



News Release

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Janssen Announces U.S. FDA Approval of CABENUVA (rilpivirine and cabotegravir), the First Long-Acting Regimen for the Treatment of HIV

CABENUVA offers adults living with HIV a new once-monthly injectable option for maintaining viral suppression

TITUSVILLE, N.J., January 21, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the U.S. Food and Drug Administration (FDA) has approved CABENUVA (consisting of Janssen’s rilpivirine and ViiV Healthcare’s cabotegravir), the first and only once-monthly, long-acting regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults. The novel regimen was co-developed as part of a collaboration with ViiV Healthcare and builds on Janssen’s 25-year commitment to make HIV history. In the U.S., ViiV Healthcare is the marketing authorization holder for CABENUVA.

CABENUVA is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen, with no history of treatment failure, and with no known or suspected resistance to either cabotegravir or rilpivirine. Prior to initiating treatment with CABENUVA, oral cabotegravir (VOCABRIA) and oral rilpivirine (EDURANT®) should be administered for approximately one month to assess the tolerability of each therapy.

CABENUVA, a co-packaged kit with two injectable medicines, offers people living with HIV a new approach for maintaining viral suppression.¹

[Click to Tweet:](#) #BREAKING: The #FDA has approved another treatment option for people living with #HIV. Read full announcement here: <http://bit.ly/38rPgFi>

“With the approval of CABENUVA, we’re proud to bring a new treatment option to people living with HIV that removes the burden of taking a daily pill,” said Paul Stoffels, M.D., Vice Chairman of the Executive Committee and Chief Scientific Officer, Johnson & Johnson. “While much more remains to be done to make HIV history, today’s milestone reminds us how far medical innovation has come since the first reported cases of the virus almost 40 years ago.”

The approval of CABENUVA is based on the pivotal Phase 3 ATLAS (Antiretroviral Therapy as Long-Acting Suppression) and FLAIR (First Long-Acting Injectable Regimen) studies that included more than 1,100 patients from 16 countries, including the U.S. The studies demonstrated that CABENUVA was as effective as continuing a daily, oral, three-drug regimen in maintaining viral suppression throughout the 48-week study period.

In the ATLAS study, CABENUVA met the primary endpoint for noninferiority (the proportion of participants with plasma HIV-1 RNA ≥ 50 copies per milliliter [c/mL] at Week 48), with a comparable number of patients receiving either CABENUVA or their daily current antiretroviral regimen (CAR) having an HIV-1 RNA level ≥ 50 c/mL. Two percent of patients receiving the long-acting injectable and 1% of patients receiving CAR had an HIV-1 RNA level ≥ 50 c/mL at Week 48 (Treatment Difference 0.7%; 95% CI: -1.2%, 2.5%).

In the FLAIR study, at Week 48, a comparable number of patients receiving either CABENUVA or daily oral dolutegravir/abacavir/lamivudine therapy had an HIV-1 RNA count ≥ 50 c/mL, meeting noninferiority criteria. Two percent of patients in both treatment arms had an HIV-1 RNA count ≥ 50 c/mL at Week 48 (Treatment Difference -0.4%; 95% CI: -2.8%, 2.1%).

Adverse reactions of at least Grade 2 severity in patients who were receiving CABENUVA or CAR were, respectively: injection site reactions (37%, 0), pyrexia (2%, 0), fatigue (1%, <1%), headache (<1%, <1%), musculoskeletal pain (1%, 0), nausea (<1%, 0), sleep disorders (<1%, 0), dizziness (<1%, 0) and rash (<1%, 0).

Results from these trials were [presented](#) at the 2019 Conference on Retroviruses and Opportunistic Infections (CROI).

“This is an exciting new option for patients and providers, as it provides an alternative strategy for effective HIV treatment,” said Susan Swindells, MBBS, Professor, Department of Internal Medicine, University of Nebraska Medical Center. “CABENUVA once-monthly injections showed comparable efficacy to daily oral antiretroviral treatment in maintaining viral suppression – a first in the treatment paradigm.”

