DOVATO (DOLUTEGRAVIR AND LAMIVUDINE TABLETS)-AN INNOVATIVE DRUG DISCOVERY IN HIV-1 TREATMENT-A REVIEW

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ABSTRACT

Dolutegravir/lamivudine (trade name Dovato) is a combination drug for the treatment of HIV/AIDS. It was approved for use in the United States in April 2019.[1] It contains dolutegravir, an integrase inhibitor, and lamivudine, a reverse-transcriptase inhibitor.

The management of HIV/AIDS normally includes the use of multiple antiretroviral drugs in an attempt to control HIV infection. The use of multiple drugs that act on different viral targets is known as highly active antiretroviral therapy (HAART). HAART decreases the patient's total burden of HIV, maintains function of the immune system, and prevents opportunistic infections that often lead to death.

Dovato is a once-daily, single-tablet, two-drug regimen that combines the integrase strand transfer inhibitor (INSTI) dolutegravir (Tivicay, 50 mg) with the nucleoside analogue reverse transcriptase inhibitor (NRTI) lamivudine (Epivir, 300 mg). Dovato is specifically indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with no antiretroviral treatment history. Dovato is supplied as a tablet for oral administration. Dovato is a fixed-dose combination product containing 50 mg of dolutegravir and 300 mg of lamivudine. The recommended dosage regimen in adults is one tablet taken orally once daily with or without food.

KEYWORDS

Human Immuno Deficiency Virus, Acquired Immuno Deficiency Syndrome, Highly Active Anti Retroviral Therapy,Integrase Strand Transfer Inhibitor],Nucleoside Analogue Reverse Transcriptase Inhibitor,CD4 cells,Hepatitis-B Virus.

INTRODUCTION

HIV1/AIDS

HIV is a variation of a virus that infects African chimpanzees. Scientists suspect the simian immunodeficiency virus (SIV) jumped to humans when people consumed infected chimpanzee meat. Once inside the human population, the virus mutated into what we now know as HIV. This likely occurred as long ago as the 1920s.Eventually, the virus migrated to other parts of the world. Scientists first discovered HIV in a human blood sample in 1959.[1]

HIV is a virus that damages the immune system. The immune system helps the body fight off infections. Untreated HIV infects and kills CD4 cells, a type of immune cell called T cells(Healthy adults generally have a CD4 count of 500 to 1,500 per cubic millimetre). A person with HIV whose CD4 count falls below 200 per cubic millimeter will be diagnosed with AIDS.[1]

Over time, as HIV kills more CD4 cells, the body is more likely to get various types of infections and cancers.HIV is transmitted through bodily fluids that include : blood,semen,vaginal or rectal fluids and breast milk. HIV is a lifelong condition and currently there is no cure. However, with medical care, including treatment called antiretroviral therapy, it’s possible to manage HIV and live with the virus for many years.[1]

Without treatment, a person with HIV is likely to develop a serious condition called AIDS. AIDS is a disease that can develop in people with HIV. At that point, the immune system is too weak to fight off other diseases and infections. Untreated, life expectancy with AIDS is about three years. With antiretroviral therapy, HIV can be well-controlled and life expectancy can be nearly the same as someone who has not contracted HIV.[1]

A person can also be diagnosed with AIDS if they have HIV and develop an opportunistic infection or cancer that's rare in people who don't have HIV. An opportunistic infection, such as pneumonia, is one that takes advantage of a unique situation, such as HIV.[1]

If AIDS does develop, it means that the immune system is severely compromised. It's weakened to the point where it can no longer fight off most diseases and infections. That makes the person vulnerable to a wide range of illnesses, including:

- pneumonia,tuberculosis, cancer, and lymphoma
- oral thrush, a fungal infection in the mouth or throat
- cytomegalovirus (CMV), a type of herpes virus
- cryptococcal meningitis, a fungal infection in the brain
- toxoplasmosis, a brain infection caused by a parasite
- cryptosporidiosis, an infection caused by an intestinal parasite

