PRESS RELEASE

Dovato (dolutegravir/lamivudine), the once-daily, single-pill, 2-drug regimen for the treatment of HIV-1 infection, granted marketing approval by Japan Ministry of Health, Labour and Welfare

Japan, London, 15 January 2020 - ViiV Healthcare, the global specialist HIV company majority owned by GSK, with Pfizer Inc. and Shionogi Limited as shareholders, announced that it has obtained approval of Dovato (dolutegravir 50 mg/lamivudine 300 mg) from the Japan Ministry of Health, Labour and Welfare (MHLW) for the treatment of HIV-1 infection in adults and adolescents above 12 years of age weighing at least 40 kg, to be administered orally, with or without food.[1]

Dovato is a once-daily, single-pill, 2-drug regimen (2DR) for treatment-naïve HIV infection that combines dolutegravir, an integrase inhibitor (INI), with the nucleoside reverse transcriptase inhibitor (NRTI) lamivudine[2].

Dustin Haines, President, ViiV Healthcare Japan said: "In Japan, the standard of care for treatment-naïve people living with HIV has been for many years with a three-drug regimen. The data from our dolutegravir-based 2-drug regimen development programme has, however, challenged this, and with the authorisation of Dovato, people living with HIV in Japan can, for the first time, start treatment on a once-daily, single-pill, 2-drug regimen with the knowledge that efficacy is non-inferior to a three-drug regimen."

Dr. Ichiro Koga, MD, Director Medical Affairs, ViiV Healthcare Japan said: "The authorisation of Dovato in Japan marks a significant development for people living with HIV. This treatment allows individuals to take a 2-drug regimen in a once-daily, single-pill with dolutegravir at its core. ViiV Healthcare's ambition and innovative R&D programme aim to reduce the number of HIV medicines people living with HIV take over a lifetime and Dovato is an important addition to our portfolio of medicines to help support this aim."

Marketing Authorisation for Dovato is supported by data from the landmark global GEMINI 1 & 2 studies that included more than 1,400 HIV-1 infected adults. In these studies, dolutegravir and lamivudine demonstrated non-inferior efficacy based on plasma HIV-1 RNA <50 copies per millilitre (c/mL), a standard measure of HIV control, at week 48 when compared to a three-drug regimen of dolutegravir and two NRTIs, tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), in treatment-naïve, HIV-1 infected adults. The safety results for dolutegravir and lamivudine seen in GEMINI 1 & 2 were consistent with the product labelling for dolutegravir and lamivudine. Four patients (1%) in both the dolutegravir and lamivudine, and the dolutegravir and TDF/FTC, study arms experienced drug-related serious adverse events, and 15 patients (2%) in the dolutegravir and

lamivudine arm and 16 patients (2%) in the dolutegravir and TDF/FTC arm had adverse events that led to discontinuation. The most common adverse reactions included headache, diarrhoea, nausea, insomnia, and fatigue. No patient who experienced virologic failure in either treatment arm developed treatment-emergent resistance also up to week 48.[3,4]

About Human Immunodeficiency Virus (HIV-1) infection

HIV-1 infects human immune cells called CD4 T lymphocytes, a type of white blood cell that plays a central role in the human immune system. CD4 T lymphocytes are destroyed gradually due to HIV infection, causing the patients' immune functions to decline. Eventually, patients exhibit various types of opportunistic infections and malignant tumours as a complication, a condition referred to as Acquired Immune Deficiency Syndrome (AIDS). According to a report by the MHLW's Committee on AIDS Trends, a total of 940 people in Japan were reportedly diagnosed with HIV infection (without AIDS) in 2018, and 377 patients suffered AIDS at the time of HIV diagnosis in Japan. The total number of newly reported cases in 2018, therefore, came to be 1,317 patients. The cumulative number of cases that have been reported up to 2018 (excluding cases of infections caused by coagulation factor preparations) is 30,149.[5]

About Dovato (dolutegravir/lamivudine)

Dovato (dolutegravir/lamivudine) is a once-daily, single-pill, 2-drug regimen that combines the INI dolutegravir (Tivicay, 50 mg) with the NRTI lamivudine (Epivir, 300 mg).[2]

It is authorised in the EU for the treatment of HIV-1 infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the INI class, or lamivudine.[2] In the US, the Food and Drug Administration (FDA) authorised Dovato, a complete, once-daily, single-tablet regimen of dolutegravir 50 mg and lamivudine 300 mg for the treatment of HIV-1 infection in adults with no antiretroviral (ARV) treatment history and with no known resistance to either dolutegravir or lamivudine.[6]

Like a dolutegravir-based three-drug regimen, dolutegravir/lamivudine inhibits the viral cycle at two different sites. INIs, like dolutegravir, 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 infection. Lamivudine is an NRTI that works by interfering with the conversion of viral ribonucleic acid (RNA) into deoxyribonucleic acid (DNA) which in turn stops the virus from multiplying.

