ViiV Healthcare submits FDA application for first dispersible single tablet regimen containing dolutegravir (DTG) for children living with HIV

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ViiV Healthcare, the global specialist HIV company majority-owned by GSK, with Pfizer Inc. and Shionogi Limited as shareholders, has announced it has made a regulatory submission to the U.S. Food and Drug Administration (FDA) for approval of a new dispersible tablet formulation of the fixed dose combination of abacavir, dolutegravir and lamivudine and, to extend its current approval for Triumeq (abacavir/ dolutegravir/ lamivudine) to lower the minimum weight at which a child can be prescribed this medicine, from 40kg and above to 14kg and above. If approved, this approval will result in further treatment options for younger children living with HIV.

Paediatric HIV remains a global issue, with children disproportionately affected by the HIV epidemic. Latest statistics show there are 1.7 million children living with HIV globally, with most AIDS-related deaths among this group occurring during the first five years of life.

Major obstacles persist for children, such as the availability of HIV testing, continued vertical transmission, slow initiation of treatment and, poor availability of optimised paediatric formulations of antiretrovirals (ARVs)., The availability of age-appropriate treatment options is essential in ensuring children around the world can access optimal care.

Deborah Waterhouse, CEO of ViiV Healthcare, said:

> UNAIDS reported that in 2020, 74% of adults living with HIV had access to treatment, compared to only 54% of children.1 This is a stark reminder of the gap between treatment options for adults and children and this submission represents another important step in ensuring that we address this disparity. By broadening the treatment options available to children living with HIV, we are one step closer to ending paediatric HIV and AIDS.

This submission is based on modelled data and in line with regulatory guidance.

Two essential steps in the HIV life cycle are replication – when the virus turns its RNA copy into DNA – and integration – the moment when viral DNA becomes part of the host cell's DNA. These processes require two enzymes called reverse transcriptase and integrase. NRTIs and integrase inhibitors interfere with the action of the two enzymes to prevent the virus from replicating and further infecting cells.

Important Safety Information (ISI) for TRIUMEQ (abacavir, dolutegravir, and lamivudine) tablets

TRIUMEQ is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and in pediatric patients weighing at least 40 kg.

TRIUMEQ alone is not recommended in patients with resistance-associated integrase substitutions or clinically suspected INSTI resistance because the dose of dolutegravir in TRIUMEQ is insufficient in these subpopulations. See full prescribing information for TIVICAY (dolutegravir).

IMPORTANT SAFETY INFORMATION

BOXED WARNING: HYPERSENSITIVITY REACTIONS AND EXACERBATIONS OF HEPATITIS B VIRUS (HBV)

Hypersensitivity Reactions:

- Serious and sometimes fatal hypersensitivity reactions, with multiple organ involvement, have occurred with abacavir-containing products

- Patients who carry the HLA-B*5701 allele are at a higher risk of experiencing a hypersensitivity reaction to abacavir, although hypersensitivity reactions have occurred in patients who do not carry the HLA-B*5701 allele

- TRIUMEQ is contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLA-B*5701-positive patients. All patients should be screened for the HLA-B*5701 allele prior to initiating therapy or reinitiation of therapy with TRIUMEQ unless patients have a previously documented HLA-B*5701 allele assessment

- Discontinue TRIUMEQ as soon as hypersensitivity reaction is suspected. Regardless of HLA-B*5701 status, permanently discontinue TRIUMEQ if hypersensitivity cannot be ruled out, even when other diagnoses are possible

- Following a hypersensitivity reaction to TRIUMEQ, NEVER restart TRIUMEQ or any other abacavir-containing product

Exacerbations of Hepatitis B:

- Severe acute exacerbations of HBV have been reported in patients who are co-infected with HBV and HIV-1 and have discontinued lamivudine, a component of TRIUMEQ. Monitor hepatic function closely in these patients and, if appropriate, initiate anti-hepatitis B treatment

- Do not use TRIUMEQ in patients who have the HLA-B*5701 allele

- Do not use TRIUMEQ in patients with previous hypersensitivity reaction to abacavir, dolutegravir, or lamivudine

- Do not use TRIUMEQ in patients receiving dofetilide

- Do not use TRIUMEQ in patients with moderate or severe hepatic impairment

Hypersensitivity Reactions:

- Hypersensitivity reactions have been reported with dolutegravir and were characterized by rash, constitutional findings, and sometimes

organ dysfunction, including liver injury

- Clinically, it is not possible to determine whether a hypersensitivity reaction with TRIUMEQ would be caused by abacavir or dolutegravir

- Discontinue TRIUMEQ immediately if signs or symptoms of hypersensitivity reactions develop, as a delay in stopping treatment may result in a life-threatening reaction. Clinical status, including liver aminotransferases, should be monitored and appropriate therapy initiated

