to treatment with VOCABRIA may be at increased risk for worsening or development of transaminase elevations.

Monitoring of liver chemistries is recommended and treatment with VOCABRIA should be discontinued if hepatotoxicity is suspected.

When VOCABRIA is Used for HIV-1 Pre-Exposure Prophylaxis

Clinical and laboratory monitoring should be considered and VOCABRIA should be discontinued if hepatotoxicity is suspected, and individuals managed as clinically indicated.

5.4 Depressive Disorders

When VOCABRIA is Used for Treatment HIV-1 Infection

Depressive disorders (including depressed mood, depression, mood altered, mood swings, suicidal ideation/suicide attempt) have been reported with VOCABRIA when used with EDURANT for treatment of HIV-1 infection *[see Adverse Reactions (6.1)]*. Promptly evaluate patients with depressive symptoms to assess whether the symptoms are related to VOCABRIA and to determine whether the risks of continued therapy outweigh the benefits.

When VOCABRIA is Used for HIV-1 Pre-Exposure Prophylaxis

Depressive disorders (including depression, depressed mood, persistent depressive disorder, suicidal ideation/suicide attempt) have been reported with VOCABRIA *[see Adverse Reactions (6.1)]*. Promptly evaluate individuals with depressive symptoms to assess whether the symptoms are related to VOCABRIA and to determine whether the risks of continued therapy outweigh the benefits.

5.5 Risk of Adverse Reactions, Loss of Efficacy, or Reduced Concentration Due to Drug Interactions

The concomitant use of VOCABRIA and other drugs may result in known or potentially significant drug interactions, some of which may lead to adverse events, loss of efficacy from VOCABRIA when used for treatment of HIV-1 infection or HIV-1 PrEP, and possible development of viral resistance *[see Contraindications (4), Drug Interactions (7.2, 7.3)]*.

See Table 1 for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations. Consider the potential for drug interactions prior to and during use of VOCABRIA; review concomitant medications during use of VOCABRIA *[see Drug Interactions (7.3)]*.

5.6 Risks Associated with Combination Treatment

VOCABRIA is indicated for use in combination with EDURANT (rilpivirine) for treatment of HIV-1 infection *[see Indications and Usage (1.1), Dosage and Administration (2.1)]*. Review the

prescribing information for EDURANT for information on rilpivirine prior to initiation of VOCABRIA in combination with EDURANT.

6 ADVERSE REACTIONS

The following adverse reactions are described below and in other sections of the labeling:

- Hypersensitivity reactions *[see Warnings and Precautions (5.2)]*
- Hepatotoxicity *[see Warnings and Precautions (5.3)]*
- Depressive disorders *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect rates observed in practice. See full prescribing information for CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) for additional safety information. Since VOCABRIA is taken in combination with EDURANT tablets, the prescribing information for EDURANT (rilpivirine) should be consulted for relevant information on rilpivirine.

Adverse Reactions of VOCABRIA in Clinical Trials for the Treatment of HIV-1 Infection

Clinical Trials Experience in Adults: The safety assessment of VOCABRIA for oral lead-in therapy prior to therapy with CABENUVA is based on the analysis of 48-week data from virologically suppressed participants with HIV-1 infection in 3 international, multicenter, open-label trials, where 590 of 1,182 participants received oral lead-in within the pivotal trials FLAIR and ATLAS (pooled analysis) and 655 of 1,045 participants received oral lead-in within ATLAS-2M *[see Clinical Studies (14.1)]*.

Adverse reactions were reported following exposure to VOCABRIA tablets and EDURANT tablets administered in combination as oral lead-in therapy (median time exposure: 5.3 weeks). Adverse reactions included those attributable to the oral formulation of cabotegravir and rilpivirine administered as a combination regimen. Refer to the prescribing information for EDURANT for other adverse reactions associated with oral rilpivirine.

The most common adverse reactions during the oral lead-in period in the pooled analyses of FLAIR and ATLAS at Week 48 were headache, nausea, abnormal dreams, anxiety, and insomnia, all of which occurred in at least 3 participants with an incidence ≤1%. The most common adverse reactions during the oral lead-in period for ATLAS-2M were fatigue, diarrhea, headache, nausea, dizziness, abdominal discomfort, abdominal distension, insomnia, and asthenia, all of which occurred in at least 3 participants across both arms, with an incidence ≤2%.

During the oral lead-in period for FLAIR and ATLAS, 6 (1%) participants discontinued due to adverse events, including asthenia, myalgia, depression suicidal, and headache. During the oral

lead-in period for ATLAS-2M, 4 (<1%) participants discontinued due to adverse events, including asthenia, skin lesion, fatigue, transaminases increased, and depression.

In the extension phase of the FLAIR study at Week 124, the overall safety profile was consistent with that observed at Week 48 and when injection therapy with CABENUVA was initiated directly without the oral lead-in phase.

Clinical Trial Experience in Adolescents: Based on data from the Week 24 analysis of the MOCHA study in 144 adolescents (aged 12 to younger than 18 years and weighing ≥35 kg), the safety profile of oral cabotegravir and oral rilpivirine administered in combination during the oral lead-in period in adolescents was consistent with the safety profile established with cabotegravir plus rilpivirine in adults.

Adverse Reactions of VOCABRIA in Clinical Trials for HIV-1 Pre-Exposure Prophylaxis

Clinical Trial Experience in Adults: In trial HPTN 083, adverse reactions were reported while participants were on blinded study product following exposure to VOCABRIA tablets as oral lead-in for HIV-1 PrEP (median time exposure: 4.1 weeks). The most common adverse reactions reported at ≥1% during the oral lead-in period were diarrhea (4% and 4%), nausea (3% and 5%), dizziness (2% and 2%), headache (2% and 2%), fatigue (1% and 2%), and abnormal dreams (1% and 2%) for VOCABRIA and TRUVADA (emtricitabine and tenofovir disoproxil fumarate), respectively. During the oral lead-in period, 24 (1%) participants receiving VOCABRIA discontinued due to adverse events, including increased alanine aminotransferase, increased aspartate aminotransferase, suicide attempt, and dizziness, which were observed in ≥2 participants.

In Trial HPTN 084, adverse reactions were reported while participants were on blinded study product following exposure to VOCABRIA tablets as oral lead-in for HIV-1 PrEP (median time exposure: 4.1 weeks). The most common adverse reactions reported at ≥1% during the oral lead-in period were headache (6% and 7%), nausea (3% and 7%), dizziness (3% and 4%), diarrhea (2% and 4%), upper respiratory tract infection (2% and 2%), somnolence (2% and 1%), fatigue (1% and 2%), abdominal pain (1% and 1%), vomiting (<1% and 3%), decreased appetite (<1% and 2%), and pruritus (<1% and 1%) for VOCABRIA and TRUVADA, respectively. During the oral lead-in period, 4 (<1%) participants receiving VOCABRIA discontinued due to adverse events of increased alanine aminotransferase (n = 3) and sleep disorders (n = 1).

Clinical Trials Experience in Adolescents: In adolescents receiving VOCABRIA for HIV-1 PrEP, the safety data were comparable to the safety data reported in adults receiving VOCABRIA for HIV-1 PrEP *[see Use in Specific Populations (8.4)]*.

Less Common Adverse Reactions

The following select adverse reactions (regardless of severity) occurred in <1% of participants receiving VOCABRIA in clinical trials for the treatment of HIV-1 infection or for HIV-1 PrEP.

Psychiatric Disorders: Suicidal ideation, and suicide attempt (these events were observed primarily in participants with a pre-existing history of depression or other psychiatric illness).

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of cabotegravir-containing regimens. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders

Hypersensitivity reactions (including angioedema and urticaria) *[see Warnings and Precautions (5.2)]*.

7 DRUG INTERACTIONS

7.1 Concomitant Use with Other Antiretroviral Medicines

VOCABRIA in combination with EDURANT (rilpivirine) is a complete regimen for the treatment of HIV-1 infection. Refer to the prescribing information for EDURANT for relevant information on rilpivirine.

