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Janssen Announces European Commission Approval of JULUCA®▼ (dolutegravir/rilpivirine), the First Two-Drug Regimen, Once-Daily, Single-Pill for the Treatment of HIV-1

Dolutegravir/rilpivirine, the result of a collaboration with ViiV Healthcare, offers a complete daily treatment regimen for virologically suppressed adults living with HIV-1 in a single-pill

Cork, Ireland, 21 May 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the European Commission has granted marketing authorisation for JULUCA® (dolutegravir 50mg [ViiV Healthcare]/rilpivirine 25mg [Janssen Sciences Ireland UC]).[1] ViiV Healthcare, as the marketing authorisation holder, will market dolutegravir/rilpivirine in all countries in the European Union and European Economic Area.

Dolutegravir/rilpivirine is the first two-drug regimen, once-daily, single-pill for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable antiretroviral regimen for at least six months with no history of virological failure and no known or suspected resistance to any non-nucleoside reverse transcriptase inhibitor (NNRTI) or integrase inhibitor (INI).[1]

"The European Commission Decision for dolutegravir/rilpivirine marks a significant milestone in our 25-year commitment to make HIV history," said Brian Woodfall, VP, Global Head Late Development, Infectious Diseases, Janssen Research & Development, LLC. "At Janssen, the driving force behind our R&D efforts is to advance science and to discover and develop transformational medicines that advance health for humanity. We are proud to be combining our internal science with that of others to ensure optimised and individualised treatment options are available for those living with HIV-1."

Dolutegravir/rilpivirine combines just two antiretrovirals in a single-pill regimen, reducing the cumulative drug exposure in people living with HIV-1, whilst maintaining the efficacy of traditional three-drug regimens at 48-weeks.[2]

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"Dolutegravir/rilpivirine signifies an evolution in HIV-1 treatment options by combining two antiretrovirals into a once-daily, single-pill. It maintains the efficacy of a three-drug regimen but reduces the number of antiretrovirals, along with their potential toxicities, that virologically suppressed HIV-1 patients have to take and are therefore exposed to in the long-term," said Dr. Josep M Llibre, Infectious Diseases Dept, University Hospital Germans Trias i Pujol, Badalona, Barcelona.

This approval brings another treatment option to the estimated 810,000 people living with HIV in Europe.[3] It follows the Positive Opinion from the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) on 22 March 2018.[4] Dolutegravir/rilpivirine was approved by the US Food and Drug Administration (FDA) in November 2017[5] and Health Canada in May 2018.[6]

Data from two pivotal Phase 3 trials (SWORD-1 and SWORD-2) published in *The Lancet*,[2] showed that the dolutegravir and rilpivirine regimen is non-inferior to three- and four-drug regimens in maintaining virologic suppression (HIV-1 RNA <50 c/mL) through 48-weeks in virologically supressed adults who are infected with HIV-1, in both pooled and individual analyses of these Phase 3 studies (dolutegravir+rilpivirine 486/513 [95%] current antiretroviral regimen (CAR) 485/511 [95%], [adjusted difference -0.2% (95% confidence interval: -3.0%, 2.5%), pooled analysis]). Participating adults had stable plasma HIV-1 RNA (viral load <50 copies/mL) for 6 months or longer at screening, with no major resistance association mutations to protease inhibitor, nucleoside reverse-transcriptase inhibitors (NRTI), NNRTI or INI. Virologic suppression rates were similar between treatment arms at 48 weeks.[2]

Adverse events were reported by 77% of participants in the dolutegravir+rilpivirine group and 71% in the CAR group. The most commonly reported adverse events were nasopharyngitis (10% dolutegravir+rilpivirine, 10% CAR) and headache (8% dolutegravir+rilpivirine, 5% CAR). Adverse events leading to discontinuation in the dolutegravir+rilpivirine group occurred in 3% of patients and 1% in the CAR group. The safety profiles for dolutegravir and rilpivirine in these studies were consistent with the product labelling for each medicine.[2]