“For more than 25 years, we have been committed to changing the course of the HIV epidemic through the pursuit of innovative treatments and effective prevention,” said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, Johnson & Johnson. “This new treatment option for people living with HIV brings us one step closer toward alleviating this global health threat.”

The once-monthly rilpivirine and cabotegravir injectable treatment was approved by Health Canada on March 20, 2020, and the European Commission approved a once-monthly and once every two-month version of the injectable treatment on December 21, 2020. Regulatory reviews continue in Australia and Switzerland, and several additional submissions are planned throughout 2021.

About CABENUVA (rilpivirine and cabotegravir)

CABENUVA is approved as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine. CABENUVA is administered by a healthcare provider once-monthly as two individual intramuscular injections in the buttocks.

The complete regimen combines rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI) developed by Janssen Sciences Ireland UC, with the integrase strand transfer inhibitor (INSTI) cabotegravir, developed by ViiV Healthcare.

INSTIs, like cabotegravir, inhibit HIV replication by preventing the viral DNA from integrating into the genetic material of human immune cells (T-cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic infection.

Rilpivirine is an NNRTI that works by interfering with an enzyme called reverse transcriptase, which in turn stops the virus from multiplying.

About EDURANT® (rilpivirine)

EDURANT® (rilpivirine), in combination with other antiretroviral agents, is a non-nucleoside reverse transcriptase inhibitor (NNRTI) indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naïve patients 12 years of age and older and weighing at least 35 kg with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy.

Limitations of Use:

- More EDURANT®-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure (HIV-1 RNA \geq 50 copies/mL) compared to EDURANT®-treated subjects with HIV-1 RNA less than or equal to 100,000 copies/mL

EDURANT® is also indicated in combination with VOCABRIA (oral cabotegravir) for short-term treatment of HIV-1 infection in adults who are virologically suppressed (HIV-1 RNA less than 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:

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

Janssen is the marketing authorization holder for EDURANT® in the U.S.

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About ATLAS and FLAIR

ATLAS (NCT02951052) is a Phase 3, open-label, active-controlled, multicenter, parallel-group, noninferiority study designed to assess the antiviral activity, safety and tolerability of a two-drug regimen of long-acting, injectable rilpivirine and cabotegravir dosed every four weeks compared to continuation of current oral antiretroviral therapy (ART) of two

nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or protease inhibitor (PI) among virally suppressed individuals. Participants were required to be virally suppressed for six months or longer, on a first or second regimen, with no prior failure. The primary endpoint for ATLAS is the proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL per the FDA Snapshot algorithm at Week 48 (Missing, Switch, or Discontinuation = Failure, Intent-to-Treat Exposed [ITT-E] population).

FLAIR (NCT02938520) is a Phase 3, randomized, open-label, multicenter, parallel-group, noninferiority study designed to assess the antiviral activity, safety and tolerability of a two-drug regimen of intramuscular, long-acting, injectable rilpivirine and cabotegravir in adults living with HIV who were virologically suppressed following 20 weeks of induction therapy with either dolutegravir/abacavir/lamivudine or dolutegravir plus 2 other NRTIs if subjects were HLA-B*5701 positive. Participants who were virologically suppressed (HIV-1 RNA less than 50 copies/mL) were then randomized (1:1) to receive either a cabotegravir plus rilpivirine regimen or remain on the current antiretroviral regimen. The primary endpoint for FLAIR is the proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL per the FDA Snapshot algorithm at Week 48 (Missing, Switch, or Discontinuation = Failure, Intent-to-Treat Exposed [ITT-E] population).

