Dovato
dolutegravir/lamivudine

DOVATO is indicated for the treatment of HIV-1 in adults and adolescents above 12 years weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.

TWO WELL-CHOSEN AGENTS CAN ACHIEVE A HIGH BARRIER TO RESISTANCE

"FORGIVENESS" OR "HIGH BARRIER TO RESISTANCE"—WHAT MATTERS MOST?

"Forgiveness" of a regimen implies that intermittent non-adherence can still maintain virological suppression with no resistance[1]

Non-adherence can lead to[2]**:**
- Virological failure
- Development of resistance
- Limited treatment options
- Increased transmission risk

All oral HIV therapies are required to be taken at least once daily.[3]

WHY WE SHOULD REFER TO "BARRIER TO RESISTANCE"

"Barrier to resistance" is well-defined by virological, pharmacological and target-binding properties, ensuring[4-17]**:**

Long-term durability
Reduced risk of resistance
Preservation of future treatment options

DOVATO and DTG-based 3-drug regimens all have a high barrier to resistance recognised by International Guidelines[3,18]**:**

EACS GUIDELINES

DHHS GUIDELINES

Clinical data and real-world experience are the **standard measures** of a regimen's barrier to resistance

THE GEMINI STUDIES: REASSURANCE FOR YOUR PATIENTS OUT TO 3 YEARS

Few Confirmed Virological Withdrawals* at 3 Years[16]

	Number of Patients in Treatment Arm	Confirmed Virological Withdrawals
DOVATO pooled, n (%)	**716**	**12** (2%)
DTG + TDF/FTC pooled, n (%)	**717**	**9** (1%)

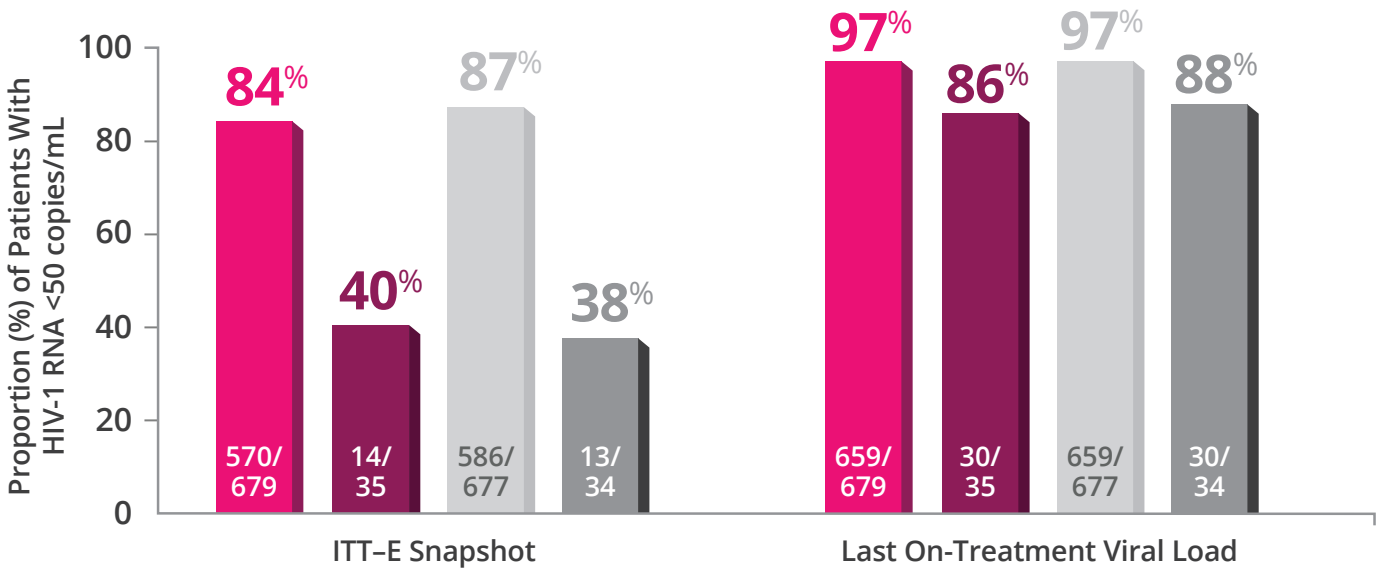
- While taking DTG + 3TC separates, 1 participant developed resistance-associated mutations

FURTHER CONFIRMED BY REAL-WORLD EVIDENCE

In 1,777 patients across 10 real-world switch studies and 135 treatment-naïve patients in the REDOLA study, 0 cases of INI or NRTI resistance-associated mutations were reported[20-30]

