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**Janssen Announces U.S. FDA Approval of First and Only  
Complete, Single-Pill, Two-Drug Regimen, JULUCA®  
(Dolutegravir and Rilpivirine), for the Treatment of HIV-1 Infection**

*Provides New Treatment Option for Stable,  
Virologically Suppressed Adults Living with HIV-1*

**TITUSVILLE, N.J., NOVEMBER 21, 2017** – Janssen Therapeutics, Division of Janssen Products, LP (Janssen), today announced that the U.S. Food and Drug Administration (FDA) has approved JULUCA®, the first, complete, single-pill, two-drug regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in certain adults living with the disease who are virologically suppressed.

JULUCA® is a once-daily, antiretroviral combination of dolutegravir, an integrase strand transfer inhibitor (INSTI) marketed by ViiV Healthcare as TIVICAY®, and rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI) marketed by Janssen as EDURANT®. With JULUCA®, people living with HIV who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable antiretroviral regimen for at least six months and have no prior history of treatment failure – and no known resistance to the individual components of JULUCA® – now have a new treatment option to consider.<sup>1</sup>

“Today’s approval of JULUCA® marks a significant milestone in the treatment of HIV,” said Brian Woodfall, Global Head of Late Development, Janssen Research & Development. “As the first single-pill, complete two-drug regimen, JULUCA® maintains the safety and efficacy of a traditional three-drug regimen without an N(t)RTI. This is

exciting because it offers those living with HIV who are compliant and stably suppressed a new, simplified treatment option to consider.”

JULUCA<sup>®</sup> received FDA approval based on data from the two pivotal Phase 3 SWORD studies, which are identical, randomized, multicenter, open-label, non-inferiority studies designed to assess the safety and efficacy of switching to the two-drug regimen of dolutegravir and rilpivirine compared with remaining on current antiretroviral regimen (CAR). The studies included more than one thousand patients who previously achieved stable viral suppression for at least six months on other antiretroviral regimens (integrase inhibitor, NNRTI, or boosted protease inhibitor-based) and had no history of virologic failure or known resistance to dolutegravir or rilpivirine.<sup>2</sup>

Reaching and maintaining suppression of viral load is a key treatment goal for people living with HIV. Results demonstrated that JULUCA<sup>®</sup> achieved non-inferior viral suppression (HIV-1 RNA <50 c/mL) at 48 Weeks compared with a three-drug CAR in both studies (dolutegravir + rilpivirine [DTG+RPV] 486/513 (95%), CAR 485/511 (95%), adjusted difference -0.2%, (95% CI: [2.5%,-3.0%])). Virologic failure rates were <1% in the DTG+RPV arm and 1% in the CAR arm. No INSTI resistance-associated mutations or clinically significant resistance to rilpivirine were reported. The proportion of patients who discontinued treatment due to an adverse event (AE) was 4% in those receiving DTG+RPV once daily and less than 1% in those who remained on their CAR. The most common AEs leading to discontinuation were psychiatric disorders in 2% receiving DTG+RPV and less than 1% on the CAR. The most common AEs (all grades) reported in at least 2% of patients were diarrhea and headache.

Switching to the two-drug regimen of JULUCA<sup>®</sup> showed a neutral effect on lipids – at 48 Weeks, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and total cholesterol to HDL ratio were similar between the treatment arms. In addition, while the long-term clinical significance of bone mineral density (BMD) changes is not known, a substudy demonstrated mean BMD increased from baseline to Week 48 in people who switched from an antiretroviral treatment (ART) regimen containing tenofovir disoproxil fumarate (TDF) to JULUCA<sup>®</sup> (1.34% total hip and 1.46% lumbar spine) compared with those who continued on treatment with a TDF-containing ART regimen (0.05% total hip and 0.15% lumbar spine). The SWORD trials are ongoing and planned to continue through 148 Weeks. Future long-term data and analyses will be presented at upcoming medical congresses.

“At Janssen, we strive to advance science and develop new treatments to help those living with HIV better manage their condition and adhere to therapy by simplifying dosing regimens and reducing pill burden,” said Rick Nettles, MD, Vice President, US Medical Affairs, Janssen Infectious Diseases. “The FDA approval of JULUCA<sup>®</sup>, which is the result of a partnership with ViiV Healthcare, exemplifies our continued commitment to meeting the diverse needs of the HIV community.”