The shortened life expectancy linked with untreated AIDS isn't a direct result of the syndrome itself. Rather, it's a result of the diseases and complications that arise from having an immune system weakened by AIDS.[1]

SYMPTOMS

- headaches and other aches and pains ,swollen lymph nodes
- recurrent fevers,night sweats, pneumonia,shingles
- recurrent or chronic diarrhoea,weight loss,skin rashes,recurrent oral or vaginal yeast infections, sores, spots, or lesions of the mouth and tongue, genitals, or anus
- neurologic problems such as trouble concentrating, memory loss,confusion,anxiety and depression.

A BRIEF HISTORY OF HIV TREATMENT

Azidothymidine, also known as zidovudine, was introduced in 1987 as the first treatment for HIV. Scientists also developed treatments to reduce mother to child transmission.In 1997, highly active antiretroviral therapy (HAART) became the new treatment standard. It caused a 47 percent decline in death rates.[2]

The Food and Drug Administration (FDA) approved the first rapid HIV diagnostic test kit in November 2002. The test kit allowed hospitals to provide results with 99.6 percent accuracy in 20 minutes.[2]

Also in 2003, the CDC reported that 40,000 new infections occurred each year. More than half of those transmissions came from people who didn't know they were infected. It was later discovered the number was closer to 56,300 infections. This number remains roughly the same since the late 1990s.[2]

The World Health Organization set a goal to bring treatment to 3 million people by 2005. By 2010, about 5.25 million people had treatment, and 1.2 million people would start treatment. The FDA approved Combivir in 1997. Combivir combines two drugs into a single medication, making HIV medications easier to take.[2]

Researchers continued to create new formulations and combinations to improve treatment outcome. By 2010, there were up to 20 different treatment options and generic drugs, which helped lower costs. As of 2017, studies have shown that a person living with HIV who is on regular antiretroviral therapy that reduces the virus to undetectable levels in the blood is NOT able to transmit HIV to a partner during sex.[2]

On april 2019 , FDA approved dovato(doultegravir and lamivudine tablets),that is the first two drug complete regimen for HIV infected patients who never received antiretroviral treatment.[2]

ANTIRETROVIRAL THERAPY [ART]

Standard antiretroviral therapy (ART) consists of the combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease. Huge reductions have been seen in rates of death and suffering when use is made of a potent ARV regimen, particularly in early stages of the disease.Furthermore, expanded access to ART can also reduce the HIV transmission at population level, impact orphan hood and preserve families.[2]

In 2011, an estimated 34 million people were living with HIV.WHO and UNAIDS estimate that at least 15 million people were in need of antiretroviral therapy in 2011. As of the end of 2012, 9.7 million people had access to ART in low- and middle-income countries. WHO is providing countries with ongoing guidance, tools and support in delivering and scaling up ART within a public health approach .In 2010, WHO and UNAIDS launched the Treatment 2.0 strategy, which promotes radical simplification of ART, with accelerated treatment scale-up and full integration with prevention, in order to reach Universal Access.
WHO launched in July 2013 new guidelines with recommendations on ART for adults and Adolescents.[2]

DOVATO [DOLUTEGRAVIR AND LAMIVUDINE TABLETS]

Dovato (dolutegravir and lamivudine) is a combination antiviral medicine that prevents the human immunodeficiency virus (HIV) from multiplying in your body. Dovato is used to treat HIV, the virus that can cause the acquired immunodeficiency syndrome (AIDS).[5] This medicine is not a cure for HIV or AIDS. DOVATO, a two-drug combination of dolutegravir (integrase strand transfer inhibitor [INSTI]) and lamivudine (nucleoside analogue reverse transcriptase inhibitor [NRTI]) is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with no antiretroviral treatment history and with no known substitutions associated with resistance to the individual components of DOVATO.[5]