Important Safety Information for Dovato (50mg dolutegravir/300mg lamivudine) tablets in Japan

The following ISI is based on the Highlights section of the Prescribing Information for Dovato.

Please consult the full Prescribing Information for all the labeled safety information for Dovato.

WARNINGS

- For paediatric patients who may develop pancreatitis (paediatric patients with a history of pancreatitis, paediatric patients who are being treated concomitantly with drugs that are known to cause pancreatitis), Dovato should be used carefully only when there are no other sufficiently effective treatments. If symptoms or clinical signs suggestive of pancreatitis, such as severe abdominal pain, nausea / vomiting or increase in serum amylase, serum lipase or triglycerides, etc., administration of Dovato should be stopped immediately.
- Because chronic hepatitis B may relapse in patients with complications of chronic hepatitis B upon discontinuation of lamivudine administration, adequate attention should be paid when the administration of Dovato is discontinued. This relapse may have severe consequences in patients with decompensated liver disease.

PRECAUTIONS CONCERNING INDICATION

Dovato should be used in patients with HIV infection who are anti-HIV treatment naïve
Dovato should be selected on the basis of viral resistance testing (genotypic or phenotypic analysis) if possible.

Since Dovato is a combination product containing fixed doses of dolutegravir and lamivudine, individual dolutegravir preparation (Tivicay Tablets) or lamivudine preparation (Epivir Tablets) should be used in patients with renal impairment (CLcr < 50 mL/min) requiring dose adjustment of lamivudine.

DOSAGE AND ADMINISTRATION

For adults and children aged 12 years or older and weighing 40 kg or heavier, the usual dosage is one tablet (50 mg as dolutegravir and 300 mg as lamivudine) administered once daily orally with or without food.

PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION

Since Dovato is a drug that treats with one agent, do not use in combination of other anti-HIV drugs excluding the case in which additional administration of dolutegravir is required. When Dovato is used in combination with carbamazepine, rifampicin, phenytoin, fosphenytoin, phenobarbital or St. John's Wort-containing foods, dolutegravir 50 mg should be administered twice daily. In this case, the dolutegravir should be administered approximately 12 hours after the dosing of Dovato. Dovato contains fixed dose of lamivudine, do not administer lamivudine in combination in addition to Dovato.

Geriatric Use

Dovato should be administered with care while monitoring the patient's condition. Generally, elderly has lower physiological function (liver, renal, cardiac) so many of them have complications or concomitantly use other drugs. Lamivudine is mainly excreted from the kidney as parent drug. Since renal function is often reduced in elderly patients, the plasma drug concentration may persist at a high level.

DRUG INTERACTIONS

Dolutegravir is primarily metabolized by UGT1A1 and partially by CYP3A4. Also, dolutegravir inhibits Organic Cation Transporter 2 (OCT2) and Multidrug and Toxin Extrusion 1 (MATE1). Lamivudine is substrate for OCT2, MATE1, and MATE2-K.

ADVERSE REACTIONS

The following adverse reactions may occur. Patients should be carefully monitored, and if any abnormalities are observed, appropriate measures such as discontinuing administration should be taken.

Clinically Significant Adverse Reactions

Drug-induced hypersensitivity syndrome (frequency unknown)

- Serious blood disorders
- Pancreatitis (frequency unknown)
- Lactic acidosis (frequency unknown) and severe hepatomegaly with steatosis (fatty liver) (0.1%)
- Rhabdomyolysis (frequency unknown)
- Neuropathy (frequency unknown), confusion state (frequency unknown), convulsion (frequency unknown)
- Cardiac failure (frequency unknown)
- Hepatic function disorder (0.1%), jaundice (frequency unknown)
- Hepatic function disorder or jaundice accompanied by increased AST, ALT, and / or bilirubin may occur.

Please refer to the full European Summary of Product Characteristics for Dolutegravir/lamivudine in the EU, including contraindications, special warnings and precautions for use. For the US, please refer to the US Prescribing Information.

About ViiV Healthcare

ViiV Healthcare LLC 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. Shionogi joined as a shareholder in October 2012. The company's aim is to take a deeper and broader interest in HIV/AIDS than any company has done before and take a new approach to deliver effective and new HIV medicines, 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.

About GSK

GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com.

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 under Item 3.D 'Principal risks and uncertainties' in the company's Annual Report on Form 20-F for 2018.

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[3] Cahn J, Sierra Madero J, Arribas J, et al. Non-inferior efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) fixed-dose combination in antiretroviral treatment-naïve adults with HIV-1 infection – 48-week results from the GEMINI studies. AIDS 2018.

[4] Cahn P, Sierra Madero J, Arribas JR, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naïve adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. Lancet. 2019;393(10167):143-155

[5] AIDS Prevention Information Network. http://api-net.jfap.or.jp/status/2017/17nenpo/h30gaiyo.pdf. Last accessed December 2019.

[6] Dovato US Prescribing Information. https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Dovato/pdf/DOVATO-PI-PIL.PDF. Last accessed December 2019.