- Hepatic adverse events have been reported, including cases of hepatic toxicity (elevated serum liver biochemistries, hepatitis, and acute liver failure), in patients receiving a dolutegravir-containing regimen without pre-existing hepatic disease or other identifiable risk factors

- Patients with underlying hepatitis B or C or marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations with use of TRIUMEQ. In some cases, the elevations in transaminases were consistent with immune reconstitution syndrome or hepatitis B reactivation, particularly in the setting where anti-hepatitis therapy was withdrawn

- Drug-induced liver injury leading to liver transplant has been reported with TRIUMEQ

- Monitoring for hepatotoxicity is recommended

Lactic Acidosis and Severe Hepatomegaly With Steatosis:

- Fatal cases have been reported with the use of nucleoside analogues, including abacavir and lamivudine. Discontinue TRIUMEQ if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations

- Assess the risks and benefits of TRIUMEQ and discuss with the patient to determine if alternative treatments should be considered at the time of conception through the first trimester of pregnancy due to the risk of neural tube defects

- Pregnancy testing is recommended before use of TRIUMEQ. Adolescents and adults of childbearing potential should be counseled on the consistent use of effective contraception

Adverse Reactions or Loss of Virologic Response Due to Drug Interactions with concomitant use of TRIUMEQ and other drugs may occur (see Contraindications and Drug Interactions).

Immune Reconstitution Syndrome, including the occurrence of autoimmune disorders with variable time to onset, has been reported with the use of TRIUMEQ.

Myocardial Infarction (MI):

- Several observational studies have reported an association with the use of abacavir and the risk of MI; meta-analyses of randomized controlled clinical trials did not show increased risk. To date, there is no established biological mechanism to explain a potential increase in risk. In totality, the available data show inconsistency; therefore, evidence for a causal relationship between abacavir and the risk of MI is inconclusive

- The underlying risk of coronary heart disease should be considered when prescribing antiretroviral therapies, including abacavir, and action taken to minimize all modifiable risk factors (e.g., hypertension, hyperlipidemia, diabetes mellitus, smoking)

- The most common adverse reactions (incidence ≥2%, Grades 2-4) in treatment-naïve adults receiving TRIUMEQ were insomnia (3%), headache (2%), and fatigue (2%).

- Consult the full Prescribing Information for TRIUMEQ for more information on potentially significant drug interactions

- Drugs that induce or inhibit CYP3A or UGT1A1 may affect plasma concentrations of dolutegravir

- Administer TRIUMEQ 2 hours before or 6 hours after taking antacids, polyvalent cation-containing products or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered medications. Alternatively, TRIUMEQ and supplements containing calcium or iron can be taken with food

Use in specific populations

- Pregnancy: There are insufficient human data on the use of TRIUMEQ during pregnancy to definitively assess a drug-associated risk for birth defects and miscarriage. An Antiretroviral Pregnancy Registry has been established. Advise adolescents and adults of childbearing potential of the potential risk of neural tube defects. Assess the risks and benefits of TRIUMEQ and discuss with the patient to determine if an alternative treatment should be considered at the time of conception through the first trimester of pregnancy or if pregnancy is confirmed in the first trimester

- Lactation: Breastfeeding is not recommended due to the potential for HIV-1 transmission, developing viral resistance in HIV-positive infants, and adverse reactions in a breastfed infant

- Females and Males of Reproductive Potential: Pregnancy testing is recommended before initiation of TRIUMEQ. Counsel adolescents and adults of childbearing potential taking TRIUMEQ on the consistent use of effective contraception

- Impaired Renal Function: TRIUMEQ is not recommended for patients with creatinine clearance

- Impaired Hepatic Function: If a dose reduction of abacavir is required for patients with mild hepatic impairment, then the individual components of TRIUMEQ should be used

Please see full prescribing information available at: US Prescribing Information, including Boxed Warning.

ViiV Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV and for people who are at risk of becoming infected with HIV. Shionogi joined as shareholders in October 2012. The company’s aims are to take a deeper and broader interest in HIV and AIDS than any company has done before and take a new approach to deliver effective and innovative medicines for HIV treatment and prevention, as well as support communities affected by HIV.

For more information on the company, its management, portfolio,

pipeline, and commitment, please visit www.viivhealthcare.com.

GSK is a science-led global healthcare company. For further information please visit https://www.gsk.com/en-gb/about-us/.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the Company's Annual Report on Form 20-F for 2020, GSK's Q2 Results and any impacts of the COVID-19 pandemic.

UNAIDS. Global HIV & AIDS statistics – 2020 fact sheet. Available at: https://www.unaids.org/en/resources/fact-sheet Last accessed: September 2021.

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