Coadministration of VOCABRIA with other antiretroviral medications for PrEP is not recommended *[see Drug Interactions (7.4), Clinical Pharmacology (12.3)]*.

Prior to initiating dosing with VOCABRIA, the prescribing information for CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) or APRETUDE should be consulted to ensure use of CABENUVA or APRETUDE will be appropriate for either the treatment of HIV-1 infection or HIV-1 PrEP, respectively.

7.2 Potential for Other Drugs to Affect VOCABRIA

Cabotegravir is primarily metabolized by UGT1A1 with some contribution from UGT1A9. Drugs that are strong inducers of UGT1A1 or UGT1A9 are expected to decrease cabotegravir plasma concentrations and may result in loss of efficacy; therefore, coadministration of VOCABRIA with these drugs is contraindicated *[see Contraindications (4)]*.

Coadministration of oral cabotegravir with polyvalent cation-containing products may lead to decreased absorption of cabotegravir *[see Drug Interactions (7.3)]*.

7.3 Established and Other Potentially Significant Drug Interactions

Information regarding potential drug interactions with cabotegravir are provided in Table 1. These recommendations are based on either drug interaction trials or predicted interactions due to the expected magnitude of the interaction and potential for loss of efficacy *[see Contraindications (4), Warnings and Precautions (5.5), Clinical Pharmacology (12.3)]*. Table 1 includes potentially significant interactions but is not all inclusive.

Refer to the prescribing information for EDURANT (rilpivirine) for established or potentially significant interactions that should be considered during concomitant administration of VOCABRIA and EDURANT for HIV-1 treatment.

Table 1. Drug Interactions with VOCABRIA

Concomitant Drug Class: Drug Name	Effect on Concentration	Clinical Comment
Antacids containing polyvalent cations (e.g., aluminum or magnesium hydroxide, calcium carbonate)	↓Cabotegravir	Administer antacid products at least 2 hours before or 4 hours after taking VOCABRIA.
Anticonvulsants: Carbamazepine Oxcarbazepine Phenobarbital Phenytoin	↓Cabotegravir	Coadministration is contraindicated with VOCABRIA due to potential for loss of efficacy and development of resistance *[see Contraindications (4)]*.
Antimycobacterials[a]: Rifampin Rifapentine	↓Cabotegravir	
Antimycobacterial: Rifabutin	↓Cabotegravir	Dose modification is not required for VOCABRIA. Dose modification is recommended for APRETUDE for HIV-1 PrEP. Coadministration is contraindicated with CABENUVA for HIV-1 treatment.

↓ = Decrease; PrEP = Pre-exposure prophylaxis.

[a] Rifabutin can be coadministered with cabotegravir; however, it is contraindicated with CABENUVA for HIV-1 treatment. Dosage modification is recommended with APRETUDE for HIV-1 PrEP.

7.4 Drugs without Clinically Significant Interactions with Cabotegravir

Based on drug interaction study results, the following drugs can be coadministered with cabotegravir without a dose adjustment: etravirine, midazolam, oral contraceptives containing levonorgestrel and ethinyl estradiol, rifabutin, and rilpivirine *[see Clinical Pharmacology (12.3)]*.

Prior to initiating oral therapy, note that use of CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension) with rifabutin is contraindicated for the treatment of HIV-1 infection. Dosage modification is recommended when APRETUDE is used with rifabutin for HIV-1 PrEP.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to VOCABRIA during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

Risk Summary

There are insufficient human data on the use of VOCABRIA during pregnancy to adequately assess a drug-associated risk of birth defects and miscarriage. Discuss the benefit-risk of using VOCABRIA with individuals of childbearing potential or during pregnancy.

The APR has been established to monitor for birth defects following prenatal exposure to antiretrovirals. The rate of miscarriage is not reported in the APR. The background risk for major birth defects and miscarriage for the indicated population is unknown. The background rate for major birth defects in a United States (U.S.) reference population of the Metropolitan Atlanta Congenital Defects Program (MACDP) is 2.7%. The estimated background rate of miscarriage in clinically recognized pregnancies in the U.S. general population is 15% to 20%. The APR uses the MACDP as the U.S. reference population for birth defects in the general population. The MACDP evaluates mothers and infants from a limited geographic area and does not include outcomes for births that occurred at <20 weeks' gestation.

In animal reproduction studies with oral cabotegravir, a delay in the onset of parturition and increased stillbirths and neonatal deaths were observed in a rat pre- and postnatal development study at >28 times the exposure at the recommended human dose (RHD). No evidence of adverse developmental outcomes was observed with oral cabotegravir in rats or rabbits (>28 times or similar to the exposure at the RHD, respectively) given during organogenesis *(see Data)*.

Data

Animal Data: Cabotegravir was administered orally to pregnant rats at 0, 0.5, 5, or 1,000 mg/kg/day from 15 days before cohabitation, during cohabitation, and from Gestation Days 0 to 17. There were no effects on fetal viability when fetuses were delivered by caesarean, although a minor decrease in fetal body weight was observed at 1,000 mg/kg/day (>28 times the exposure in humans at the RHD). No drug-related fetal toxicities were observed at 5 mg/kg/day (approximately 13 times the exposure in humans at the RHD), and no drug-related fetal malformations were observed at any dose.

Cabotegravir was administered orally to pregnant rabbits at 0, 30, 500, or 2,000 mg/kg/day from Gestation Days 7 to 19. No drug-related fetal toxicities were observed at 2,000 mg/kg/day (approximately 0.7 times the exposure in humans at the RHD).

In a rat pre- and postnatal development study, cabotegravir was administered orally to pregnant rats at 0, 0.5, 5, or 1,000 mg/kg/day from Gestation Day 6 to Lactation Day 21. A delay in the onset of parturition and increases in the number of stillbirths and neonatal deaths by Lactation Day 4 were observed at 1,000 mg/kg/day (>28 times the exposure in humans at the RHD); there were no alterations to growth and development of surviving offspring. In a cross-fostering study, similar incidences of stillbirths and early postnatal deaths were observed when rat pups born to cabotegravir-treated mothers were nursed from birth by control mothers. There was no effect on neonatal survival of control pups nursed from birth by cabotegravir-treated mothers. A lower dose of 5 mg/kg/day (13 times the exposure at the RHD) was not associated with delayed parturition or neonatal mortality in rats. Studies in pregnant rats showed that cabotegravir crosses the placenta and can be detected in fetal tissue.

8.2 Lactation

Risk Summary

There are no data on the presence of cabotegravir in human milk, the effects on the breastfed infant, or the effects on milk production. Cabotegravir is present in animal milk *(see Data)*. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Potential risks of breastfeeding include: (1) HIV-1 transmission (in HIV-1–negative infants), (2) developing viral resistance (in HIV-1–positive infants), and (3) adverse reactions in a breastfed infant similar to those seen in adults.

In mothers without HIV-1, breastfeeding should only be considered if the expected benefit justifies the potential risk to the infant, including the potential risk for adverse reaction in the breastfed child, along with the risk of HIV-1 acquisition due to nonadherence and subsequent vertical transmission to the child. Breastfeeding is not recommended if acute HIV-1 infection is suspected to avoid the risk of postnatal transmission of HIV-1 infection.

Data

Animal lactation studies with cabotegravir have not been conducted. However, cabotegravir was detected in the plasma of nursing pups on Lactation Day 10 in the rat pre- and postnatal development study.

8.4 Pediatric Use

Treatment of HIV-1 Infection

The safety and effectiveness of VOCABRIA have been established in adolescents aged 12 to younger than 18 years and weighing at least 35 kg, which is supported by the following:

- Trials in adults *[see Clinical Studies (14.1)]*
- MOCHA (NCT03497676) trial in adolescents, in which virologically suppressed adolescents (aged 12 to younger than 18 years and weighing at least 35 kg) with HIV-1 received either cabotegravir or rilpivirine in addition to their background antiretroviral regimen (cohort 1),

or cabotegravir plus rilpivirine as a complete regimen (cohort 2) *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14.3)]*.

