POWER MAINTAINED

Tivicay + lamivudine
dolutegravir

A COMPLETE REGIMEN

48-WEEK RESULTS

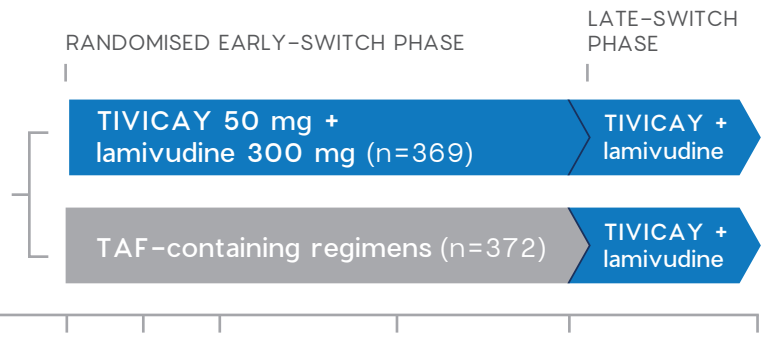
TANGO

Suitable to treat HIV-1 infection only in adults with no known or suspected resistance to integrase inhibitors or lamivudine.

POWERED BY DOLUTEGRAVIR AT THE CORE

OPEN LABEL STUDY OF TIVICAY + LAMIVUDINE vs TAF-CONTAINING REGIMENS IN MORE THAN 700 VIROLOGICALLY SUPPRESSED PATIENTS[1]

- Virologically suppressed adults with HIV-1 RNA <50 copies/mL for >6 months
- TAF/FTC + PI or INI or NNRTI as initial regimen
- Stable TAF-containing regimen
- No prior virological failure and no documented NRTI or INI resistance
- HBV negative
- CrCl >50ml/min



Fixed dose combination of DTG 50mg/3TC 300 mg used in the TANGO study.

PRIMARY ENDPOINT:
Proportion of patients with plasma HIV-1 RNA ≥50 copies/mL (by Snapshot algorithm; ITT-E)

POWERFUL, NON-INFERIOR EFFICACY WITH 0 RESISTANCE AT 48 WEEKS[1]

NO INCREASED RISK OF VIROLOGICAL FAILURE vs TAF-CONTAINING REGIMENS (ITT-E SNAPSHOT ANALYSIS)

0.3% (n=1/369) TIVICAY + lamivudine

0.5% (n=2/372) TAF-containing regimens

Proportion (%) of patients with HIV-1 RNA ≥50 copies/mL

Adjusted difference: −0.3 (95% CI: −1.2, 0.7)

93.2% (n=344/369) TIVICAY + lamivudine

93.0% (n=346/372) TAF-containing regimens

Proportion (%) of patients with HIV-1 RNA <50 copies/mL

6.5% (n=24/369) TIVICAY + lamivudine

6.5% (n=24/372) TAF-containing regimens

No virological data

REASSURANCE WITH A HIGH BARRIER TO RESISTANCE

0
CASES

OF RESISTANCE-ASSOCIATED MUTATIONS IN BOTH ARMS

- No confirmed virological withdrawals* on TIVICAY + lamivudine (0) vs TAF-containing regimens (1 [<1%])
  - —No INI mutations observed
  - —No NRTI mutations observed (including M184V/I)

FEWER ANTIRETROVIRALS vs A 3-DRUG REGIMEN: TDF, TAF AND ABC FREE[2,3]

OVERALL ADVERSE EVENTS WERE COMPARABLE ACROSS BOTH ARMS AT 48 WEEKS[1]

For the majority of patients in the TIVICAY + lamivudine arm, the introduction of 2 new ARVs may have contributed to the numerical differences observed

	Any AE	Any drug-related AE, Grade 2 to Grade 5	AEs leading to withdrawal
TIVICAY + lamivudine (n=369)	295 (80%)	17 (5%)	13 (4%)
TAF-containing regimens (n=371)	292 (79%)	3 (1%)	2 (1%)

METABOLIC PARAMETERS AT 48 WEEKS[1]

MINIMAL CHANGES in bone turnover biomarkers in both treatment arms. The TANGO study did not deteremine whether these changes translate to clinical differences.

MINIMAL CHANGES in renal function biomarkers in both treatment arms. The TANGO study did not deteremine whether these changes translate to clinical differences.

