Viatris Announces U.S. FDA Tentative Approval of a Paediatric Formulation of Abacavir (ABC)/Dolutegravir (DTG)/Lamivudine (3TC), a Once-daily Treatment for Children Living with HIV

September 5, 2023

Tentative approval will help enhance access to WHO-recommended paediatric regimen with the goal of improved adherence of HIV treatment for children in low- and middle-income countries

PITTSBURGH and BANGALORE, India, Sept. 5, 2023 /PRNewswire/ -- Viatris Inc. (NASDAQ: VTRS), a global healthcare company, today announced U.S. Food and Drug Administration (FDA) tentative approval for a New Drug Application for abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension for the treatment of HIV-1 infection in paediatric patients.

The World Health Organization (WHO) recommends abacavir/dolutegravir/lamivudine as a preferred first-line regimen for paediatric patients. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), treatment coverage for children and adolescents lags behind adults. Some 660,000 children living with HIV – about 43 percent of the estimated total 1.5 million [1.2 million–2.1 million] children living with HIV – did not receive antiretroviral (ARV) therapy in 2022. Accordingly, children accounted for 13 per cent of AIDS-related deaths in 2022, even though they comprise only about 4 percent of people living with HIV.

The fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension is indicated for the treatment of HIV-1 infection in paediatric patients weighing at least 6 kg. The fixed-dose combination tablets for oral suspension are strawberry-flavoured. Historically, it has been challenging to treat paediatric HIV patients because children require special medicine formulations.

The FDA's tentative approval through the President's Emergency Plan for AIDS Relief (PEPFAR) program means the formulation meets all the agency's quality, safety, and efficacy standards. Viatris has signed a licensing agreement for paediatric dolutegravir from the Medicines Patent Pool (MPP) and development agreement with ViiV Healthcare (ViiV) and the Clinton Health Access Initiative (CHAI) for producing and distributing the fixed-dose combination of abacavir/ dolutegravir/lamivudine.

Rakesh Bamzai, President of India, Emerging Asia & Access Markets at Viatris, said, "At Viatris, we have expanded access at scale to high-quality HIV/AIDS treatment for more than a decade. Over the years, we have continued to seek improvements to existing molecules to better meet patient needs – we have introduced novel heat-stable generic formulations, more convenient packaging options, and paediatric therapies. We have also built strong partnerships with multiple stakeholders to improve access to ARVs, with particular attention to vulnerable populations like children. The approval of this single tablet regimen – the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg - will reduce the pill burden for children living with HIV."

This milestone supports the company's sustainability goal to provide ARV therapy equivalent to a total of 30 million patients, including more than 2 million children living with HIV/AIDS, between 2022 and the end of 2025.

The fixed-dose combination of abacavir/dolutegravir/lamivudine is approved for once-daily treatment of paediatric patients weighing at least 6 kg to <25 kg with HIV-1 infection and the recommended dose of the fixed-dose combination of abacavir/dolutegravir/lamivudine tablets for oral suspension is determined according to weight. The fixed-dose combination of abacavir/dolutegravir/lamivudine are contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLAB*5701-positive patients. The tentative approval facilitates regulatory authority submissions, production and distribution of the new child friendly formulation across 123 low- and middle-income countries as per the license agreement.

About the fixed-dose combination of abacavir/dolutegravir/lamivudine tablets for oral suspension
Abacavir/dolutegravir/lamivudine is a fixed-dose combination containing two nucleoside reverse transcriptase inhibitors (NRTIs) and integrase strand transfer inhibitor (INSTI). NRTIs interfere with the action of the reverse transcriptase enzyme and INSTI interferes with the action of integrase enzyme to prevent the virus from replicating. All patients with HIV-1 should be tested for the presence of hepatitis B virus (HBV) prior to or when initiating the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg as severe acute exacerbations of HBV have been reported in patients who are co-infected with HBV and HIV-1 and have discontinued the medication.