The safety and efficacy of VOCABRIA in adolescents (aged 12 to younger than 18 years and weighing at least 35 kg) were similar to that in adults and there was no clinically significant change in drug exposure *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3)]*.

Please refer to the CABENUVA prescribing information for additional information.

The safety, efficacy, and pharmacokinetics of VOCABRIA have not been established in pediatric patients younger than 12 years of age or weighing <35 kg.

HIV-1 Pre-Exposure Prophylaxis

The safety and effectiveness of VOCABRIA for HIV-1 PrEP in adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition is supported by data from 2 adequate and well-controlled trials of VOCABRIA for HIV-1 PrEP in adults with additional safety and pharmacokinetic data from studies in adults with HIV-1 who were administered CABENUVA and in adolescent participants with HIV-1 who were administered separate components of CABENUVA in addition to their current antiretroviral therapy *[see Dosage and Administration (2.2), Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14.2)]*.

APRETUDE for HIV-1 PrEP was evaluated in 2 open-label multicenter clinical trials, HPTN 083-01 and HPTN 084-01, in adolescent individuals 12 to less than 18 years of age weighing at least 35 kg who are at risk for HIV-1 acquisition. Sixty-four adolescents were enrolled. Of these, 62 adolescent participants received one or more injections after receiving VOCABRIA. In adolescents receiving VOCABRIA and APRETUDE for HIV-1 PrEP, the safety data were comparable to the safety data reported in adults receiving APRETUDE for HIV-1 PrEP.

While using APRETUDE, HIV-1 testing should be conducted prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) and prior to each injection of APRETUDE. Adolescents may benefit from more frequent visits and counseling to support adherence to the dosing schedule *[see Dosage and Administration (2.2), Warnings and Precautions (5.1)]*.

The safety, efficacy, and pharmacokinetics of VOCABRIA in pediatric participants younger than 12 years of age or weighing <35 kg have not been established.

8.5 Geriatric Use

Clinical trials of VOCABRIA did not include sufficient numbers of participants aged 65 years and older to determine whether they respond differently from younger participants. In general, caution should be exercised in administration of VOCABRIA in elderly patients, reflecting greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy *[see Clinical Pharmacology (12.3)]*.

8.6 Renal Impairment

No dosage adjustment of VOCABRIA is necessary for patients with mild to moderate (creatinine clearance equal to 30 mL/min to <90 mL/min) or severe renal impairment (creatinine clearance equal to 15 mL/min to <30 mL/min) *[see Clinical Pharmacology (12.3)]*. The effect of end-stage renal disease (creatinine clearance <15 mL/min) on the pharmacokinetics of cabotegravir is unknown. As cabotegravir is >99% protein bound, dialysis is not expected to alter exposures of cabotegravir.

Since VOCABRIA is taken in combination with EDURANT for the treatment of HIV-1 infection, the prescribing information for EDURANT should be consulted for additional recommendations in patients with severe impairment or end-stage renal disease.

8.7 Hepatic Impairment

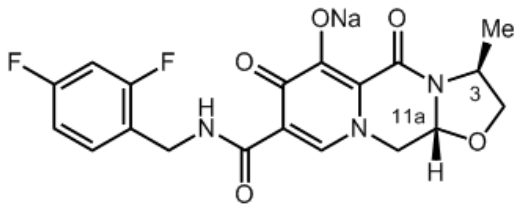
No dosage adjustment of VOCABRIA is necessary for patients with mild or moderate hepatic impairment (Child-Pugh A or B). The effect of severe hepatic impairment (Child-Pugh C) on the pharmacokinetics of cabotegravir is unknown *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

There is no known specific treatment for overdose with VOCABRIA. If overdose occurs, monitor the patient and apply standard supportive treatment as required as well as observation of the clinical status of the individual. As cabotegravir is highly bound to plasma proteins, it is unlikely that it will be significantly removed by dialysis.

11 DESCRIPTION

VOCABRIA contains cabotegravir, as cabotegravir sodium, an HIV integrase strand transfer inhibitor (INSTI). The chemical name of cabotegravir sodium is sodium (*3S,11aR*)-N-[(2,4-difluorophenyl)methyl]-6-hydroxy-3-methyl-5,7-dioxo-2,3,5,7,11,11a-hexahydro[1,3]oxazolo [3,2-a]pyrido [1,2-d]pyrazine-8-carboxamide. The empirical formula is $C_{19}H_{16}F_2N_3NaO_5$ and the molecular weight is 427.34 g/mol. It has the following structural formula:



Cabotegravir sodium is a white to almost white crystalline solid that is slightly soluble in water.

Each immediate-release film-coated tablet of VOCABRIA for oral administration contains 30 mg of cabotegravir (equivalent to 31.62 mg cabotegravir sodium) and the inactive ingredients: hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium

starch glycolate. The tablet film-coating contains hypromellose, polyethylene glycol, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cabotegravir is an HIV-1 antiretroviral drug *[see Microbiology (12.4)]*.

12.2 Pharmacodynamics

Cardiac Electrophysiology

At a dose of cabotegravir 150 mg orally every 12 hours (10 times the recommended total daily oral lead-in dosage of VOCABRIA), the QT interval is not prolonged to any clinically relevant extent. Administration of 3 doses of cabotegravir 150 mg orally every 12 hours resulted in a geometric mean C_{max} approximately 2.8-fold above the geometric mean steady-state C_{max} associated with the recommended 30-mg dose of oral cabotegravir.

For additional QT information related to the injectable formulations of cabotegravir and rilpivirine (CABENUVA), the injectable formulation of cabotegravir (APRETUDE), and the oral formulation of rilpivirine (EDURANT), refer to the prescribing information for CABENUVA, APRETUDE, and EDURANT.

12.3 Pharmacokinetics

Absorption, Distribution, and Elimination

The pharmacokinetic properties of cabotegravir are provided in Table 2. The multiple-dose pharmacokinetic parameters are provided in Table 3.

Table 2. Pharmacokinetic Properties of Cabotegravir

Absorption	
T_{max} (h), median	3
Effect of high-fat meal (relative to fasting): $AUC_{(0\text{-}inf)}$ ratio[a]	1.14 (1.02, 1.28)
Distribution	
% Bound to human plasma proteins	>99.8
Blood-to-plasma ratio	0.52
CSF-to-plasma concentration ratio (median [range])[b]	0.003 (0.002 to 0.004)
Elimination	
$t_{1/2}$ (h), mean	41
Metabolism	
Metabolic pathways	UGT1A1 UGT1A9 (minor)

Excretion	
Major route of elimination	Metabolism
% of dose excreted as total ^{14}C (unchanged drug) in urine[b]	27 (0)
% of dose excreted as total ^{14}C (unchanged drug) in feces[b]	59 (47)

CSF = Cerebrospinal fluid.

[a] Geometric mean ratio (fed/fasted) in pharmacokinetic parameters and 90% confidence interval. High-calorie/high-fat meal = 870 kcal, 53% fat.

[b] Dosing in mass balance studies: single-dose oral administration of [^{14}C] cabotegravir.

Table 3. Multiple-Dose Pharmacokinetic Parameters of Oral Cabotegravir in Adults

Parameter	Geometric Mean (5^{th}, 95^{th} Percentile)[a]
C_{max} (mcg/mL)	8.0 (5.3, 11.9)
$AUC_{(0\text{-}tau)}$ (mcg•h/mL)[b]	145 (93.5, 224)
C_{tau} (mcg/mL)[b]	4.6 (2.8, 7.5)

[a] Pharmacokinetic parameter values were based on individual post-hoc estimates from the final population pharmacokinetic model for participants receiving 30 mg of oral cabotegravir once daily in FLAIR and ATLAS trials.

[b] tau is dosing interval: 24 hours for oral cabotegravir.

Specific Populations

No clinically significant differences in the pharmacokinetics of cabotegravir were observed based on age, sex, race/ethnicity, body mass index, or UGT1A1 polymorphisms. The effect of hepatitis B and C virus co-infection on the pharmacokinetics of cabotegravir is unknown.