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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 collaboration to investigate the potential of combining dolutegravir and rilpivirine in a single-pill in order to expand the treatment options available to people living with HIV-1.[7]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, 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/emea. Follow us at

@JanssenEMEA. Janssen Sciences Ireland UC and Janssen Research & Development, LLC are each part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

About HIV

HIV stands for the Human Immunodeficiency Virus. Unlike some other viruses, the human body cannot get rid of HIV, so once someone has HIV they have it for life. There is no cure for HIV, but effective treatment can control the virus so that people with HIV can enjoy healthy and productive lives.

HIV has largely become a chronic treatable disease with improved access to antiretroviral treatment. This has led to a 22% drop in global HIV mortality between 2009 and 2013,[8] but more can be done for the estimated 36.7 million people living with HIV[9] of which 160,000 were newly diagnosed in the European region alone in 2016.[10]

About dolutegravir/rilpivirine

Dolutegravir/rilpivirine was approved by the US Food and Drug Administration (FDA) on 21 November 2017[5] and Health Canada on 18 May 2018[6], as a complete regimen for the treatment of HIV-1 infection in adults 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 dolutegravir/rilpivirine.[5]

Dolutegravir/rilpivirine is a two-drug regimen, single-pill that combines the INI dolutegravir (50mg), with the NNRTI rilpivirine (25mg) taken once-daily with food as a complete regimen for people living with HIV-1 who are virologically suppressed.[1]

Two essential steps in the HIV life cycle include reverse transcription – when the virus turns its RNA (ribonucleic acid) copy into DNA (deoxyribonucleic acid) – and integration – the moment when viral DNA becomes part of the host cell's DNA. These processes require two enzymes called nucleoside reverse transcriptase and integrase. NNRTIs and INSTIs interfere with the action of these two enzymes to prevent the virus from replicating. This decrease in replication can lead to less virus being available to cause subsequent infection of uninfected cells.

ViiV Healthcare has also submitted regulatory marketing applications in other countries worldwide.

About the SWORD phase 3 programme for dolutegravir (Tivicay▼)[11] and rilpivirine (EDURANT®)[12]

The SWORD phase 3 clinical trial programme evaluates the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current integrase inhibitor-, non-nucleoside reverse transcriptase inhibitor-, or protease inhibitor (+2 NRTI)-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed with a three or four-drug regimen. SWORD-1 (NCT02429791) and SWORD-2 (NCT02422797) are replicate 148-week, randomised, open-label, non-inferiority studies to assess the

antiviral activity and safety of a two-drug, once-daily oral regimen of dolutegravir plus rilpivirine compared with current antiretroviral therapy (full 148-week data will be shared in 2019). In the SWORD clinical trials, dolutegravir and rilpivirine are provided as individual tablets.[2]

The primary endpoint is the proportion of patients with plasma HIV-1 RNA <50 copies per millilitre (c/mL) at 48-weeks (intention to treat analysis). Key secondary endpoints include evaluation of the development of viral resistance, measurements of safety and tolerability, and changes in renal, bone and cardiovascular biomarkers. The studies also include exploratory measures to assess change in health-related quality of life, willingness to switch and adherence to treatment regimens.[2]

For more information on the trials please visit: www.clinicaltrials.gov

JULUCA® and Tivicay (dolutegravir)[11] are trademarks owned by the ViiV Healthcare group of companies. It is important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at https://www.gsk.com/en-gb/contact-us/report-a-possible-side-effect/. Adverse events should also be reported to GlaxoSmithKline 0800 221 441.

EDURANT® (rilpivirine)[12] is a registered trademark of Janssen Sciences Ireland UC. It is important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Ltd on 01494 567447 or at dsafety@its.jnj.com.

Important Safety Information for dolutegravir/rilpivirine in the European Union: Please refer to the full European Summary of Product Characteristics.[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 potential approval, availability and benefits of a 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 materialise, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, 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 31, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company'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:

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