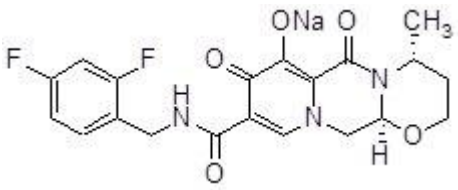
DOVATO DISCRIPTION

WARNING: PATIENTS CO-INFECTED WITH HEPATITIS B VIRUS (HBV) AND HUMAN IMMUNODEFICIENCY VIRUS (HIV-1): EMERGENCE OF LAMIVUDINE-RESISTANT HBV AND EXACERBATIONS OF HBV

All patients with HIV-1 should be tested for the presence of HBV prior to or when initiating DOVATO. Emergence of lamivudine-resistant HBV variants associated with lamivudine-containing antiretroviral regimens has been reported. If DOVATO 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 HIV-1 and HBV and have discontinued lamivudine, a component of DOVATO. Closely monitor hepatic function in these patients and, if appropriate, initiate anti-HBV treatment. Prior to or when initiating DOVATO, test patients for HBV infection.[9]

Dolutegravir

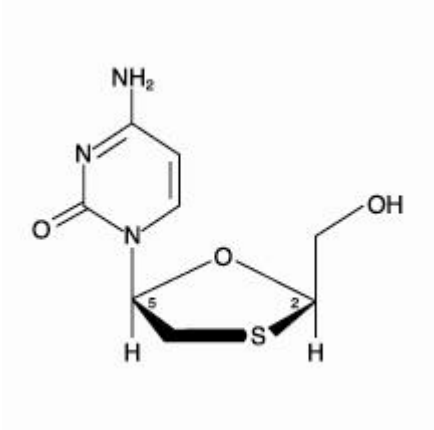
The chemical name of dolutegravir sodium is sodium (4R,12aS)-9-{[(2,4-difluorophenyl)methyl]carbamoyl}-4-methyl-6,8-dioxo-3,4,6,8,12,12a-hexahydro-2H-pyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazin-7-olate. The empirical formula is C20H18F2N3NaO5 and the molecular weight is 441.36 g/mol.[9] It has the following structural formula:



Dolutegravir sodium is a white to light yellow powder and is slightly soluble in water.

Lamivudine

The chemical name of lamivudine is (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one. Lamivudine is the (-)enantiomer of a dideoxy analogue of cytidine. Lamivudine has also been referred to as (-)2′,3′-dideoxy, 3′-thiacytidine. It has a molecular formula of C8H11N3O3S and a molecular weight of 229.3 g/mol. [9] It has the following structural formula:



Lamivudine is a white to off-white crystalline solid and is soluble in water.

CLINICAL TRIALS ON DOVATO

The US FDA's approval for Dovato was based on the positive results obtained from two Phase III clinical trials named GEMINI 1 and GEMINI 2, which together enrolled 1,433 adult HIV-1 patients with no ARV treatment history. [10]

Dovato was administered once daily for 148 weeks in patients with baseline HIV-1 viral loads up to 500,000 copies per millilitre during both the trials. [10]

The drug was also compared to a three-drug regimen comprising dolutegravir, two NRTIs, and tenofovir disoproxil fumarate/emtricitabine (Truvada; TDF/FTC). The primary efficacy endpoint of each trial was the achievement of plasma HIV-1 RNA rebinucleaic acid (RNA) copies to less than 50 per ml after week 48 in 91% cases. [10]

A mean change of 0.116mg/dl was observed in fasted lipid values of patients treated with a two-drug combination of dolutegravir and lamivudine from baseline to week 48. The mean change for patients treated with a three-drug regimen was noticed as 0.154mg/dl from baseline to week 48. [10]

Dovato achieved a 10% non-inferior efficacy compared to the three-drug regimen during the trials and resulted in reducing exposure to the number of ARVs. [10]