Renal Impairment: No clinically significant differences in the pharmacokinetics of cabotegravir are expected with mild, moderate, or severe renal impairment. Cabotegravir has not been studied in patients with end-stage renal disease not on dialysis. As cabotegravir is >99% protein bound, dialysis is not expected to alter exposures of cabotegravir *[see Use in Specific Populations (8.6)]*.

Hepatic Impairment: No clinically significant differences in the pharmacokinetics of cabotegravir are expected in mild to moderate (Child-Pugh A or B) hepatic impairment. The effect of severe hepatic impairment (Child-Pugh C) on the pharmacokinetics of cabotegravir has not been studied *[see Use in Specific Populations (8.7)]*.

Gender: Population pharmacokinetic analyses revealed no clinically relevant effect of gender on the exposure of cabotegravir. In addition, no clinically relevant differences in plasma cabotegravir concentrations were observed in PrEP studies by gender, including cisgender men and transgender women (+/-hormone use). Therefore, no dose adjustment is necessary based on gender.

Geriatric Patients: No dose adjustment is required in elderly individuals. There are limited data available on the use of cabotegravir in individuals aged 65 years and older. In general, caution should be exercised in administration of cabotegravir in elderly individuals, reflecting greater

frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy *[see Use in Specific Populations (8.5)]*.

Pediatric Patients: Population pharmacokinetic analyses revealed no clinically relevant differences in exposure between adolescent participants (weighing ≥35 kg) and adult participants with and without HIV-1 from the cabotegravir development program; therefore, no dosage adjustment is needed for adolescents weighing ≥35 kg (Table 4).

Table 4. Pharmacokinetic Parameters following Once-Daily Oral Cabotegravir in Adolescents Aged 12 to Younger than 18 Years (≥35 kg)

Parameter	Geometric Mean (5th, 95th Percentile)[a]
C_{max} (mcg/mL)	10.7 (7.36, 16.6)
$AUC_{(0\text{-}tau)}$ (mcg•h/mL)[b]	203 (136, 320)
C_{tau} (mcg/mL)[b]	6.43 (4.15, 10.5)

[a] Pharmacokinetic parameter values were based on individual post-hoc estimates from population pharmacokinetic models in both adolescents with HIV-1 (n = 147) weighing 35.2 to 98.5 kg and adolescents without HIV-1 (n = 62) weighing 39.9 to 167 kg.

[b] tau is dosing interval: 24 hours for oral administration.

Drug Interaction Studies

Cabotegravir is not a clinically relevant inhibitor of the following enzymes and transporters: cytochrome P450 (CYP)1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, and 3A4; UGT1A1, 1A3, 1A4, 1A6, 1A9, 2B4, 2B7, 2B15, and 2B17; P-glycoprotein (P-gp); breast cancer resistance protein (BCRP); bile salt export pump (BSEP); organic cation transporter (OCT)1, OCT2; organic anion transporter polypeptide (OATP)1B1, OATP1B3; multidrug and toxin extrusion transporter (MATE) 1, MATE 2-K; and multidrug resistance protein (MRP)2 or MRP4.

In vitro, cabotegravir inhibited renal OAT1 (IC_{50} = 0.81 microM) and OAT3 (IC_{50} = 0.41 microM). Based on physiologically based pharmacokinetic (PBPK) modeling, cabotegravir may increase the AUC of OAT1/3 substrates up to approximately 80%.

In vitro, cabotegravir did not induce CYP1A2, CYP2B6, or CYP3A4.

Simulations using PBPK modeling show that no clinically significant interaction is expected during coadministration of cabotegravir with drugs that inhibit UGT1A1.

In vitro, cabotegravir was not a substrate of OATP1B1, OATP1B3, OATP2B1, or OCT1.

Cabotegravir is a substrate of P-gp and BCRP in vitro; however, because of its high permeability, no alteration in cabotegravir absorption is expected with coadministration of P-gp or BCRP inhibitors.

The effects of coadministered drugs on the exposure of cabotegravir are summarized in Table 5, and the effects of cabotegravir on the exposure of coadministered drugs are summarized in Table 6.

Table 5. Effect of Coadministered Drugs on the Pharmacokinetics of Cabotegravir

Coadministered Drug(s) and Dose(s)	Dose of Cabotegravir	n	Geometric Mean Ratio (90% CI) of Cabotegravir Pharmacokinetic Parameters with/without Coadministered Drugs No Effect = 1.00		
			C_{max}	AUC	C_{tau} or C_{24}
Etravirine 200 mg twice daily	30 mg once daily	12	1.04 (0.99, 1.09)	1.01 (0.96, 1.06)	1.00 (0.94, 1.06)
Rifabutin 300 mg once daily	30 mg once daily	12	0.83 (0.76, 0.90)	0.79 (0.74, 0.83)	0.74 (0.70, 0.78)
Rifampin 600 mg once daily	30-mg single dose	15	0.94 (0.87, 1.02)	0.41 (0.36, 0.46)	0.50 (0.44, 0.57)
Rilpivirine 25 mg once daily	30 mg once daily	11	1.05 (0.96, 1.15)	1.12 (1.05, 1.19)	1.14 (1.04, 1.24)

n = Maximum number of participants with data, CI = Confidence Interval.

Table 6. Effect of Cabotegravir on the Pharmacokinetics of Coadministered Drugs

Coadministered Drug(s) and Dose(s)	Dose of Cabotegravir	n	Geometric Mean Ratio (90% CI) of Pharmacokinetic Parameters of Coadministered Drug with/without Cabotegravir No Effect = 1.00		
			C_{max}	AUC	C_{tau} or C_{24}
Ethinyl estradiol 0.03 mg once daily	30 mg once daily	19	0.92 (0.83, 1.03)	1.02 (0.97, 1.08)	1.00 (0.92, 1.10)
Levonorgestrel 0.15 mg once daily	30 mg once daily	19	1.05 (0.96, 1.15)	1.12 (1.07, 1.18)	1.07 (1.01, 1.15)
Midazolam 3 mg	30 mg once daily	12	1.09 (0.94, 1.26)	1.10 (0.95, 1.26)	NA
Rilpivirine 25 mg once daily	30 mg once daily	11	0.96 (0.85, 1.09)	0.99 (0.89, 1.09)	0.92 (0.79, 1.07)

n = Maximum number of participants with data, CI = Confidence Interval, NA = Not available.

12.4 Microbiology

Mechanism of Action

Cabotegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration that is essential for the HIV replication cycle. The mean 50% inhibitory concentration (IC_{50}) value of cabotegravir in a strand transfer assay using purified recombinant HIV-1 integrase was 3.0 nM.

Antiviral Activity in Cell Culture

Cabotegravir exhibited antiviral activity against laboratory strains of HIV-1 (subtype B, n = 4) with mean 50 percent effective concentration (EC_{50}) values of 0.22 to 1.7 nM in peripheral blood mononuclear cells (PBMCs) and 293 cells. Cabotegravir demonstrated antiviral activity in PBMCs against a panel of 24 HIV-1 clinical isolates (3 in each of group M subtypes A, B, C, D, E, F, and G and 3 in group O) with a median EC_{50} value of 0.19 nM (range: 0.02 to 1.06 nM, n = 24). The median EC_{50} value against subtype B clinical isolates was 0.05 nM (range: 0.02 to 0.50 nM, n = 3). Against clinical HIV-2 isolates, the median EC_{50} value was 0.12 nM (range: 0.10 to 0.14 nM, n = 3).

In cell culture, cabotegravir was not antagonistic in combination with the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine, or the nucleoside reverse transcriptase inhibitors (NRTIs) emtricitabine (FTC), lamivudine (3TC), or tenofovir disoproxil fumarate (TDF).