To learn more about Janssen’s commitment to the prevention and treatment of HIV, please visit [jnj.com/HIV](http://jnj.com/HIV).

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### **Notes to editors**

In June 2014, ViiV Healthcare and Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson announced a partnership to investigate the potential of combining dolutegravir and rilpivirine in a single tablet in order to expand the treatment options available to people living with HIV.

### **About JULUCA<sup>®</sup>**

JULUCA<sup>®</sup> 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 <50 copies per mL) on a stable antiretroviral regimen for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of JULUCA<sup>®</sup>.<sup>1</sup>

ViiV Healthcare has also submitted regulatory marketing applications in Europe, Canada, Australia and Switzerland. Outside of the U.S., the two-drug regimen of dolutegravir and rilpivirine is an investigational product and is currently still under review.

### **HIGHLIGHTS OF PRESCRIBING INFORMATION**

**These highlights do not include all the information needed to use JULUCA safely and effectively. See [full prescribing information](#) for JULUCA.**

**JULUCA (dolutegravir and rilpivirine) tablets, for oral use Initial U.S. Approval: 2017**

### **INDICATIONS AND USAGE**

JULUCA, a two-drug combination of dolutegravir, a human immunodeficiency virus type 1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, a HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI), 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 for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of JULUCA.

### **DOSAGE AND ADMINISTRATION**

- One tablet taken orally once daily with a meal.
- Rifabutin coadministration: Take an additional 25-mg tablet of rilpivirine with JULUCA once daily with a meal for the duration of the rifabutin coadministration.

### **DOSAGE FORMS AND STRENGTHS**

Each tablet contains: 50 mg of dolutegravir (equivalent to 52.6 mg dolutegravir sodium) and 25 mg of rilpivirine (equivalent to 27.5 mg rilpivirine hydrochloride).

### **CONTRAINDICATIONS**

- Previous hypersensitivity reaction to dolutegravir or rilpivirine.
- Coadministration with dofetilide.
- Coadministration with drugs where significant decreases in rilpivirine plasma concentrations may occur, which may result in loss of virologic response.

### **WARNINGS AND PRECAUTIONS**

- Severe skin and hypersensitivity reactions characterised by rash, constitutional findings, and sometimes organ dysfunction, including liver injury, have been reported with the individual components. Discontinue JULUCA immediately if signs or symptoms of severe skin or hypersensitivity reactions develop, as a delay in stopping treatment may result in a life-threatening reaction.
- Hepatotoxicity has been reported in patients receiving a dolutegravir- or rilpivirine-containing regimen. Monitoring for hepatotoxicity is recommended.
- Depressive disorders have been reported with the use of rilpivirine- or dolutegravir-containing regimens. Immediate medical evaluation is recommended for severe depressive symptoms.

### **ADVERSE REACTIONS**

The most common adverse reactions (all Grades) observed in at least 2% of subjects were diarrhoea and headache.

**To report SUSPECTED ADVERSE REACTIONS, contact ViiV Healthcare at 1-888-844-8872 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### **DRUG INTERACTIONS**

- Because JULUCA is a complete regimen, coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.
- Refer to the full prescribing information for important drug interactions with JULUCA.
- Drugs that induce or inhibit CYP3A4 or UGT1A1 may affect the plasma concentrations of the components of JULUCA.
- Drugs that increase gastric pH or containing polyvalent cations may decrease plasma concentrations of the components of JULUCA
- Consider alternatives to prescribing JULUCA with drugs with a known risk of Torsade de Pointes.

### **USE IN SPECIFIC POPULATIONS**

Lactation: Breastfeeding is not recommended due to the potential for HIV transmission.

### **About the Janssen Pharmaceutical Companies**

At Janssen, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at [www.janssen.com](http://www.janssen.com). Follow us at [www.twitter.com/JanssenUS](https://www.twitter.com/JanssenUS) and [www.twitter.com/JanssenGlobal](https://www.twitter.com/JanssenGlobal).

Tivicay® is a registered trademark of the ViiV Healthcare group of companies.

EDURANT® is a registered trademark of Janssen Sciences Ireland UC.