Insomnia, diarrhoea, headache, nausea, and fatigue were Dovato's most common adverse events noticed during the GEMINI I and II clinical trials.[10]

DOVATO'S MECHANISM OF ACTION

Dovato is a combination of 50mg of the integrase strand transfer inhibitor (INSTI) dolutegravir (Tivicay; DTG) and 300mg of the nucleoside analogue reverse transcriptase inhibitor (NRTI) lamivudine (Epivir; 3TC), which is a synthetic nucleoside analogue. [10]

Dolutegravir binds to the active site of the integrase produced by HIV virus and blocks the strand transfer activity, which will stop the formation of integrated proviral DNA. [10]

Lamivudine is metabolised intracellularly by phosphorylation to its active 5-triphosphate metabolite, lamivudine triphosphate (3TC-TP), which inhibits reverse transcriptase (RT) via DNA chain termination. [10]

The drug is available in the form of a fixed-dose tablet for oral administration.

PHARMACODYNAMICS

Cardiac Electrophysiology

The effect of combination therapy as Dovato or lamivudine given alone on the QT interval has not been studied. At a 250-mg suspension dose (exposures approximately 3–fold that of the 50-mg once-daily dose at steady state), dolutegravir given alone did not prolong the QTc interval to any clinically relevant extent.[12]

Effects of Dolutegravir on Renal Function

No clinically significant dolutegravir exposure-response relationship on the glomerular filtration rate or effective renal plasma flow was observed. The effect of dolutegravir on renal function was evaluated in an open-label, randomized, 3-arm, parallel, placebo-controlled trial in healthy subjects (n = 37) who received dolutegravir 50 mg once daily (n = 12), dolutegravir 50 mg twice daily (n = 13), or placebo once daily (n = 12) for 14 days. [12]

PHARMACOKINETICS

Absorption

When 50 mg of dolutegravir once daily was orally administered to HIV-1 infected adults, the AUC, Cmax, and Cmin is 53.6 mcg h/mL, 3.67 mcg/mL, and 1.11 mcg/mL, respectively. The peak plasma concentration was observed 2 to 3 hours post-dose. Steady state is achieved within approximately 5 days with average accumulation ratios for AUC, Cmax, and C24h ranging from 1.2 to 1.5. When 50 mg once daily is given to pediatric patients (12 to < 18 years and weighing ≥40 kg) the Cmax, AUC, and C24 is 3.49 mcg/mL, 46 mcg.h/mL, and 0.90 mcg/mL respectively.

Volume of distribution

The administration of a dose of 50 mg of dolutegravir presents an apparent volume of distribution of 17.4 L. The median dolutegravir concentration in CSF was 18 ng/mL after 2 weeks of treatment.

Protein binding

Dolutegravir is highly protein bound to human plasma proteins reaching a percentage 98.9% of the administered dose.

Metabolism

Dolutegravir is highly metabolized through three main pathways and it forms no long-lived metabolites. The first pathway is defined by the glucuronidation by UGT1A1, the second pathway by carbon oxidation by CYP3A4 and the third pathway is what appears to be a sequential oxidative defluorination and glutathione conjugation. The main metabolite found in blood plasma is the ether glucuronide form (M2) and its chemical properties disrupt its ability to bind metal ions, therefore, it is inactive.

Route of elimination

When a single oral dose of dolutegravir is given, nearly all complete dose is recovered in a proportion of 53% excreted unchanged in the feces and 31% excreted in urine. The renal eliminated recovered dose consists of ether glucuronide of dolutegravir (18.9%), a metabolite formed by oxidation at the benzylic carbon (3.0%), a hydrolytic N-dealkylation product (3.6%) and unchanged drug (< 1%)

HALF LIFE

The half-life of dolutegravir is 14 hours.

CLEARANCE

The apparent clearance rate of dultegravir is 1.0 L/h.