Resistance

Cell Culture: Cabotegravir-resistant viruses were selected during passage of HIV-1 strain IIIB in MT-2 cells in the presence of cabotegravir. Amino acid substitutions in integrase that emerged and conferred decreased susceptibility to cabotegravir included Q146L (fold change: 1.3 to 4.6), S153Y (fold change: 2.8 to 8.4), and I162M (fold change: 2.8). The integrase substitution T124A also emerged alone (fold change: 1.1 to 7.4 in cabotegravir susceptibility), in combination with S153Y (fold change: 3.6 to 6.6 in cabotegravir susceptibility) or I162M (2.8-fold change in cabotegravir susceptibility). Cell culture passage of virus harboring integrase substitutions Q148H, Q148K, or Q148R selected for additional substitutions (C56S, V72I, L74M, V75A, T122N, E138K, G140S, G149A, and M154I), with substituted viruses having reduced susceptibility to cabotegravir of 2.0- to 410-fold change. The combinations of E138K+Q148K and V72I+E138K+Q148K conferred the greatest reductions of 53- to 260-fold change and 410-fold change, respectively.

Clinical Trials: Treatment of HIV-1 Infection: In the pooled Phase 3 FLAIR (Week 124) and ATLAS (Week 96) analysis, there were 8 confirmed virologic failures (2 consecutive HIV-1 RNA ≥200 copies/mL) on cabotegravir plus rilpivirine (8/591, 1.4%) and 8 confirmed virologic failures on current antiretroviral regimen (8/591, 1.4%). Of the 8 confirmed virologic failures in the cabotegravir plus rilpivirine arm, 7 (88%) had treatment-emergent NNRTI resistance-associated substitutions K101E, V106V/A, V108I, E138A, E138G, E138K, H221H/L, or M230L in reverse transcriptase, and 6 of them showed reduced phenotypic susceptibility to rilpivirine (range: 2- to 27-fold). One additional participant in the ATLAS Extension Switch on cabotegravir plus rilpivirine had emergent NNRTI resistance substitution E138A at Week 80 with HIV-1 RNA >50 copies/mL and <200 copies/mL.

Additionally, 5 of the 8 (63%) cabotegravir plus rilpivirine confirmed virologic failures had treatment-emergent INSTI resistance-associated substitutions and reduced phenotypic susceptibility to cabotegravir: Q148R (n = 2; 5- and 9-fold decreased susceptibility to

cabotegravir), G140R (n = 1; 7-fold decreased susceptibility to cabotegravir), N155H (n = 1; 3-fold decreased susceptibility to cabotegravir), or N155H+R263K (n = 1; 9-fold decreased susceptibility to cabotegravir).

There was another confirmed virologic failure participant at Week 112 in FLAIR who had switched to cabotegravir plus rilpivirine direct to injection at Week 100; there were no INSTI resistance-associated substitutions detected at failure.

In comparison, in the current antiretroviral regimen arm with 8 confirmed virologic failures, 2 of 7 (29%) who had post-baseline resistance data had treatment-emergent resistance substitutions and phenotypic resistance to their antiretroviral drugs; both had treatment-emergent NRTI substitutions, M184V or I, which conferred resistance to emtricitabine or lamivudine in their regimen, and one of them also had the treatment-emergent NNRTI resistance substitution G190S, which conferred resistance to efavirenz in their regimen.

In the ATLAS-2M trial, there were 11 confirmed virologic failures (2 consecutive HIV-1 RNA ≥200 copies/mL) through Week 48: 9 participants (1.7%) in the every-2-month treatment arm and 2 participants (0.4%) in the monthly treatment arm. Of note, 8 of the 11 (73%) participants met confirmed virologic failure criteria at or before the Week 24 injection visit.

Four of the 9 confirmed virologic failure participants in the every-2-month arm transitioned from the oral current antiretroviral regimen arm of ATLAS into this trial.

In the every-2-month treatment arm, 8 of 9 (89%) confirmed virologic failure participants had NNRTI resistance-associated substitutions (E138E/K+V179V/I, K101E+E138A, A98G+K103N, E138K, V179I+Y188L+P225H, Y188L, K103N+E138A, or K101E) at virologic failure. Decreases in rilpivirine susceptibility for these 8 participant isolates ranged from 2- to 30-fold. Six of the 8 participants with NNRTI resistance-associated substitutions also had INSTI resistance-associated substitutions (L74I+Q148Q/R+N155N/H (n = 2), L74I+T97A+N155H, L74I+N155H, N155H, or L74I+Q148R) at failure with cabotegravir fold changes ranging from 1- to 9-fold. The INSTI polymorphism L74I was detected at baseline in 5 of the virologic failure participants by a HIV-1 proviral DNA assay.

In the monthly treatment arm, both of the confirmed virologic failure participants had NNRTI resistance-associated substitutions (K101E+M230L or Y188F+G190Q) at virologic failure with decreased susceptibility to rilpivirine of 17- and >119.2-fold, respectively. Both participants also had INSTI resistance-associated substitutions (N155N/H or Q148R+E138E/K) at failure with decreased susceptibility to cabotegravir of 2- and 5-fold, respectively. Neither participant had the L74I integrase polymorphism at baseline.

Genotypic Baseline Factors Associated with Virologic Failure

An increased risk of cabotegravir plus rilpivirine confirmed virologic failure is associated with baseline virological factors: HIV-1 subtype A1, the presence of baseline integrase L74I polymorphism, and archived NNRTI resistance-associated substitutions.

Association of Subtype A1 and Baseline L74I Polymorphism in Integrase with Cabotegravir plus Rilpivirine Virologic Failure

Eight of the 18 (44%) cabotegravir plus rilpivirine confirmed virologic failures in FLAIR, ATLAS, and ATLAS-2M had HIV-1 subtype A1 with 7 of the 8 subtype A1 failures having the integrase polymorphism L74I detected at baseline and failure timepoints (Table 7). There was no detectable phenotypic resistance to cabotegravir conferred by the presence of L74I at baseline.

Subtype A1 is uncommon in the U.S.

The presence of the integrase polymorphism L74I in subtype B commonly seen in the U.S. was not associated with virologic failure. In contrast to FLAIR and ATLAS, where all virologic failures were subtype A, A1, or AG, subtypes of the cabotegravir plus rilpivirine virologic failures in ATLAS-2M included A (n = 1), A1 (n = 3), B (n = 4), C (n = 2), and complex/A1 (n = 1).

Association of Archived Baseline NNRTI Substitutions with Cabotegravir plus Rilpivirine Virologic Failure

The presence of archived NNRTI resistance-associated substitutions at baseline detected using an exploratory HIV-1 proviral DNA assay was associated with a higher virologic failure rate in the every-2-month arm of ATLAS-2M and in the cabotegravir plus rilpivirine arm (monthly) of ATLAS compared to without archived NNRTI resistance-associated substitutions (Table 7). However, in clinical practice, it is unlikely baseline resistance testing will be performed on virologically suppressed patients (HIV-1 RNA <50 copies/mL). Thus, in patients with an incomplete or uncertain NNRTI treatment history, consideration should be given before starting cabotegravir plus rilpivirine treatment.

Table 7. Rate of Confirmed Virologic Failure in FLAIR, ATLAS, and ATLAS-2M: Baseline[a] Analysis (Subtype Al, Presence of lntegrase Polymorphism L74I, and Presence of Archived NNRTI Resistance-Associated Substitutions)

	FLAIR CAB+RPV N = 283	**FLAIR CAR N = 283**	**ATLAS CAB+RPV N = 308**	**ATLAS CAR N = 308**	**ATLAS-2M Q4W N = 523**	**ATLAS-2M Q8W N = 522**
Total confirmed virologic failures	5	4	3	4	2	9
Subtype A1[b]	4/8 (50%)	1/4 (25%)	1/17 (6%)	0/21 (0%)	0/30 (0%)	4/31 (13%)
+L74I[c]	4/5 (80%)	1/3 (33%)	1/16 (6%)	0/19 (0%)	2/28 (0%)	3/26 (12%)
-L74I	0/3 (0%)	0/1 (0%)	0/1 (0%)	0/2 (0%)	0/2 (0%)	1/5 (20%)
Other subtypes	2/268 (0.7%)	3/272 (1%)	2/240 (0.8%)	4/252 (1.6%)	2/409 (0.5%)	5/415 (1.2%)

+L74I[c]	0/49 (0%)	1/43 (2.3%)	1/29 (3%)	1/39 (2.6%)	0/42 (0%)	2/48 (4%)
-L74I	0/219 (2.5%)	2/229 (0.9%)	1/211 (0.5%)	3/213 (1.4%)	2/367 (0.5%)	3/367 (0.8%)
Missing data	7	7	51	35	84	76
With NNRTI RAS[d]	NA	NA	3/78 (4%)	2/83 (2%)	1/128 (0.8%)	7/117 (6%)
Without NNRTI RAS	NA	NA	0/179 (0%)	2/190 (1%)	1/310 (0.3%)	2/327 (0.6%)
Missing data	NA	NA	51	35	84	76

NNRTI = Non-Nucleoside Reverse Transcriptase Inhibitor, CAB+RPV = Cabotegravir + Rilpivirine, CAR = Current Antiretroviral Regimen, RAS = resistance-associated substitutions, NA = Not available.

