News Release

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U.S. FDA Approves CABENUVA (cabotegravir and rilpivirine) for Adolescents, Expanding the Indication of the First and Only Complete Long-Acting Injectable HIV Regimen

CABENUVA offers virologically suppressed adolescents 12 years of age or older living with HIV-1 an injectable treatment option with as few as six dosing days per year

TITUSVILLE, N.J., March 29, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the U.S. Food and Drug Administration (FDA) has approved CABENUVA (cabotegravir and rilpivirine) for the treatment of HIV-1 in virologically suppressed adolescents (HIV-1 RNA less than 50 copies per milliliter [c/mL]) who are 12 years of age or older, weigh at least 35 kg and are on a stable antiretroviral regimen, with no history of treatment failure, nor known or suspected resistance to either cabotegravir or rilpivirine.[1,2] Co-developed as part of a collaboration with ViiV Healthcare, CABENUVA is the first and only complete long-acting HIV-1 treatment regimen, and the first to be made available for eligible adolescents, building on Janssen's ongoing commitment to fighting HIV and improving HIV treatment options for young people living with HIV.

CABENUVA is approved as a once-monthly or every-two-months treatment for HIV-1 in virologically suppressed adults and adolescents. It contains ViiV Healthcare's cabotegravir extended-release injectable suspension in a single-dose vial and rilpivirine extended-release injectable suspension in a single-dose vial, a product of Janssen Sciences Ireland Unlimited Company, one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

"HIV remains one of the most significant challenges in global health, and as part of our decades-long commitment to fighting HIV, Janssen is working tirelessly to advance innovative new treatment options for young people living with HIV," said James Merson, Ph.D., Global Therapeutic Area Head, Infectious Diseases, Janssen Research & Development, LLC. "With this milestone, we're continuing to redefine how HIV can be managed so that even more people, including adolescents, can benefit from long-acting injectable therapies."

The expanded indication for CABENUVA is supported by studies in adults and by data from the Week 16 interim analysis of the ongoing More Options for Children and Adolescents (MOCHA) study from ViiV Healthcare's collaboration with the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT). The efficacy of CABENUVA in adolescents is extrapolated from adults with support from pharmacokinetic analyses showing similar drug exposure. The safety profile in adolescents with the addition of either oral cabotegravir followed by injectable cabotegravir (n=8) or oral rilpivirine (n=15) followed by injectable rilpivirine (n=13) was consistent with the safety profile established with cabotegravir plus rilpivirine in adults.

Based on data from the Week 16 analysis of the MOCHA study in 23 adolescents, adverse reactions were reported in 61% of patients receiving either cabotegravir or rilpivirine in addition to their current antiretroviral treatment. The majority of these individuals (86%) had a Grade 1 or Grade 2 adverse reaction. The adverse reactions reported by more than one patient (regardless of severity) were injection site pain (n=13) and insomnia (n=2). Two patients had Grade 3 adverse reactions of hypersensitivity (n=1) and insomnia (n=1). The Grade 3 adverse reaction of drug hypersensitivity led to discontinuation of rilpivirine during oral lead-in. Sixty-two percent of patients who received at least one injection of cabotegravir or rilpivirine reported at least one injection site reaction. All injection site reactions were Grade 1 or Grade 2.[1]

"We're proud of our longstanding efforts to address the needs of young people living with HIV," said Candice Long, President, Infectious Diseases & Vaccines, Janssen Therapeutics, a Division of Janssen Products, LP. "By advancing new treatment options to meet the unique needs of adolescents living with HIV, we can help build a future where young people are not defined or limited by their diagnosis."

The U.S. Centers for Disease Control and Prevention reported that people aged 13-24 accounted for 21% of all new HIV diagnoses in the U.S. and dependent areas in 2018.[3] Adhering to treatment regimens can be difficult for children and adolescents, who may skip HIV medicine doses to hide their HIV-positive status from others.[3] Having more treatment options available, including simplified and long-acting injectable regimens, may be important to ensuring that adolescents can receive treatment on their own terms.

CABENUVA Regulatory Status

In January 2021, the FDA approved CABENUVA to be administered every month to adults living with HIV-1. In February 2022, the FDA approved an expanded label for CABENUVA to be administered every two months to adults living with HIV-1. The FDA approved a label update in March 2022 that made the oral lead-in period optional for adults living with HIV-1 who planned to begin the injectable treatment regimen. The oral lead-in period is also optional for adolescent patients.

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

Johnson & Johnson's Commitment to HIV

Johnson & Johnson has been committed to the fight against HIV for decades, playing a central role in bringing nine therapeutics to people living with HIV, and continuing to drive innovation in HIV prevention and care. Johnson & Johnson also works with vulnerable communities on the frontlines of the HIV epidemic through initiatives such as Positively Fearless, DREAMS Thina Abantu Abasha, the MenStar Coalition and the New Horizons Collaborative.

To learn more, visit jnj.com/hiv

About CABENUVA (cabotegravir and rilpivirine)
CABENUVA is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents who are 12 years of age or older and weighing at least 35 kg 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.

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

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

About MOCHA/IMPAACT 2017
MOCHA (NCT03497676) is a Phase 1/2, multi-center, open-label, non-comparative study of oral cabotegravir or rilpivirine and long-acting cabotegravir or rilpivirine in virologically suppressed adolescents living with HIV-1 who are 12 to less than 18 years old. The study is designed to confirm the dose and evaluate the safety, tolerability, acceptability, and pharmacokinetics of cabotegravir and rilpivirine in adolescents living with HIV. Caregivers of adolescent participants in the United States are also enrolled to take part in a single in-depth qualitative interview to contribute to the evaluation of tolerability and acceptability of long-acting therapy, with favorable feedback overall.[4] The study is being conducted at research centers in Botswana, South Africa, Thailand, Uganda and the United States.

Important Safety Information for CABENUVA (cabotegravir 200 mg/mL; rilpivirine 300 mg/mL) extended-release injectable suspensions

CABENUVA is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents who are 12 years of age or older and weighing at least 35 kg 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.

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 ≥2%, all grades) with CABENUVA were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash
- The safety of CABENUVA in adolescents is expected to be similar to adults

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 Research & Development, LLC; and Janssen Therapeutics, a Division of Janssen Products, LP 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 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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.

References

1. CABENUVA (cabotegravir, rilpivirine) Prescribing Information. US Approval March 2022.
2. Moore CB, Capparelli E, Calabrese K, et al. Safety and PK of Long-Acting Cabotegravir and Rilpivirine in Adolescents. Presented at CROI 2022.
3. HIV and Children and Adolescents. National Institutes of Health. Available: https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-children-and-adolescents. Last updated August 2021. Last accessed March 2022.
4. Lowenthal E, Chapman, J, Calabrese, K, et al. Adolescent and Parent Experiences with Long-Acting Injectables in the MOCHA Study. Presented at CROI 2022.

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