BEFORE TAKING THIS MEDICINE

One should not use Dovato if you are allergic to dolutegravir or lamivudine, or if you are also taking dofetilide (Tikosyn).

To make sure Dovato is safe for you, tell your doctor if you have ever had:

- liver disease, especially hepatitis B or C.

You may develop lactic acidosis, a dangerous build-up of lactic acid in your blood. This may be more likely if you have other medical conditions, if you are overweight, or if you are a woman.

You may need to have a negative pregnancy test before starting treatment with Dovato.Dolutegravir and lamivudine may harm an unborn baby if you take the medicine at the time of conception or during the first 12 weeks of pregnancy.

Women with HIV or AIDS should not breastfeed a baby. Even if your baby is born without HIV, the virus may be passed to the baby in your breast milk.[5]

DOVATO DOSING INFORMATION

Recommended Dosage:Dovato is a fixed-dose combination product containing 50 mg of dolutegravir and 300 mg of lamivudine. The recommended dosage regimen of Dovato in adults is one tablet taken orally once daily with or without food.

1)Usual Adult Dose for HIV Infection:one tablet orally once a day
Use: As a complete regimen, for the treatment of HIV-1 infection in patients with no antiretroviral treatment history and with no known substitutions associated with resistance to the individual components

2)Renal Dose Adjustments:CrCl less than 50 mL/min: Not recommended.

3)Liver Dose Adjustments:Mild or moderate liver dysfunction (Child-Pugh A or B): No adjustment recommended.Severe liver dysfunction (Child-Pugh C): Not recommended.[5]

DOSE ADJUSTMENTS

Co-administration with carbamazepine or rifampin: An additional 50 mg/day of dolutegravir is recommended, separated from this combination product by 12 hours. [5]

OVER DOSAGE

There is no known specific treatment for overdose with Dovato. If overdose occurs, the patient should be monitored and standard supportive treatment applied as required.[15]

Dolutegravir

As dolutegravir is highly bound to plasma proteins, it is unlikely that it will be significantly removed by dialysis. [15]

Lamivudine

Because a negligible amount of lamivudine was removed via (4-hour) hemodialysis, continuous ambulatory peritoneal dialysis, and automated peritoneal dialysis, it is not known if continuous hemodialysis would provide clinical benefit in a lamivudine overdose event. [15]

SIDE EFFECTS/ADVERSE EFFECTS

Even though it may be rare, some people may have very bad and sometimes deadly side effects when taking a drug.

Signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat. [5]

- Signs of liver problems like dark urine, feeling tired, not hungry, upset stomach or stomach pain, light-colored stools, throwing up, or yellow skin or eyes.

- Signs of too much lactic acid in the blood (lactic acidosis) like fast breathing, fast heartbeat, a heartbeat that does not feel normal, very bad upset stomach or throwing up, feeling very sleepy, shortness of breath, feeling very tired or weak, very bad dizziness, feeling cold, or muscle pain or cramps.
- Signs of a pancreas problem (pancreatitis) like very bad stomach pain, very bad back pain, or very bad upset stomach or throwing up.
- Fever,Muscle /joint pain,Mouth sores,Eye irritation,Shortness of breath.
- Changes in your immune system can happen when you start taking drugs to treat HIV. If you have an infection that you did not know you had, it may show up when you take this drug. [5]

DRUG INTERACTION'S OF DOVATO

A total of 169 drugs are known to interact with Dovato (dolutegravir / lamivudine).

- 64 major drug interactions
- 27 moderate drug interactions
- 78 minor drug interactions.