*Patients met virological withdrawal criteria if a second and consecutive HIV-1 RNA value met any of the following definitions: decrease from baseline in HIV-1 RNA of <1 $\log_{10}$ copies/mL unless HIV-1 RNA <200 copies/mL by Week 12; confirmed plasma HIV-1 RNA of ≥200 copies/mL after confirmed consecutive HIV-1 RNA <200 copies/mL.[19]

Comparable Suppression vs DTG + TDF/FTC Across Adherence Subgroups at 3 Years[31]



- Increased risk of not being suppressed if DOVATO or DTG + TDF/FTC is taken less than once daily

Adapted from Fernvik et al, 2021.[31]

IT IS TIME TO RECONSIDER THE VALUE OF THE SECOND NRTI

DTG 50 mg + 3TC 300 mg used for the GEMINI studies.
ITT–E=intent-to-treat–exposed.

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Dovato
dolutegravir/lamivudine

Abridged Prescribing Information

Dovato (dolutegravir 50mg/lamivudine 300mg) tablets See Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** Film-coated tablet containing dolutegravir sodium equivalent to 50 mg dolutegravir and 300 mg lamivudine debossed with "SV-137" on one face. **Indication:** HIV-1 in adults & adolescents above 12 years of age weighing ≥40kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine. **Dosing:** One tablet once daily with or without food. Use an additional 50mg tablet of dolutegravir approximately 12 hours after the dose of Dovato when co-administered with efavirenz, nevirapine, tipranavir/ritonavir, etravirine (without boosted PI), carbamazepine, oxcarbazepine, phenytoin, phenobarbital, St John's Wort or rifampicin. *Elderly:* Limited data in 65+ yrs. *Renal impairment:* Not recommended in patients with creatinine clearance < 30 mL/min. For patients with a sustained creatinine clearance between 30 and 49 mL/min see SmPC section 4.4. *Hepatic impairment:* Caution in severe hepatic impairment (Child-Pugh grade C). **Contraindications:** Hypersensitivity to any ingredient. Co-administration with substrates of OCT-2 with narrow therapeutic windows, such as fampridine. **Special warnings/precautions:** Risk of hypersensitivity reactions. Discontinue dolutegravir and other suspect agents immediately. Risks of osteonecrosis, immune reactivation syndrome. Monitor LFTs in Hepatitis B/C co-infection and ensure effective Hepatitis B therapy. Caution with metformin: monitor renal function and consider metformin dose adjustment. Use with etravirine requires boosted PI or increased dose of dolutegravir. Use with Mg/Al-containing antacids requires dosage separation. Use with calcium, multivitamins or iron also requires dosage separation if not taken at the same time with food. Use with cladribine or emtricitabine not recommended. When possible, avoid chronic co-administration of sorbitol or other osmotic acting alcohols (see SmPC section 4.5). If unavoidable, consider more frequent viral load monitoring. **Fertility, pregnancy and lactation:** Human fertility - no data; animal fertility - studies indicate no effects. Women of childbearing potential (WOCBP) should be counselled about the potential risk of neural tube defects including consideration of effective contraceptive measures. If a woman plans pregnancy, the benefits and the risks of continuing treatment should be discussed with the patient. The safety and efficacy of a duel regime has not been studied in pregnancy. If a pregnancy is confirmed in the first trimester while on Dovato, the benefits and risks of continuing Dovato versus switching to another antiretroviral regimen should be discussed with the patient taking the gestational age and the critical time period of neural tube defect development into account (see SmPC section 4.6). There have been reports of mitochondrial dysfunction in HIV-negative infants exposed in utero and/or post-natally to nucleoside analogues. Do not breast-feed. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, abnormal dreams, depression, anxiety, dizziness, somnolence, rash, pruritus, alopecia, fatigue, arthralgia, myalgia, hypersensitivity, completed suicide, suicidal ideation or suicide attempt, panic attack, hepatitis, blood dyscrasias, acute hepatic failure, pancreatitis, angioedema, rhabdomyolysis, lactic acidosis, peripheral neuropathy. Elevations of bilirubin, ALT, AST and CPK. Weight increased. **MA Nr:** EU/1/19/1370/001. **MA holder:** ViiV Healthcare BV, Van Asch van Wijckstraat 55H, 3811 LP Amersfoort, Netherlands. **Legal Category:** POM A. **Date of preparation of API:** September 2022. **Code:** PI-6305. Further information available from GlaxoSmithKline, 12 Riverwalk, Citywest, Business Campus, Dublin 24. Tel: 01-4955000.

Adverse events should be reported directly to the Health Products Regulatory Authority (HPRA) on their website: www.hpra.ie. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

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