Important Safety Information for CABENUVA

CABENUVA is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

CONTRAINDICATIONS

- Do not use CABENUVA in patients with previous hypersensitivity reaction to cabotegravir or rilpivirine.
- Do not use CABENUVA in patients receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (>1 dose), and St John's wort.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions:

- Hypersensitivity reactions, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), have been reported during postmarketing experience with rilpivirine-containing regimens. While some skin reactions were accompanied by constitutional symptoms such as fever, other skin reactions were associated with organ dysfunctions, including elevations in hepatic serum biochemistries.
- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with CABENUVA.
- Discontinue CABENUVA immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated. Prescribe the oral lead-in prior to administration of CABENUVA to help identify patients who may be at risk of a hypersensitivity reaction.

Post-Injection Reactions:

- Serious post-injection reactions (reported in less than 1% of subjects) were reported within minutes after the injection of rilpivirine, including dyspnea, agitation, abdominal cramping, flushing, sweating, oral numbness, and changes in blood

pressure. These events may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after the injection.

- Carefully follow the Instructions for Use when preparing and administering CABENUVA to avoid accidental intravenous administration. Observe patients briefly (approximately 10 minutes) after the injection. If a post-injection reaction occurs, monitor and treat as clinically indicated.

Hepatotoxicity:

- Hepatotoxicity has been reported in patients receiving cabotegravir or rilpivirine with or without known pre-existing hepatic disease or identifiable risk factors.
- Patients with underlying liver disease or marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations.
- Monitoring of liver chemistries is recommended and treatment with CABENUVA should be discontinued if hepatotoxicity is suspected.

Depressive Disorders:

- Depressive disorders (including depressed mood, depression, major depression, mood altered, mood swings, dysphoria, negative thoughts, suicidal ideation or attempt) have been reported with CABENUVA or the individual products.
- Promptly evaluate patients with depressive symptoms.

Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:

- The concomitant use of CABENUVA and other drugs may result in known or potentially significant drug interactions (see Contraindications and Drug Interactions).
- Rilpivirine doses 3 and 12 times higher than the recommended oral dosage can prolong the QTc interval. CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes.

Long-Acting Properties and Potential Associated Risks with CABENUVA:

- Residual concentrations of cabotegravir and rilpivirine may remain in the systemic circulation of patients for prolonged periods (up to 12 months or longer). Select appropriate patients who agree to the required monthly injection dosing schedule because non-adherence to monthly injections or missed doses could lead to loss of virologic response and development of resistance.
- To minimize the potential risk of developing viral resistance, it is essential to initiate an alternative, fully suppressive antiretroviral regimen no later than 1 month after the final injection doses of CABENUVA. If virologic failure is suspected, switch the patient to an alternative regimen as soon as possible.

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 2\%$, all grades) with CABENUVA were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash.

DRUG INTERACTIONS

- Refer to the applicable full Prescribing Information for important drug interactions with CABENUVA, Vocabria, or rilpivirine.
- Because CABENUVA is a complete regimen, coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.

- Drugs that are strong inducers of UGT1A1 or 1A9 are expected to decrease the plasma concentrations of cabotegravir. Drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine.
- CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** There are insufficient human data on the use of CABENUVA during pregnancy to adequately assess a drug-associated risk for birth defects and miscarriage. Discuss the benefit-risk of using CABENUVA during pregnancy and conception and consider that cabotegravir and rilpivirine are detected in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA. An Antiretroviral Pregnancy Registry has been established.
- **Lactation:** The CDC recommends that HIV-1–infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. Breastfeeding is also not recommended due to the potential for developing viral resistance in HIV-positive infants, adverse reactions in a breastfed infant, and detectable cabotegravir and rilpivirine concentrations in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA.

Please see full [Prescribing Information](#).

