

Dovato (dolutegravir, lamivudine)



NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Dovato
- **Generic name:** Dolutegravir, lamivudine
- **Pharmacological class:** HIV-1 integrase strand transfer inhibitor (INSTI) + nucleoside analog reverse transcriptase inhibitors (NRTIs)
- **Strength and Formulation:** 50mg/300mg; tablets
- **Manufacturer:** ViiV Healthcare
- **How supplied:** Bottles—30
- **Legal Classification:** Rx

Dovato



Indication

- As a complete regimen for the treatment of HIV-1 infection in adults with no antiretroviral treatment history and with no known substitutions associated with resistance to the individual components of Dovato

Dosage & Administration

- **Test for HBV** infection prior to initiation
- Take with or without food
- 1 tab daily
- Concomitant carbamazepine, rifampin: give additional dolutegravir 50mg separated by 12hrs from Dovato
- **Renal impairment** (CrCl <50mL/min) or **severe hepatic impairment** (Child-Pugh C): not recommended

Considerations for Special Populations

- **Pregnancy:** increased risk of **neural tube defects** (avoid use at time of conception through 1st trimester); exclude status prior to initiation; if confirmed, switch to alternative HIV therapy
- **Nursing mothers:** not recommended
- **Pediatric:** not established
- **Elderly:** use caution
- **Renal impairment:** CrCl <50mL/min: not recommended
- **Hepatic impairment:** severe impairment (Child-Pugh C): not recommended

Contraindications

- Previous hypersensitivity reaction to dolutegravir or lamivudine
- Concomitant dofetilide

Boxed Warning

- Patients co-infected with HBV and HIV-1: emergence of lamivudine-resistant HBV and exacerbations of HBV

Warnings/Precautions

- Emergence of lamivudine-resistant HBV variants associated with lamivudine-containing antiretroviral regimens
- Discontinuation of lamivudine-containing products and possibly Dovato may be associated with severe acute exacerbations of hepatitis B
- Closely monitor **patients co-infected with HBV and HIV** for several months after stopping treatment; if appropriate, anti-HBV therapy may be warranted (esp. in advanced liver disease or cirrhosis)

Warnings/Precautions

- Discontinue immediately if **hypersensitivity reactions** develop
- Increased risk for worsening/development of elevated transaminases in patients with underlying hepatitis B or C; monitor for hepatotoxicity
- Suspend if **lactic acidosis** or pronounced hepatotoxicity (eg, hepatomegaly, steatosis) occurs
- Immune reconstitution syndrome
- Renal impairment: if lamivudine dose reduction is required, use individual components
- Embryo-fetal toxicity
- Advise females of reproductive potential to use effective contraception

Interactions

- See Contraindications
- Concomitant other antiretrovirals: not recommended
- Dolutegravir may be affected by drugs that induce or inhibit UGT1A1, CYP3A, UGT1A3, UGT1A9, BCRP, and P-gp enzymes or transporters
- May potentiate drugs eliminated via OCT2 or MATE1
- Avoid concomitant oxcarbazepine, phenytoin, phenobarbital, St. John's wort

Interactions

- Antagonized by carbamazepine, rifampin: requires extra dolutegravir dose (see Dosing)
- Potentiates metformin
- Avoid concomitant sorbitol-containing products
- Concomitant cation-containing antacids, laxatives, sucralfate, buffered drugs, or oral iron/calcium supplements (also can give together with a meal): give Dovato 2hrs before or 6hrs after

Adverse Reactions

- **Most common** ($\geq 2\%$ in those receiving Dovato): headache, diarrhea, nausea, insomnia, fatigue
- **Others**: hypersensitivity reactions (may be fatal), hepatotoxicity (monitor)

Mechanism of Action

- Dolutegravir, an INSTI, inhibits HIV integrase by binding to the active site and blocking the strand transfer step of retroviral DNA integration which is vital for the HIV replication cycle
- Lamivudine, a NRTI, is a synthetic nucleoside analogue that is phosphorylated intracellularly to its active 5'-triphosphate metabolite, lamivudine triphosphate (3TC-TP)
- The 3TC-TP integrates into the viral DNA and causes DNA chain termination through inhibition of reverse transcriptase

Clinical Studies

- The efficacy of Dovato was evaluated in two identical Phase 3, randomized, multicenter, parallel-group, non-inferiority, 148-week trials (GEMINI-1 and GEMINI-2) in HIV-1 infected adults with no history of antiretroviral treatment
- Patients (N=1433) were randomized to receive either Tivicay 50mg + Epivir 300mg once daily or Tivicay 50mg + fixed-dose Truvada once daily

Clinical Studies

- The primary efficacy endpoint for both trials was the difference in proportion <50 copies/mL plasma HIV-1 RNA at Week 48 (Snapshot algorithm) for the 2 treatment arms
- At Week 48, the adjusted difference was -2.6 (95% CI: -6.7, 1.5) for GEMINI-1 and -0.7 (95% CI: -4.3, 2.9) for GEMINI-2 with a prespecified non-inferiority margin of 10%
- Additionally, no patients had any detectable treatment-emergent substitutions associated with resistance to dolutegravir or NRTIs

New Product Monograph

- For more information view the product monograph available at:

<https://www.empr.com/drug/dovato/>