Tivicay + lamivudine
dolutegravir

A COMPLETE REGIMEN

Prescribing Information

Tivicay dolutegravir 10mg, 25mg and 50mg tablets
See Summary of Product Characteristics before prescribing

Indication: HIV in >6 years and >15kg as part of combination therapy. **Dosing:** *Adults & adolescents >40kg*: 50mg once daily with or without food if no proven/ suspected integrase resistance. Children 6 to <12 years: dose according to bodyweight: 15-<20kg: 20mg once daily (2x10mg); 20-<30kg: 25mg once daily; 30-<40kg: 35mg once daily (1 x 25mg + 1 x 10mg); When co-administered with efavirenz, nevirapine, tipranavir/ritonavir, etravirine (without boosted PI), carbamazepine, oxcarbazepine, phenytoin, phenobarbital, St John's Wort or rifampicin, Tivicay 50mg twice daily in adults/ adolescents or the weight-based once daily dose twice daily in paediatric patients. *Adults with proven or suspected integrase resistance:* 50mg twice daily preferably with food. Limited data in paediatric patients with proven/suspected integrase resistance. *Elderly:* Limited data in 65+ yrs. Caution in severe hepatic impairment. **Contraindications:** Hypersensitivity to any ingredient. Co-administration with dofetilide. **Warnings/precautions:** Risk of hypersensitivity reactions. Discontinue dolutegravir and other suspect agents immediately if suspected. The two-drug regimen of dolutegravir and lamivudine is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine. 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, calcium, multivitamins or iron requires dosage separation. **Pregnancy/ lactation:** Before initiating dolutegravir, women of childbearing potential (WOCBP) should undergo pregnancy testing. WOCBP who are taking dolutegravir should use effective contraception. Dolutegravir should not be used during the first trimester due to the potential risk of neural tube defects, unless there is no alternative. Dolutegravir should only be used during the second and third trimester of pregnancy when the expected benefit justifies the potential risk to the foetus. Avoid breast-feeding. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, abnormal dreams, depression, anxiety, dizziness, rash, pruritus, fatigue, elevations of ALT, AST and CPK, arthralgia, myalgia, hypersensitivity, suicidal ideation or suicide attempt, acute hepatic failure. **Basic NHS costs:** £498.75 for 30 x 50mg tablets (EU/1/13/892/001). £99.75 for 30 x 10mg tablets (EU/1/13/892/003). £249.38 for 30 x 25mg tablets (EU/1/13/892/005). MA holder: ViiV Healthcare BV, Huis ter Heideweg 62, 3705 LZ Zeist, Netherlands. Further information available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

Date of approval: April 2019 PI-1290

Prescribing Information

Epivir - Lamivudine 300mg tablets
See Summary of Product Characteristics (SmPC) before prescribing

Indications: HIV in adults, adolescents and children weighing at least 25 kg as part of combination therapy. **Dose:** Adults: one 300mg tablet daily with or without food. See SmPC for dosage in children and adolescents. Additional formulations available: 150mg tablets and Oral Solution (10mg/mL) – see SmPCs. *Elderly:* No specific data. *Renal impairment*: Creatinine clearance <50ml/min: see SmPC for dosage adjustment. *Hepatic impairment*: no dose adjustment required. **Contraindications:** Hypersensitivity to any ingredient. **Warnings/precautions:** High risk of virological failure (when used in a triple nucleoside regimen), immune reactivation syndrome, osteonecrosis, increased weight, lipids, glucose. Monitor LFTs in Hepatitis B/C co-infection. Use with cladribine, emtricitabine or high doses of co-trimoxazole 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. **Pregnancy/lactation:** Not recommended. Avoid breast-feeding. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, cough, nasal symptoms, rash, alopecia, arthralgia, muscle disorders, fatigue, malaise, fever, blood dyscrasias, pancreatitis, hepatitis, angioedema, rhabdomyolysis, lactic acidosis, peripheral neuropathy. Transient increases in liver enzymes. **Basic NHS costs:** 30 tablets: £157.51 EU/1/04/298/002. MA holder: ViiV Healthcare BV, Huis ter Heideweg 62, 3705 LZ Zeist, Netherlands. Further information is available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

Date of approval: January 2019 UK/3TC/0001/18(1)

Adverse events should be reported. For the UK, reporting forms and information can be found at *www.mhra.gov.uk/yellowcard* or search for **MHRA Yellowcard** in the **Google Play** or **Apple App store.** Adverse events should also be reported to GlaxoSmithKline on 0800 221441.

Adverse events should be reported. For Ireland, adverse events should be reported directly to the HPRA; Freepost, Pharmacovigilance Section, Health Products Regulatory Authority, Earlsfort Terrace, Dublin 2, Tel: +353 1 676 4971, *medsafety@hpra.ie*. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

*Patients met confirmed virological withdrawal criteria if they had 1 assessment with HIV-1 RNA ≥200 copies/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 copies/mL.[1]

References: 1. van Wyk J, Ajana F, Bisshop F, et al. Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen in maintaining virologic suppression through 48 weeks (TANGO study). Presented at: International AIDS Conference; July 21-24, 2019; Mexico City, Mexico. Slides WEAB0403LB. **2.** TIVICAY Summary of Product Characteristics. March 2019. **3.** EPIVIR Summary of Product Characteristics. February 2019.

Abbreviations: ABC=abacavir; AE=adverse event; FTC=emtricitabine; HBV=hepatitis B virus; INI=integrase inhibitor; ITT–E=intent-to-treat exposed; NRTI=nucleoside reverse transcriptase inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; TAF=tenofovir alafenamide; TC/HDL=total cholesterol/high-density lipoprotein cholesterol; TDF=tenofovir disoproxil fumarate.

ViiV Healthcare

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