MultiVitamin Plus Zinc (multivitamin with minerals):Dolutegravir and multivitamin with minerals should not be taken orally at the same time. Products that contain aluminum, calcium, iron, magnesium and/or other minerals may interfere with the absorption of dolutegravir and reduce its effectiveness in treating HIV infection. You should take dolutegravir at least two hours before or six hours after the multivitamin with minerals dose. Talk to your doctor if you have any questions or concerns, or if you have trouble separating the dosing times. Your doctor may be able to prescribe alternatives that do not interact. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.[5]

DRUG	INTERACTION
Abemaciclib	The serum concentration of Dolutegravir can be increased when it is combined with Abemaciclib.
Acebutolol	The serum concentration of Dolutegravir can be increased when it is combined with Acebutolol.
Acetaminophen	The serum concentration of Dolutegravir can be increased when it is combined with Acetaminophen.
Acetylcysteine zinc	Acetylcysteine zinc can cause a decrease in the absorption of Dolutegravir resulting in a reduced serum concentration and potentially a decrease in efficacy.
Acetylsalicylic acid	The serum concentration of Dolutegravir can be increased when it is combined with Acetylsalicylic acid.
Acyclovir	The excretion of Acyclovir can be decreased when combined with Dolutegravir.
Adefovir dipivoxil	The excretion of Adefovir dipivoxil can be decreased when combined with Dolutegravir.
Adenine	The metabolism of Dolutegravir can be decreased when combined with Adenine.
Adenovirus type 7 vaccine live	The therapeutic efficacy of Adenovirus type 7 vaccine live can be decreased when used in combination with Dolutegravir.
Afatinib	The serum concentration of Dolutegravir can be increased when it is combined with Afatinib.

PHARMACOGENOMIC EFFECTS/ADR

INTERACTING GENE/ENZYME	ALLELE NAME	GENOTYPE(S)	DEFINING CHANGE(S)	TYPE(S)	DESCRIPTION
UDP-glucuronosyl transferase 1-1	UGT1A1*28 or UGT1A 7/7	Not Available	extra TA in promoter	Effect Directly Studied	Poor drug metabolizer.
UDP-glucuronosyl transferase 1-1	UGT1A1*6	Not Available	G > A	Effect Directly Studied	The presenceof this Polymorphism in UGT1A1is associated with reduction in dolutegravirmetabolism.

UDP-glucuronosyl transferase 1-1	UGT1A1*37	Not Available	TA pair insertion	Effect Directly Studied	The presence of this polymorphism in UGT1A1isassociatedwith reduction in dolutegravir metabolism.

STORAGE

- Store Dovato below 86°F (30°C).
- Keep Dovato in the container that it came in and keep the container tightly closed.
- Do not use Dovato if the original seal over the container opening is broken or missing.
- Throw away Dovato that is no longer needed or expired (out of date). Follow FDA guidelines on how to safely dispose of unused medicine.
- Keep Dovato and all medicines out of reach of children.[14]

USE IN SPECIFIC POPULATION

- Pregnancy,Lactation
- Males and females with child bearing potential
- Paediatric patients,Elderly patients
- Patients with creatinine clearance <50 mL/min,Patients with mild or moderate hepatic impairment.[15]

NONCLINICAL TOXICOLOGY

Carcinogenicity

Dolutegravir: Two-year carcinogenicity studies in mice and rats were conducted with dolutegravir. Mice were administered doses of up to 500 mg/kg, and rats were administered doses of up to 50 mg/kg. In mice, no significant increases in the incidence of drug-related neoplasms were observed at the highest doses tested, resulting in dolutegravir AUC exposures approximately 26 times higher than those in humans at the recommended dose. In rats, no increases in the incidence of drug-related neoplasms were observed at the highest dose tested, resulting in dolutegravir AUC exposures 17 times higher than those in humans at the recommended dose. [15]

Lamivudine: Long-term carcinogenicity studies with lamivudine in mice and rats showed no evidence of carcinogenic potential at exposures up to 12 times (mice) and 57 times (rats) the human exposures at the recommended dose. [15]

Mutagenicity

Dolutegravir: Dolutegravir was not genotoxic in the bacterial reverse mutation assay, in a mouse lymphoma assay, or in the in vivo rodent micronucleus assay. [15]

