GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Coadministration With Metformin

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) and coadministration with metformin. For more information about metformin, please refer to its product labeling.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/~/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi.

Product Labeling[1]

The BIC/FTC/TAF US Prescribing Information does not provide specific recommendations for additional monitoring or metformin dosage limitations. Coadministration can lead to increased metformin exposures. Available PK data regarding the effects of BIC/FTC/TAF on metformin are presented in Table 1 below. Refer to the FDA-approved prescribing information of metformin to assess the benefit and risk of concomitant use of BIC/FTC/TAF and metformin.

Table 1. Effect of BIC/FTC/TAF Components on Metformin[1a]

Coadminstered Drug	Dose of Coadministered Drug	BIC	TAF	Mean Ratio of Coadministered Drug PK Parameters (90% CI); No Effect=1		
				C_{max}	AUC	C_{min}
Metformin	500 mg twice daily	50 mg once daily	25 mg once daily	1.28 (1.21–1.36)	1.39 (1.31–1.48)	1.36 (1.21–1.53)

Abbreviations: C_{max}=maximum observed concentration of drug; C_{min}=minimum observed concentration of drug.
[a]All interaction studies were conducted in healthy volunteers.

Clinical Data on Coadministration of BIC/FTC/TAF and Metformin

PK DDI Evaluation[2]

A phase 1, blinded, placebo-controlled, multiple-dose, 2-period crossover study in healthy individuals (N=32) was conducted to evaluate the effect of BIC on the PK and pharmacodynamics of metformin. When BIC/FTC/TAF was coadministered with metformin, there was a modest increase in metformin exposure (metformin AUC increased by 39%) due to inhibition of the OCT2 and MATE1 renal transporters. Coadministration of metformin with BIC/FTC/TAF and placebo resulted in similar decreases in the AUC of serum glucose at

60 minutes after a glucose tolerance test (-16.6 mg/dL vs -12.7 mg/dL, respectively; *P*=0.26), and similar increases in serum lactate levels (1.6 pmol/L vs 0.8 pmol/L, respectively; *P*=0.37). The increase in metformin levels due to the BIC-mediated drug interaction did not lead to clinically significant changes in serum glucose and lactate levels.

Coadministration of metformin with BIC/FTC/TAF was well tolerated in these healthy individuals; all adverse events were Grade 1 or 2 in severity, and no adverse events led to study drug discontinuation.

BIC/FTC/TAF PK[1,3]

Table 2. BIC/FTC/TAF PK[1,3]

DDI Mechanism		BIC	FTC	TAF
Drug Transporters	OCT2	Inhibitor	N/A	N/A
	MATE1	Inhibitor	N/A	N/A
	P-gp/BCRP	N/A	N/A	Substrate
	OATP1B1	N/A	N/A	Substrate
	OATP1B3	N/A	N/A	Substrate
Drug Metabolizing Enzymes	CYP3A	Substrate[a]	N/A	Minor substrate
	UGT1A1	Substrate[a]	N/A	N/A

Abbreviations: BCRP=breast cancer resistance protein; OATP=organic anion transporting polypeptide; P-gp=p-glycoprotein; UGT1A1=uridine diphosphate glucourosyl transferase family 1 member A1.
[a]A drug that is a strong inducer of CYP3A and an inducer of UGT1A1 can substantially decrease the plasma concentrations of BIC. Similarly, the use of BIC/FTC/TAF with a drug that is a strong inhibitor of CYP3A and also an inhibitor of UGT1A1 may significantly increase the plasma concentrations of BIC.[1]

Retrospective Analysis[4]

A retrospective analysis verifying the clinical relevance of the PK DDI study was conducted in 20 patients with diabetes and HIV. Eligible patients were diagnosed with type 2 diabetes mellitus for ≥1 year, were on metformin therapy for ≥1 year, were receiving a BIC-based ARV regimen for ≥3 months, and had no changes in metformin dose after initiating the BIC-based ARV regimen. Glycemic control was analyzed before and after initiation of BIC using a paired t-test. Most patients were male (75%), Caucasian (95%), and were a mean age of 62 years. The mean (range) metformin dose was 1455 (500–3000 mg per day).

When comparing pre– and post–BIC initiation periods, there were no significant differences in fasting blood glucose (134 mg/dL vs 128 mg/dL, respectively; mean difference: -2.2%; *P*=0.311) or HbA1c (48 mmol/mol vs 50 mmol/mol, respectively; mean difference: +2%; *P*=0.907) when including all doses of metformin in the study. The same trends were observed in the subgroup of patients treated with >1000 mg of metformin daily (n=11). There were no instances of hypoglycemia or lactic acidosis after BIC was initiated.

Literature Search

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and September 4, 2025, using search terms that included Biktarvy, bictegravir, tenofovir alafenamide, emtricitabine, metformin, and other related search terms. No additional relevant citations were identified.

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Zhang H, West SK, Vu A, et al. Lack of Clinically Relevant Effect of Bictegravir on Metformin Pharmacokinetics and Pharmacodynamics [Poster 50]. Paper presented at: 18th International Workshop on Clinical Pharmacology of Antiviral Therapy (IWCPAT); 14-16 June, 2017; Chicago, IL.
3. Enclosed. Gilead Sciences Inc, DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U. S. Prescribing Information. Foster City, CA.
4. Cattaneo D, Formenti T, Minisci D, Casalini G, Meraviglia P, Gervasoni C. Lack of clinically relevant interactions between bictegravir and metformin in persons with diabetes and HIV. *J Antimicrob Chemother.* 2021.

Abbreviations

ARV=antiretroviral
AUC=area under the curve
BIC=bictegravir
DDI=drug-drug interaction
FTC=emtricitabine
MATE=multidrug and toxin extrusion protein
OCT=organic cation transporter
PK=pharmacokinetic(s)
TAF=tenofovir alafenamide

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Biktarvy and Descovy US Prescribing Information available at:
www.gilead.com/~/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi.

Follow Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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