



News Release

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U.S. FDA Approves CABENUVA (rilpivirine and cabotegravir) for Use Every Two Months, Expanding the Label of the First and Only Long-Acting HIV Treatment

CABENUVA offers virologically suppressed adults living with HIV an injectable treatment option administered as few as six times a year.

TITUSVILLE, N.J., February 1, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the U.S. Food and Drug Administration (FDA) has approved an expanded label for CABENUVA (rilpivirine and cabotegravir) to be administered every two months for the treatment of HIV-1 in virologically suppressed adults (HIV-1 RNA less than 50 copies per milliliter [c/ml]) on a stable regimen, with no history of treatment failure, and with no known or suspected resistance to either rilpivirine or cabotegravir. 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. ViiV Healthcare is the marketing authorization holder for CABENUVA in the U.S.

CABENUVA was [approved](#) by the U.S. FDA in January 2021 as a once-monthly, 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).¹ CABENUVA is comprised of two separate injectable medicines, rilpivirine extended-release injectable suspension in a single-dose vial, a product of Janssen Sciences Ireland Unlimited

Company, and ViiV Healthcare's cabotegravir extended-release injectable suspension in a single dose vial. Prior to initiating treatment of CABENUVA, oral dosing of rilpivirine and cabotegravir should be administered for approximately one month to assess the tolerability of each therapy. The U.S. FDA Approval allows CABENUVA to be dosed monthly or every two months.

"The expanded label approval for CABENUVA—to be administered every two months—marks an important step forward in advancing the treatment landscape for people living with HIV," said Candice Long, President, Infectious Diseases & Vaccines, Janssen Therapeutics, a Division of Janssen Products, LP. "With this milestone, adults living with HIV have a treatment option that further reduces the frequency of medication."

[Click to Tweet](http://bit.ly/38rPgFi): #BREAKING: The @US_FDA has approved a new dosing option for people living with #HIV. Learn more about this exciting milestone in the HIV treatment landscape: <http://bit.ly/38rPgFi>

"An important goal for us in HIV is alleviating the need for daily medication, which can serve as a constant reminder for people living with the condition," said James Merson, Ph.D., Global Therapeutic Area Head, Infectious Diseases, Janssen Research & Development, LLC. "With this new treatment option that reduces CABENUVA dosing frequency to just six times per year, we are revolutionizing HIV therapy for people living with HIV in the U.S."

The U.S. FDA approval of long-acting rilpivirine and cabotegravir for use every two months is based on the global ATLAS-2M phase 3b trial results, which demonstrated that every-two-month dosing was non-inferior to once-monthly dosing.² Non-inferiority was determined by comparing the proportion of participants with plasma HIV-1 RNA \geq 50 c/ml using the U.S. FDA Snapshot algorithm at Week 48 (Intent-to-Treat Exposed population), which showed that the every-two-month arm (9/522 [1.7%]) and once-monthly arm (5/523 [1.0%]) were similarly effective (adjusted difference: 0.8%, 95% confidence interval [CI]: -0.6%, 2.2%). The study also found that rates of virologic suppression, a key secondary endpoint, were similar for every-two-month dosing (492/522 [94.3%]) and once-monthly dosing (489/523 [93.5%]) (adjusted difference: 0.8%, 95% CI: -2.1%, 3.7%). The most common adverse reactions (Grades 1 to 4) observed in \geq 2% of participants receiving long-acting rilpivirine and cabotegravir were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash. In ATLAS-2M, the type and frequency of adverse reactions reported in participants receiving long-acting rilpivirine and cabotegravir once monthly or every two months for 48 weeks were similar. In the every-two-month arm, rates of serious adverse events (SAEs: 27/522[5.2%]) and withdrawals due to adverse events (AEs: 12/522 [2.3%]) were low and similar to those experienced in the once-monthly arm (SAEs: 19/523 [3.6%], withdrawals due to AEs 13/523 [2.5%]).²

"Every clinician wants to be able to provide a patient with a treatment that is right for them, and there are a number of factors that go into that decision," said Tony Mills, MD*, CEO of Men's Health Foundation in Los Angeles, CA. "With this approval, there is an important added option for physicians to address patient's preferences for less frequent dosing."

The once-monthly version of rilpivirine and cabotegravir injectable treatment has also been approved by the European Commission, Health Canada, the Australia Therapeutic Goods Administration, and the Swiss Agency for Therapeutic Products. The every-two-months version has also been approved by the European Commission, Health Canada, and the Swiss Agency for Therapeutic Products. Regulatory reviews continue with additional submissions planned throughout 2022.

**Tony Mills, MD, has received research support from Janssen and has served as a paid consultant to the company. He has not been compensated for any media work.*

About ATLAS-2M (NCT03299049)

The ATLAS-2M Phase 3b trial is an ongoing, randomized, open-label, active-controlled, multicenter, parallel-group trial designed to assess the non-inferior antiviral activity and safety of long-acting rilpivirine and cabotegravir administered every eight weeks (every two months, 3ml dose of each medicine) compared to every four weeks (once monthly, 2ml dose of each medicine) over a 48-week treatment period in 1,045 adults living with HIV-1.² Subjects were required to be virologically suppressed for six months or greater, on a first or second antiretroviral regimen, with no prior virologic failure. The primary outcome measure for the trial is the proportion of participants with HIV-1 RNA ≥ 50 c/ml at Week 48 using the U.S. FDA Snapshot algorithm (intent-to-treat exposed population).

For further information please see <https://clinicaltrials.gov/ct2/show/NCT03299049>.

About CABENUVA (rilpivirine and cabotegravir)

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 rilpivirine or cabotegravir. CABENUVA is administered by a healthcare provider as two intramuscular injections (rilpivirine and cabotegravir) in the buttocks.

The complete regimen combines rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI) developed by Janssen Sciences Ireland Unlimited Company, with the integrase strand transfer inhibitor (INSTI) cabotegravir, developed by ViiV Healthcare. Rilpivirine is approved in the U.S. as a 25mg tablet taken once a day for the treatment of HIV-1 in combination with other antiretroviral agents in antiretroviral treatment-naïve patients 12 years of age and older and weighing at least 35kg with a viral load $\leq 100,000$ HIV RNA copies/ml.

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

INSTIs 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 disease.

IMPORTANT SAFETY INFORMATION

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, bronchospasm, agitation, abdominal cramping, rash/urticaria, dizziness, flushing, sweating, oral numbness, changes in blood pressure, and pain (e.g., back and chest). 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. The suspensions should be injected slowly via intramuscular injection and 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 or every-2-month injection dosing schedule because non-adherence 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 when dosed monthly and no later than 2 months after the final injections of CABENUVA when dosed every 2 months. 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.
- The most common injection site reactions (grades 1-3, $\geq 1\%$) were pain/discomfort, nodules, induration, swelling, erythema, pruritus, bruising/dyscoloration, warmth, and hematoma

DRUG INTERACTIONS

- Refer to the applicable full Prescribing Information for important drug interactions with CABENUVA, VOCABRIA, or EDURANT
- 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](#).

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 <http://www.janssen.com> and follow us at <http://www.twitter.com/JanssenGlobal> and www.twitter.com/JanssenUS. Janssen Sciences Ireland Unlimited Company, Janssen Therapeutics, a Division of Janssen Products, LP, and

Janssen Research & Development, LLC are part 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 Unlimited Company, 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 January 3, 2021, 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.
2. Overton E et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. *The Lancet*. 2020;396(10267):1994-2005.

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