[a] Baseline and/or Screening result used.

[b] Per Standard Monogram Nomenclature Reports. Based on June 2020 Los Alamos National Library panel, the majority of HIV-1 subtype A1 was reclassified as HIV-1 subtype A6.

[c] L74I and L74L/I mixture.

[d] Baseline/Screening NNRTI substitutions at L100, K101, K103, V106, V108, E138, V179, Y181, Y188, G190, H221, P225, M230.

HIV-1 PrEP: There were 12 incident infections and 4 prevalent infections among participants receiving cabotegravir injection for HIV-1 PrEP in HPTN 083. Genotypic data were generated for viruses from 13 of these 16 participants (4 participants with prevalent infections and 9 participants with incident infections) and phenotypic data were generated for 3 of these viruses. INSTI resistance-associated substitutions were detected in 5 viruses from participants who achieved target plasma concentrations of cabotegravir (≥0.65 mcg/mL [1.6 microM]) and included R263K (2-fold less susceptible to cabotegravir), E138A+Q148R (6-fold less susceptible to cabotegravir), E138K+Q148K, G140A+Q148R (13-fold less susceptible to cabotegravir), and L74I+E138E/K+G140G/S+Q148R+E157Q.

There were 3 incident infections and 1 prevalent infection among participants receiving cabotegravir injection for HIV-1 PrEP in HPTN 084. All 3 incident infections occurred during periods with cabotegravir exposures below the target concentration. No variants expressing INSTI resistance-associated substitutions were detected.

Cross-Resistance

Cross-resistance has been observed among INSTIs. Cabotegravir had reduced susceptibility (>5-fold change) to recombinant HIV-1 strain NL432 viruses harboring the following integrase amino acid substitutions: G118R, Q148K, Q148R, T66K+L74M, E92Q+N155H, E138A+Q148R, E138K+Q148K/R, G140C+Q148R, G140S+Q148H/K/R, Y143H+N155H, and

Q148R+N155H (range: 5.1- to 81-fold). The substitutions E138K+Q148K and Q148R+N155H conferred the greatest reductions in susceptibility of 81- and 61-fold, respectively.

Cabotegravir was active against viruses harboring the NNRTI substitutions K103N or Y188L, or the NRTI substitutions M184V, D67N/K70R/T215Y, or V75I/F77L/F116Y/Q151M.

Virologic failure isolates from cabotegravir plus rilpivirine treatment in FLAIR, ATLAS, and ATLAS-2M exhibited cross-resistance to INSTIs and NNRTIs. All confirmed virologic isolates with genotypic evidence of cabotegravir resistance had cross-resistance to elvitegravir and raltegravir but retained phenotypic susceptibility to dolutegravir and when tested bictegravir.

Viruses harboring E138A+Q148R or G140A+Q148R with reduced susceptibility to cabotegravir were isolated from participants using cabotegravir injection for HIV-1 PrEP in HPTN 083. These viruses remained susceptible to bictegravir and dolutegravir but had cross-resistance to elvitegravir and raltegravir.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Two-year carcinogenicity studies in mice and rats were conducted with cabotegravir. In mice, no drug-related increases in tumor incidence were observed at cabotegravir exposures (AUC) up to approximately 8 times (males) and 7 times (females) higher than those in humans at the RHD. In rats, no drug-related increases in tumor incidence were observed at cabotegravir exposures up to approximately 26 times higher than those in humans at the RHD.

Mutagenesis

Cabotegravir was not genotoxic in the bacterial reverse mutation assay, mouse lymphoma assay, or in the in vivo rodent micronucleus assay.

Impairment of Fertility

In rats, no effects on fertility were observed at cabotegravir exposures (AUC) >20 times (male) and 28 times (female) the exposure in humans at the RHD.

14 CLINICAL STUDIES

14.1 Clinical Trials in Adults for Treatment of HIV-1 Infection

The use of VOCABRIA in combination with EDURANT as an oral lead-in and in patients who miss planned injections with CABENUVA was evaluated in 3 Phase 3 randomized, multicenter, active-controlled, parallel-arm, open-label, non-inferiority trials (Trial 201584: FLAIR [NCT02938520], Trial 201585: ATLAS [NCT02951052], and Trial 207966: ATLAS-2M [NCT03299049]) in participants who were virologically suppressed (HIV-1 RNA

<50 copies/mL). Please refer to the CABENUVA prescribing information for additional information.

In the FLAIR study during the Extension Phase (Week 100 to Week 124), the efficacy of CABENUVA was evaluated in participants who switched (at Week 100) from their current antiretroviral regimen to CABENUVA, with and without an oral lead-in phase. A total of 121 participants chose to start the treatment with oral lead-in and 111 participants chose direct to injection. Participants were not randomized during the Extension Phase. At Week 124, the proportion of participants with HIV-1 RNA ≥50 copies/mL was 0.8% and 0.9% for the oral lead-in and direct to injection groups, respectively. The rates of virologic suppression (HIV-1 RNA <50 copies/mL) were similar in both the oral lead-in (93%) and direct to injection (99%) groups.

14.2 Clinical Trials in Adults for HIV-1 Pre-Exposure Prophylaxis

The use of VOCABRIA as an oral lead-in and in participants who miss planned injections with APRETUDE to reduce the risk of acquiring HIV-1 infection were evaluated in 2 randomized, double-blind, controlled, multinational trials, Trial 201738 (HPTN 083 [NCT02720094]) in men and transgender women without HIV-1 who have sex with men and have evidence of high-risk behavior for HIV-1 infection and Trial 201739 (HPTN 084 [NCT03164564]) in cisgender women without HIV-1 at risk of acquiring HIV-1. Please refer to the APRETUDE prescribing information for additional information.

14.3 Clinical Trial in Adolescents for Treatment of HIV-1 Infection

Trial 208580 (MOCHA, [NCT03497676])

The safety, tolerability, and pharmacokinetics of oral and injectable cabotegravir and oral and injectable rilpivirine were assessed in an ongoing Phase 1/2 multicenter, open-label, non-comparative study, MOCHA (IMPAACT 2017), in virologically suppressed adolescents with HIV-1 aged 12 to younger than 18 years and weighing ≥35 kg *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3)]*.

The primary objective at Week 24 was to confirm the safety of injectable cabotegravir plus injectable rilpivirine in virologically suppressed adolescents with HIV-1. Antiviral activity was assessed as a secondary objective. A total of 144 adolescent participants with HIV-1 received oral cabotegravir in combination with oral rilpivirine as an oral lead-in. Please refer to the CABENUVA prescribing information for additional information.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each VOCABRIA tablet contains 30 mg of cabotegravir and is a white, oval, film-coated, biconvex tablet debossed with “SV CTV” on one side.

Bottle of 30 tablets with child-resistant closure NDC 49702-248-13.