Abacavir/dolutegravir/lamivudine was approved in the US on 30 March 2022 under the brand name Triumeq PD.

Triumeq PD is registered trademark of the ViiV Healthcare group of companies.

About Viatris
Viatris Inc. (NASDAQ: VTRS) is a global healthcare company empowering people worldwide to live healthier at every stage of life. We provide access to medicines, advance sustainable operations, develop innovative solutions and leverage our collective expertise to connect more people to more products and services through our one-of-a-kind Global Healthcare Gateway®. Formed in November 2020, Viatris brings together scientific, manufacturing and distribution expertise with proven regulatory, medical, and commercial capabilities to deliver high-quality medicines to patients in more than 165 countries and territories. Viatris' portfolio comprises more than 1,400 approved molecules across a wide range of therapeutic areas, spanning both non-communicable and infectious diseases, including globally recognized brands, complex generic and branded medicines, and a variety of over-the-counter consumer products. With more than 38,000 colleagues globally, Viatris is headquartered in the U.S., with global centers in Pittsburgh, Shanghai and Hyderabad, India. Learn more at viatris.com and investor.viatris.com, and connect with us on Twitter, LinkedIn, Instagram

and YouTube.

Important Safety Information (ISI) for the fixed-dose combination of abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg tablets and the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension.

INDICATION
The fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension is indicated for the treatment of HIV-1 infection in paediatric patients aged at least 3 months weighing at least 6 kg. to less than 25 kgs.

Limitations of Use:
The fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension is not recommended in patients with resistance-associated integrase substitutions or clinically suspected INSTI resistance because the dose of dolutegravir in the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg is insufficient in these subpopulations. See full prescribing information for 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, a component of the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg.
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.
The fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg are contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLAB*5701-positive patients. All patients should be screened for the HLA-B*5701 allele prior to initiating therapy or re-initiation of therapy with the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg unless patients have a previously documented HLA-B*5701 allele assessment.

Discontinue the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg immediately if a hypersensitivity reaction is suspected, regardless of HLA-B*5701 status and even when other diagnoses are possible.

Following a hypersensitivity reaction to the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg, NEVER restart the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension or any other abacavir-containing product.

Exacerbations of Hepatitis B:
All patients with HIV-1 should be tested for the presence of hepatitis B virus (HBV) prior to or when initiating the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg. Emergence of lamivudine-resistant HBV variants associated with lamivudine-containing antiretroviral regimens has been reported. If the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg is used in patients co-infected with HIV-1 and HBV, additional treatment should be considered for appropriate treatment of chronic HBV; otherwise, consider an alternative regimen.

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 the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg. Monitor hepatic function closely in these patients and, if appropriate, initiate anti-hepatitis B treatment.

Contraindications
Do not use the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg in patients who have the HLA-B*5701 allele.

Do not use the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg in patients with previous hypersensitivity reaction to abacavir, dolutegravir, or lamivudine.

Do not use the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg in patients receiving dofetilide.

Do not use the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg in patients with moderate or severe hepatic impairment.

Warnings and precautions

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 the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg would be caused by abacavir or dolutegravir.

Discontinue the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg 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.

Hepatotoxicity:
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 may be at increased risk for worsening or development of transaminase elevations with use of the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg. 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 the fixed-dose combination of abacavir/dolutegravir/lamivudine.

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 the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

Embryo-Fetal Toxicity:
Assess the risks and benefits of the fixed-dose combination of abacavir/dolutegravir/lamivudine 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 the fixed-dose combination of abacavir/dolutegravir/lamivudine. Adolescents and adults of childbearing potential should be counseled on the consistent use of effective contraception.

The fixed-dose combination of abacavir/dolutegravir/lamivudine may be considered during the second and third trimesters of pregnancy if the expected benefit justifies the potential risk to the pregnant woman and the fetus.