### **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 with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy.

The following points should be considered when initiating therapy with EDURANT®:

- 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
- Regardless of HIV-1 RNA at the start of therapy, more EDURANT®-treated subjects with CD4+ cell count less than 200 cells/mm<sup>3</sup> experienced virologic failure compared to EDURANT®-treated subjects with CD4+ cell count greater than or equal to 200 cells/mm<sup>3</sup>
- The observed virologic failure rate in EDURANT®-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz

- More subjects treated with EDURANT® developed tenofovir and lamivudine/emtricitabine-associated resistance compared to efavirenz

EDURANT® is not recommended for patients less than 12 years of age.

## 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 a 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
- **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
- **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
- **Fat Redistribution:** Redistribution and/or accumulation of body fat have been observed in patients receiving 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, and Guillain-Barré syndrome) 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 H<sub>2</sub>-receptor antagonists

- 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 Category B:** EDURANT® should be used during pregnancy only if the potential benefit justifies the potential risk. No adequate and well-controlled studies have been conducted in pregnant women

#### **Adverse Reactions**

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

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Please see full [Prescribing Information](#) for more details.

## **TIVICAY (dolutegravir) tablets**

### **Important Safety Information for TIVICAY® (dolutegravir) 10-, 25-, and 50-mg tablets, for oral use**

The following Important Safety Information (ISI) is based on the Highlights section of the US Prescribing Information for TIVICAY and local variations apply. Please consult the full Prescribing Information for all the labeled safety information for TIVICAY or please refer to applicable local labelling.

## **FDA INDICATIONS AND USAGE**

TIVICAY is a human immunodeficiency virus type 1 (HIV-1) integrase strand transfer inhibitor (INSTI) indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 30 kg.

Limitations of Use:

- Use of TIVICAY in integrase strand transfer inhibitor (INSTI)-experienced patients should be guided by the number and type of baseline INSTI substitutions. The efficacy of TIVICAY 50 mg twice daily is reduced in patients with an INSTI-resistance Q148 substitution plus 2 or more additional INSTI-resistance substitutions including T66A, L74I/M, E138A/K/T, G140S/A/C, Y143R/C/H, E157Q, G163S/E/K/Q, or G193E/R.

## **CONTRAINDICATIONS**

- Previous hypersensitivity reaction to dolutegravir.
- Coadministration with dofetilide.

## **WARNINGS AND PRECAUTIONS**

- Hypersensitivity reactions characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury, have been reported. Discontinue TIVICAY and other suspect agents immediately if signs or symptoms of hypersensitivity reactions develop, as a delay in stopping treatment may result in a life-threatening reaction.
- Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of TIVICAY. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with TIVICAY is recommended in patients with underlying hepatic disease such as hepatitis B or C.
- Redistribution/accumulation of body fat and immune reconstitution syndrome have been reported in patients treated with combination antiretroviral therapy.

## **ADVERSE REACTIONS**

The most common adverse reactions of moderate to severe intensity and incidence at least 2% (in those receiving TIVICAY in any one adult trial) are insomnia, fatigue, and headache.

## **DRUG INTERACTIONS**

- Drugs that are metabolic inducers may decrease the plasma concentrations of dolutegravir.
- TIVICAY should be taken 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or



buffered medications. Alternatively, TIVICAY and supplements containing calcium or iron can be taken together with food.

## **USE IN SPECIFIC POPULATIONS**

- Pregnancy: TIVICAY should be used during pregnancy only if the potential benefit justifies the potential risk.
- Lactation: Breastfeeding is not recommended.

Please visit the following link for the full US prescribing and patient information:

[https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing\\_Information/Tivicay/pdf/TIVICAY-PI-PIL.PDF#page=1](https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Tivicay/pdf/TIVICAY-PI-PIL.PDF#page=1)

## **Cautions Concerning Forward-Looking Statements**

*This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding development and benefits of new treatment options for HIV-1. 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 Therapeutics, Division of Janssen Products, LP, 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 development, including uncertainty of clinical success and 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; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description 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 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including under the caption "Cautionary Note Regarding Forward-Looking Statements," and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies or 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. Juluca US label information
2. Llibre JM, Hung C-C, Brinson C, et al. SWORD 1 & 2: Switch to DTG + RPV maintains virologic suppression through 48 weeks, a Phase III study. Presented

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