Store below 30°C (86°F).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Important Information for Individuals without HIV-1 Taking VOCABRIA for HIV-1 PrEP

Advise individuals without HIV-1 about the following *[see Warnings and Precautions (5.1)]*:

- VOCABRIA should be used for PrEP as part of an overall HIV-1 infection prevention strategy, including adherence to the dosing schedule and safer sex practices, including condoms, to reduce the risk of STIs.
- VOCABRIA is not always effective in preventing HIV-1 acquisition *[see Clinical Studies (14.2)]*. The time from initiation of VOCABRIA for HIV-1 PrEP to maximal protection against HIV-1 infection is unknown.
- Counsel individuals on the use of other prevention measures (e.g., knowledge of partner HIV-1 status, testing for STIs condom use). Inform individuals about and support their efforts in reducing sexual risk behavior.
- VOCABRIA should be used to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV-1 negative *[see Contraindications (4), Warnings and Precautions (5.1)]*. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only VOCABRIA, because VOCABRIA alone does not constitute a complete regimen for HIV-1 treatment; therefore, care should be taken to minimize the risk of initiating or continuing VOCABRIA before confirming the individual is HIV-1 negative.
- If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute or primary HIV-1 infection.
- If an HIV-1 test indicates possible HIV-1 infection, or if symptoms consistent with acute HIV-1 infection develop following an exposure event, additional HIV testing to determine HIV status is needed. If an individual has confirmed HIV-1 infection, then the individual must be transitioned to a complete HIV-1 treatment regimen.

Hypersensitivity Reactions

Advise patients to immediately contact their healthcare provider if they develop a rash. Instruct patients to immediately stop taking VOCABRIA and seek medical attention if they develop a rash associated with any of the following symptoms: fever; generally ill feeling; extreme tiredness; muscle or joint aches; blisters; oral blisters or lesions; eye inflammation; facial swelling; swelling of the eyes, lips, tongue, or mouth; difficulty breathing; and/or signs and symptoms of liver problems (e.g., yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored stools or bowel movements; nausea; vomiting; loss of appetite; or pain, aching, or sensitivity on the right side below the ribs). Advise patients that if hypersensitivity

occurs, they will be closely monitored, laboratory tests will be ordered, and appropriate therapy will be initiated *[see Warnings and Precautions (5.2)]*.

Hepatotoxicity

Inform patients that hepatotoxicity has been reported with cabotegravir *[see Warnings and Precautions (5.3), Adverse Reactions (6.1)]*. Inform patients that monitoring for liver transaminases is recommended when VOCABRIA is used for HIV-1 treatment. Inform individuals that clinical and laboratory monitoring should be considered and APRETUDE should be discontinued if hepatoxicity is confirmed when VOCABRIA is used for HIV-1 PrEP *[see Warnings and Precautions (5.3)]*.

Depressive Disorders

Inform patients that depressive disorders (including depressed mood, depression, mood altered, mood swings, suicidal ideation/suicide attempt) have been reported with VOCABRIA for treatment of HIV-1. Inform patients that depressive disorders (including depression, depressed mood, persistent depressive disorder, suicidal ideation/suicide attempt) have been reported with VOCABRIA for HIV-1 PrEP. Promptly evaluate patients with severe depressive symptoms to assess whether the symptoms are related to VOCABRIA and to determine whether the risks of continued therapy outweigh the benefits *[see Warnings and Precautions (5.4), Adverse Reactions (6.1)]*.

Drug Interactions

Inform patients that VOCABRIA may interact with other drugs and may reduce exposure of VOCABRIA; therefore, advise patients to report to their healthcare provider the use of any other prescription or nonprescription medication or herbal products *[see Contraindications (4), Warnings and Precautions (5.5), Drug Interactions (7.2, 7.3)]*.

Dosage and Administration

Inform patients that it is important to take VOCABRIA once daily on a regular dosing schedule with a meal at the same time as EDURANT for HIV-1 treatment and to avoid missing doses, as this can result in development of resistance. Instruct patients that if they miss a dose of VOCABRIA to take it as soon as they remember *[see Dosage and Administration (2.1), Clinical Pharmacology (12.3)]*.

Pregnancy Registry

Inform patients that there is an antiretroviral pregnancy registry to monitor fetal outcomes in those exposed to VOCABRIA during pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation

Inform individuals with HIV-1 infection that the potential risks of breastfeeding include: (1) HIV-1 transmission (in HIV-1–negative infants), (2) developing viral resistance (in HIV-1-positive infants), and (3) adverse reactions in a breastfed infant similar to those seen in adults.

In mothers without HIV-1, the benefits and risks of VOCABRIA while breastfeeding should be evaluated, including the risk of HIV-1 acquisition due to medication nonadherence and subsequent mother to child transmission. Instruct mothers not to breastfeed if acute HIV-1 infection is suspected because of the risk of passing the HIV-1 virus to the baby *[see Use in Specific Populations (8.2)]*.

Manufactured for:

ViiV Healthcare
Durham, NC 27701

VCB:xPI

PHARMACIST—DETACH HERE AND GIVE LEAFLET TO PATIENT

PATIENT INFORMATION
VOCABRIA [voe-KAB-ree-ah]
(cabotegravir)
tablets, for oral use

This Patient Information provides information about two different ways that VOCABRIA may be used. See the section **"What is VOCABRIA?"** for detailed information about how VOCABRIA may be used.

What is the most important information I should know about VOCABRIA?

Important information for people who take VOCABRIA to help reduce their risk of getting human immunodeficiency virus-1 (HIV-1) infection, also called pre-exposure prophylaxis or "PrEP":

Before taking VOCABRIA to reduce your risk of getting HIV-1:

- **You must be HIV-1 negative to start VOCABRIA. You must get tested to make sure that you do not already have HIV-1 infection.**
- **Do not take VOCABRIA for HIV-1 PrEP unless you are confirmed to be HIV-1 negative.**
- Some HIV-1 tests can miss HIV-1 infection in a person who has recently become infected. If you have flu-like symptoms, you could have recently become infected with HIV-1. Tell your healthcare provider if you had a flu-like illness within the last month before starting VOCABRIA or at any time while taking VOCABRIA. Symptoms of new HIV-1 infection include:
  - tiredness
  - joint or muscle aches
  - sore throat
  - rash
  - enlarged lymph nodes in the neck or groin
  - fever
  - headache
  - vomiting or diarrhea
  - night sweats

While you are taking VOCABRIA for HIV-1 PrEP:

- **VOCABRIA does not prevent other sexually transmitted infections. Practice safer sex by using a latex or polyurethane condom to reduce the risk of getting sexually transmitted infections.**
- **You must stay HIV-1 negative to keep taking VOCABRIA for HIV-1 PrEP.**
  - Know your HIV-1 status and the HIV-1 status of your partners.
  - Ask your partners with HIV-1 if they are taking anti-HIV-1 medicines and have an undetectable viral load. An undetectable viral load is when the amount of virus in the blood is too low to be measured in a lab test. To maintain an undetectable viral load, your partners must keep taking HIV-1 medicine as prescribed. Your risk of getting HIV-1 is lower if your partners with HIV-1 are taking effective treatment.
  - Get tested for HIV-1 when your healthcare provider tells you.
  - Get tested for other sexually transmitted infections such as syphilis, chlamydia, and gonorrhea. These infections make it easier for HIV-1 to infect you.
  - If you think you were exposed to HIV-1, tell your healthcare provider right away. They may want to do more tests to be sure you are still HIV-1 negative.
  - Get information and support to help reduce sexual risk behaviors.
  - Do not miss any doses of VOCABRIA. Missing doses increases your risk of getting HIV-1 infection.

- If you do become HIV-1 positive, you will need to take other medicines to treat HIV-1. VOCABRIA by itself is not a complete treatment for HIV-1.

If you have HIV-1 and take only VOCABRIA, over time your HIV-1 may become harder to treat.

What is VOCABRIA?