Adverse Reactions or Loss of Virologic Response Due to Drug Interactions with concomitant use of the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg 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 fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg.

Different Formulations Are Not Interchangeable:
The fixed-dose combination of abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg tablets and the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets for oral suspension are not bioequivalent and are not interchangeable on a milligram-per-milligram basis. If a patient switches from one formulation to the other, the dose must be adjusted.

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).

Adverse reactions:
The most common adverse reactions (incidence ≥2%, Grades 2-4) in treatment-naïve adults receiving the fixed-dose combination of abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg tablets were insomnia (3%), headache (2%), and fatigue (2%).

Drug interactions:
Consult the full Prescribing Information for more information on potentially significant drug interactions.

Use in specific populations:
Pregnancy: Assess the risks and benefits of the fixed-dose combination of abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg tablets and discuss with the patient to determine if an alternative treatment should be considered at the time of conception through the first trimester or if pregnancy is confirmed in the first trimester due to the risk of neural tube defects.

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.

Impaired Renal Function: the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg are not recommended for patients with creatinine clearance <30 mL/min. Patients with a sustained creatinine clearance between 30 and 49 mL/min should be monitored for hematologic toxicities, which may require a dosage adjustment of lamivudine as an individual component.

Impaired Hepatic Function: If a dose reduction of abacavir is required for patients with mild hepatic impairment, then the individual components of the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg tablets should be used.

References:

1. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: Recommendations for a public health approach
2. The path that ends AIDS: UNAIDS Global AIDS Update 2023

Forward-Looking Statements
This press release includes statements that constitute "forward-looking statements." These statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward looking statements may include statements that tentative approval will help enhance access to WHO-recommended paediatric regimen with the goal of improved adherence of HIV treatment for children in low- and middle-income countries; the approval of this single tablet regimen – the fixed-dose combination of abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg - will reduce the pill burden for children living with HIV; and the milestone supports the company's sustainability goal to provide ARV therapy equivalent to a total of 30 million patients, including more than 2 million children living with HIV/AIDS, between 2022 and the end of 2025. Factors that could cause or contribute to such differences include, but are not limited to: actions and decisions of healthcare and pharmaceutical regulators; changes in healthcare and pharmaceutical laws and regulations in the U.S. and abroad; any regulatory, legal or other impediments to Viatris' ability to bring new products to market, including but not limited to "at-risk" launches; Viatris' or its partners' ability to develop, manufacture, and commercialize products; the

possibility that the Company may be unable to realize the intended benefits of, or achieve the intended goals or outlooks with respect to, its strategic initiatives; the possibility that the Company may be unable to achieve expected benefits, synergies and operating efficiencies in connection with acquisitions, divestitures, or its global restructuring program, within the expected timeframe or at all; impairment charges or other losses related to the divestiture or sale of businesses or assets; the Company's failure to achieve expected or targeted future financial and operating performance and results; the potential impact of public health outbreaks, epidemics and pandemics, including the ongoing challenges and uncertainties posed by COVID-19; the scope, timing and outcome of any ongoing legal proceedings, and the impact of any such proceedings; any significant breach of data security or data privacy or disruptions to our information technology systems; risks associated with international operations; the ability to protect intellectual property and preserve intellectual property rights; changes in third-party relationships; the effect of any changes in Viatris' or its partners' customer and supplier relationships and customer purchasing patterns; the impacts of competition; changes in the economic and financial conditions of Viatris or its partners; uncertainties and matters beyond the control of management, including general economic conditions, inflation and exchange rates; failure to execute stock repurchases consistent with current expectations; stock price volatility; and the other risks described in Viatris' filings with the Securities and Exchange Commission (SEC). Viatris routinely uses its website as a means of disclosing material information to the public in a broad, non-exclusionary manner for purposes of the SEC's Regulation Fair Disclosure (Reg FD). Viatris undertakes no obligation to update these statements for revisions or changes after the date of this release other than as required by law.

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