Lamivudine: Lamivudine was mutagenic in an L5178Y mouse lymphoma assay and clastogenic in a cytogenetic assay using cultured human lymphocytes. Lamivudine was not mutagenic in a microbial mutagenicity assay, in an in vitro cell transformation assay, in a rat micronucleus test, in a rat bone marrow cytogenetic assay, and in an assay for unscheduled DNA synthesis in rat liver. [15]

Impairment of Fertility

Dolutegravir or lamivudine did not affect male or female fertility in rats at doses associated with exposures approximately 44 or 112 times, respectively, higher than the exposures in humans at the recommended dose. [15]

PRECAUTIONS

- BOXED WARNINGS:

  PATIENTS COINFECTED WITH HBV AND HIV-1:

  -EMERGENCE OF LAMIVUDINE-RESISTANT HBV: All patients with HIV-1 should be tested for HBV before/when starting this drug. Emergence of lamivudine-resistant HBV variants associated with lamivudine-containing antiretroviral regimens reported. If this drug is used in HBV/HIV-1-coinfected patients, additional treatment should be considered to appropriately treat chronic HBV; otherwise, an alternative regimen should be considered.[5]
  -EXACERBATIONS OF HBV: Severe acute exacerbations of HBV reported in HBV/HIV-1-coinfected patients who have stopped lamivudine, a component of this drug. Hepatic function of HBV/HIV-1-coinfected patients should be monitored closely; if appropriate, anti-HBV therapy should be stared. [5]

- When taken with food, DOVATO and supplements or multivitamins containing calcium or iron can be taken at the same time. Under fasting conditions, DOVATO should be taken 2 hours before or 6 hours after taking supplements containing calcium or iron. When possible, avoid use of sorbitol-containing medicines with DOVATO.
- Safety and efficacy have not been established in patients younger than 18 years. [5]

CONCLUSION

Dolutegravir/lamivudine (trade name Dovato) is a combination drug for the treatment of HIV/AIDS. It was approved for use in the United States in April 2019.[1] It contains dolutegravir, an integrase inhibitor, and lamivudine, a reverse-transcriptase inhibitor.HIV is a virus that damages the immune system. The immune system helps the body fight off infections. Untreated HIV infects and kills CD4 cells, a type of immune cell called T cells(Healthy adults generally have a CD4 count of 500 to 1,500 per cubic millimetre). A person with HIV whose CD4 count falls below 200 per cubic millimeter will be diagnosed with AIDS.Standard antiretroviral therapy (ART) consists of the combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease.The use of multiple drugs that act on different viral targets is known as highly active antiretroviral therapy (HAART). HAART decreases the patient's total burden of HIV, maintains function of the immune system, and prevents opportunistic infections that often lead to death. The chemical name of dolutegravir sodium is sodium (4R,12aS)-9-{[(2,4-difluorophenyl)methyl]carbamoyl}-4-methyl-6,8-dioxo-3,4,6,8,12,12a-hexahydro-2H-pyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazin-7-olate.The chemical name of lamivudine is (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one. Lamivudine is the (-)enantiomer of a dideoxy analogue of cytidine.Dovato is a combination of 50mg of the integrase strand transfer inhibitor (INSTI) dolutegravir (Tivicay; DTG) and 300mg of the nucleoside analogue reverse transcriptase inhibitor (NRTI) lamivudine (Epivir; 3TC), which is a synthetic nucleoside analogue.Dolutegravir and lamivudine may harm an unborn baby if you take the medicine at the time of conception or during the first 12 weeks of pregnancy.WARNING: PATIENTS CO-INFECTED WITH HEPATITIS B VIRUS (HBV) AND HUMAN IMMUNODEFICIENCY VIRUS (HIV-1): EMERGENCE OF LAMIVUDINE-RESISTANT HBV AND EXACERBATIONS OF HBV.

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