VOCABRIA is a prescription medicine that may be used in two different ways when a person's healthcare provider determines that they meet certain requirements. VOCABRIA is used:

- to treat HIV-1 infection
  - in combination with another HIV-1 medicine called EDURANT (rilpivirine) for short-term treatment of HIV-1 infection in people 12 years of age and older who weigh at least 77 pounds (35 kg) to replace their current HIV-1 medicines to assess the tolerability of cabotegravir before receiving the long-acting medicine called CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension).
  - as oral therapy for people who will miss planned injection dosing with CABENUVA.
- for HIV-1 PrEP to reduce the risk of getting HIV-1 infection
  - for short-term PrEP in adults and adolescents who weigh at least 77 pounds (at least 35 kg) to assess the tolerability of cabotegravir before receiving the long-acting medicine called APRETUDE (cabotegravir extended-release injectable suspension).
  - as oral dosing for people who will miss planned injection dosing with APRETUDE.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

If you are taking VOCABRIA to treat HIV-1 infection, you should also read the Patient Information for EDURANT.

It is not known if VOCABRIA for treatment of HIV-1 infection is safe and effective in children younger than 12 years of age or weighing less than 77 pounds (35 kg).

It is not known if VOCABRIA is safe and effective in reducing the risk of HIV-1 infection in children younger than 12 years of age or weighing less than 77 pounds (less than 35 kg).

Do not take VOCABRIA if you:

- have ever had an allergic reaction to cabotegravir.
- are taking any of the following medicines:
  - carbamazepine
  - oxcarbazepine
  - phenobarbital
  - phenytoin
  - rifampin
  - rifapentine

For people taking VOCABRIA for treatment of HIV-1 infection:

Do not take VOCABRIA for HIV-1 infection if you are taking rifabutin.

For people taking VOCABRIA for HIV-1 PrEP:

Do not take VOCABRIA for HIV-1 PrEP if you:

- **already have HIV-1 infection**. If you are HIV-1 positive, you will need to take other medicines to treat HIV-1. VOCABRIA by itself is not a complete treatment for HIV-1.
- **do not know your HIV-1 infection status.** You may already be HIV-1 positive. You need to take other medicines to treat HIV-1. VOCABRIA can only help reduce your risk of getting HIV-1 infection **before** you are infected.

- are allergic to cabotegravir.
- are taking any of the medicines listed above. See **"Do not take VOCABRIA for HIV-1 infection if you:"**

Before taking VOCABRIA, tell your healthcare provider about all your medical conditions, including if you:

- have ever had a skin rash or an allergic reaction to medicines that contain cabotegravir.
- have or have had liver problems, including hepatitis B or C infection.
- have ever had mental health problems.
- are pregnant or plan to become pregnant. It is not known if VOCABRIA will harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with VOCABRIA.
  Pregnancy Registry. There is a pregnancy registry for those who take VOCABRIA during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. VOCABRIA may pass into your breast milk.
  - If you take VOCABRIA to treat HIV-1 infection, talk to your healthcare provider about the following risks to your baby from breastfeeding during treatment with VOCABRIA:
    - the HIV-1 virus may pass to your baby if your baby does not have HIV-1 infection.
    - the HIV-1 virus may become harder to treat if your baby has HIV-1 infection.
    - your baby may get side effects from VOCABRIA.
  - If you take VOCABRIA for HIV-1 PrEP, talk with your healthcare provider about the best way to feed your baby while receiving VOCABRIA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Some medicines may interact with VOCABRIA. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

You can ask your healthcare provider or pharmacist for a list of medicines that interact with VOCABRIA.

Do not start taking a new medicine without telling your healthcare provider. Your healthcare provider can tell you if it is safe to take VOCABRIA with other medicines.

How should I take VOCABRIA?

- **For treatment of HIV-1 infection:**
  - Take 1 VOCABRIA tablet and 1 EDURANT tablet 1 time a day for 1 month (at least 28 days) exactly as your healthcare provider tells you.
  - Your healthcare provider may have you take VOCABRIA tablets in combination with EDURANT tablets for 1 month (at least 28 days) before you receive CABENUVA for the first time. This will allow your healthcare provider to assess how well you will tolerate these medicines.
  - Your final dose of VOCABRIA and EDURANT should be taken on the same day you receive your first injections of CABENUVA.
  - If you miss or plan to miss a scheduled monthly or every-2-month injections of CABENUVA by more than 7 days, call your healthcare provider right away to discuss your options.
  - If you take VOCABRIA at the same time as EDURANT, you should take it with a meal.

- Do not run out of VOCABRIA. The virus in your blood may increase and the virus may become harder to treat when using VOCABRIA to treat HIV-1 infection.

- **For HIV-1 PrEP:**
  - Take 1 VOCABRIA tablet 1 time a day for 1 month (at least 28 days) exactly as your healthcare provider tells you.
  - Your healthcare provider may have you take VOCABRIA tablets for 1 month (at least 28 days) before you receive APRETUDE for the first time. This will allow your healthcare provider to assess how well you will tolerate APRETUDE.
  - You should receive your first injection of APRETUDE on the day of your last dose of VOCABRIA or within 3 days.
  - If you miss or plan to miss a scheduled every-2-month injection of APRETUDE by more than 7 days, call your healthcare provider right away to discuss your options.
- VOCABRIA may be taken with or without food.
- If you take antacid products that contain aluminum or magnesium hydroxide or calcium carbonate, they should be taken at least 2 hours before or 4 hours after you take VOCABRIA.
- Stay under the care of a healthcare provider while taking VOCABRIA.
- Do not change your dose or stop taking VOCABRIA without talking to your healthcare provider.
- Do not miss a dose of VOCABRIA. If you miss a dose of VOCABRIA, take it as soon as you remember.
- If you take too much VOCABRIA, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of VOCABRIA?

VOCABRIA may cause serious side effects including:

- **Allergic reactions.** Call your healthcare provider right away if you develop a rash with VOCABRIA**. Stop taking VOCABRIA and get medical help right away if you develop a rash with any of the following signs or symptoms:**
  - fever
  - generally ill feeling
  - tiredness
  - muscle or joint aches
  - trouble breathing
  - blisters or sores in mouth
  - blisters
  - redness or swelling of the eyes
  - swelling of the mouth, face, lips, or tongue
- **Liver problems**. Liver problems have happened in people with or without history of liver problems or other risk factors. Your healthcare provider may do blood tests to check your liver function. People with a history of liver problems or people who have certain liver function test changes may have an increased risk of developing new or worsening changes in certain liver tests during treatment with VOCABRIA. **Call your healthcare provider right away if you develop any of the following signs or symptoms of liver problems:**
  - your skin or the white part of your eyes turns yellow (jaundice)
  - dark or “tea-colored” urine
  - light-colored stools (bowel movements)
  - loss of appetite
  - pain, aching, or tenderness on the right side of your stomach area
  - itching

- nausea or vomiting

- **Depression or mood changes. Call your healthcare provider or get medical help right away if you develop any of the following symptoms:**
  - feeling sad or hopeless
  - feeling anxious or restless
  - have thoughts of hurting yourself (suicide) or have tried to hurt yourself

The most common side effects of VOCABRIA for HIV-1 treatment include:

- fatigue
- headache
- diarrhea
- nausea
- dizziness
- abnormal dreams
- anxiety
- sleep disorders
- stomach pain
- stomach bloating
- weakness

The most common side effects of VOCABRIA for HIV-1 PrEP include:

- headache
- diarrhea
- nausea
- dizziness
- upper respiratory tract infection
- tiredness
- drowsiness
- abnormal dreams
- stomach pain

These are not all the possible side effects of VOCABRIA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store VOCABRIA?

Store VOCABRIA below 86°F (30°C).

Keep VOCABRIA and all medicines out of the reach of children.

General information about the safe and effective use of VOCABRIA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use VOCABRIA for a condition for which it was not prescribed. Do not give VOCABRIA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about VOCABRIA that is written for health professionals.

What are the ingredients in VOCABRIA?

Active ingredient: cabotegravir

Inactive ingredients: hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate.

The tablet film-coating contains: hypromellose, polyethylene glycol and titanium dioxide.

Manufactured for:

ViiV Healthcare

ViiV Healthcare
Durham, NC 27701

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 12/2023