EDURANT® Important Safety Information

Contraindications

- Coadministration of EDURANT® with the following drugs is contraindicated because significant decreases in rilpivirine plasma concentrations may occur due to CYP3A enzyme induction or gastric pH increase, which may result in loss of virologic response and possible resistance and cross-resistance: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors such as esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole, systemic dexamethasone (more than single dose), and products containing St. John’s wort (*Hypericum perforatum*)

Warnings and Precautions

- **Skin and Hypersensitivity Reactions:** Severe skin and hypersensitivity reactions have been reported during the postmarketing experience, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), with rilpivirine-containing regimens. While some skin reactions were accompanied by constitutional symptoms such as fever, other skin reactions were associated with organ dysfunctions, including elevations in hepatic serum biochemistries. EDURANT® should be discontinued immediately if signs or symptoms of severe skin or hypersensitivity reactions develop, including but not limited to, severe rash or rash accompanied by fever, blisters, mucosal involvement, conjunctivitis, facial edema, angioedema, hepatitis or eosinophilia. Clinical status including laboratory parameters should be monitored and appropriate therapy should be initiated
- **Hepatotoxicity:** Hepatic adverse events were reported. Patients with underlying hepatic disease, including hepatitis B or C, or marked elevations in transaminases before treatment may be at increased risk for worsening or development of transaminase elevations. Monitor liver function tests (LFTs) before and during

treatment. A few hepatotoxicity cases occurred in patients with no pre-existing hepatic disease or other identifiable risk factors; therefore, monitoring of LFTs should be considered in all patients

- **Depressive Disorders:** Severe depressive disorders, defined as depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, and suicidal ideation, have been reported with EDURANT®. Immediate medical evaluation is recommended for severe depressive symptoms
- **Fat Redistribution:** Redistribution and/or accumulation of body fat have been observed in patients receiving antiretroviral (ARV) therapy. The causal relationship, mechanism, and long-term consequences of these events have not been established
- **Immune Reconstitution Syndrome** has been reported in patients treated with combination ARV therapy, including EDURANT®. Autoimmune disorders (such as Graves disease, polymyositis, Guillain-Barré syndrome and autoimmune hepatitis) have also been reported to occur in the setting of immune reconstitution; however, the time to onset is more variable and can occur many months after initiation of treatment

Drug Interactions

- EDURANT® should be used with caution when coadministered with drugs that may reduce the exposure of rilpivirine, such as antacids and H₂-receptor antagonists. If EDURANT® is used with CABENUVA (cabotegravir, rilpivirine injections), use with rifampin is contraindicated
- Concomitant use of EDURANT® with rifabutin may cause a decrease in the plasma concentrations of rilpivirine. Please read the Dosage and Administration Section of the Prescribing Information for more details regarding the concomitant use of EDURANT® and rifabutin
- EDURANT® should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes
- EDURANT® should not be used in combination with NNRTIs

**This is not a complete list of potential drug interactions.
Please see full [Prescribing Information](#) for more details.**

Use in Specific Populations

- **Hepatic Impairment:** EDURANT® should be used with caution in patients with severe hepatic impairment (Child-Pugh Class C) as pharmacokinetics of EDURANT® have not been evaluated in these patients
- **Pregnancy:** In a clinical trial, total rilpivirine exposures were generally lower during pregnancy compared to the postpartum period
- **Lactation:** Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission

**This list of uses in specific populations is not complete.
Please refer to the EDURANT® [Prescribing Information](#) for additional information.**

Adverse Reactions

- The most common adverse drug reactions reported (incidence >2%) of at least moderate intensity (≥ Grade 2) in patients taking EDURANT® through 96 weeks were depressive disorders (5%), headache (3%), insomnia (3%), and rash (3%)

This is not a complete list of all adverse drug reactions reported with the use of EDURANT®.

Please read the full [Prescribing Information](#) for a complete list of adverse drug reactions.

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About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com and follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Janssen Research & Development and Janssen Sciences Ireland Unlimited Company are members of the Janssen Pharmaceutical Companies of Johnson & Johnson.

To learn more about Janssen's commitment to the prevention and treatment of HIV, please visit jnj.com/HIV.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding rilpivirine and development of potential preventive and treatment regimens for HIV. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Sciences Ireland UC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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REFERENCES

1. CABENUVA (cabotegravir, rilpivirine) Prescribing Information. US Approval January 2021.

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