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Biktarvy® (BIC/FTC/TAF) Use in Participants With HIV/HCV Co-Infection

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in participants with both HIV-1 and HCV.

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/liver-disease/epclusa/epclusa_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/harvoni/harvoni_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vosevi/vosevi_pi.

Summary

Product Labeling[1]

Based on drug interaction studies conducted with BIC/FTC/TAF or its components, no clinically significant drug interactions have been observed when BIC/FTC/TAF is combined with the following medications used for the treatment of HCV: LDV/SOF, SOF, SOF/VEL, and SOF/VEL/VOX.

Clinical Data on BIC/FTC/TAF Use in Participants With HIV-1 and HCV

- HCV co-infection had no clinically relevant effect on BIC or TAF exposure in PWH in a PK model evaluating the effect of HCV and HIV in participants treated with BIC/FTC/TAF daily.[2]
- In treatment-naïve participants with HIV and HCV, BIC/FTC/TAF was well tolerated, and no participants with HIV and HCV reported hepatic AEs over 96 weeks of treatment.[3]
- Two crossover studies demonstrated that coadministration of BIC/FTC/TAF with LDV/SOF or SOF/VEL/VOX did not cause any clinically relevant changes in the PK of any of the drug components.[4]

Clinical Data on BIC/FTC/TAF Use in Participants With HIV-1 and HCV

PK Model Study: Effect of Hepatitis on BIC and TAF[2]

A population-based PK model used pooled intensive and sparse plasma concentration data from eighteen phase 1 and phase 3 studies to evaluate the effect of covariates such as HCV on the exposure of BIC (n=1318) and TAF (n=1409) in participants treated with BIC/FTC/TAF once daily. The AUC_{τ}, C_{max}, and C_{τ} of BIC and the AUC_{τ} and C_{max} of TAF were used to measure the effect of the covariates. HCV had no clinically relevant effect on BIC or TAF exposure in PWH. Study authors concluded that HCV did not require dose adjustments of BIC or TAF.

Safety Analysis of BIC/FTC/TAF in Participants With HIV and HCV[3]

The hepatic safety profile of BIC/FTC/TAF in treatment-naïve participants in two phase 3, randomized, double-blind studies (Studies GS-US-380-1489 and GS-US-380-1490) was evaluated. Eligible participants had no resistance to FTC or TFV (Studies 1489 and 1490) or to abacavir or lamivudine (Study 1489). Eleven of the participants included in these two studies had both HIV and HCV; 5 participants had chronic HCV at baseline, and 6 participants had incident HCV. Two of the 5 participants with chronic HCV were treated during the study with LDV/SOF and SOF/VEL, respectively, and achieved sustained virologic response. BIC/FTC/TAF was well-tolerated, and no participants with both HIV and HCV reported hepatic AEs over 96 weeks of treatment.

Drug Interactions Between BIC/FTC/TAF and LDV/SOF or SOF/VEL/VOX[4]

Study design and demographics

Two crossover studies were performed to examine the safety and potential drug-drug interactions of the coadministration of BIC/FTC/TAF and LDV/SOF or SOF/VEL/VOX in healthy volunteers. Treatment was taken in a fed state, after a meal of approximately 600 kcal/27% fat. PK samples were collected over 24 hours on the 10th day of each treatment period, and safety was measured throughout the duration of the study.

Table 1. Baseline Demographics (Garrison et al)[4]

Key Demographics		Study 1 (N=30)	Study 2 (N=30)
Male, n (%)		20 (67)	19 (63)
Weight, mean (range), kg		76.1 (56.6–99.7)	75.4 (53–99)
Race, n (%)	White	15 (50)	17 (57)
	Black	15 (50)	12 (40)
	Other	0	1 (3)

Results

PK drug interactions

Coadministration of BIC/FTC/TAF with LDV/SOF or SOF/VEL/VOX did not cause any clinically relevant changes in the PK of any of the drug components. BIC/FTC/TAF and LDV/SOF coadministration led to a modest increase in TFV exposure (<2-fold), and coadministration of BIC/FTC/TAF and SOF/VEL/VOX led to modest increases in both TAF and TFV exposure (Table 2). With these observed increases, TFV exposures were 4- to 7-fold less than what was observed when LDF/SOF or SOF/VEL/VOX were coadministered with tenofovir disoproxil fumarate. The increases in TAF exposure were a result of increased TAF absorption and were not considered clinically meaningful. Coadministration of BIC/FTC/TAF with LDV/SOF or SOF/VEL/VOX did not affect the PK of SOF, GS-331007, LDV, VEL, or VOX (Table 3).

Table 2. Effect of HCV DAAs on BIC/FTC/TAF (Garrison et al)[4]

BIC, Mean (%CV)	BIC/FTC/TAF + SOF/VEL/VOX (n=30)		BIC/FTC/TAF 50/200/25 mg (n=30)		GMR (90% CI)	
AUC_T, h·ng/mL	128,000 (20)		120,000 (20)		107 (103–110)	
C_{max}, ng/mL	8270 (15)		8530 (20)		98 (94–101)	
C_T, ng/mL	3570 (31)		3220 (30)		111 (105–117)	
BIC, Mean (% CV)	**BIC/FTC/TAF + LDV/SOF (n=30)**		**BIC/FTC/TAF 75/200/25 mg (n=30)**		**GMR (90% CI)**	
AUC_T, h·ng/mL	189,000 (21)		188,000 (19)		100 (97–103)	
C_{max}, ng/mL	13,300 (15)		13,600 (17)		98 (94–103)	
C_T, ng/mL	5190 (29)		4990 (30)		104 (99–109)	
FTC, Mean (% CV)	**BIC/FTC/TAF + SOF/VEL/VOX (n=30)**		**BIC/FTC/TAF 50/200/25 mg (n=30)**		**GMR (90% CI)**	
AUC_T, h·ng/mL	9440 (14)		9920 (12)		95 (93–97)	
C_{max}, ng/mL	1630 (26)		1830 (22)		89 (83–94)	
C_T, ng/mL	71 (22)		64 (21)		110 (105–116)	
FTC, Mean (% CV)	**BIC/FTC/TAF + LDV/SOF (n=30)**		**BIC/FTC/TAF 75/200/25 mg (n=30)**		**GMR (90% CI)**	
AUC_T, h·ng/mL	11,300 (15)		11,500 (20)		99 (96–102)	
C_{max}, ng/mL	2040 (27)		2010 (15)		99 (94–105)	
C_T, ng/mL	75 (19)		73 (22)		103 (99–107)	
TAF/TFV, Mean (% CV)	**BIC/FTC/TAF + SOF/VEL/VOX (n=30)**		**BIC/FTC/TAF 50/200/25 mg (n=30)**		**GMR (90% CI)**	
	TAF	**TFV**	**TAF**	**TFV**	**TAF**	**TFV**
AUC_T, h·ng/mL	443 (38)[a]	480 (20)	282 (36)[a]	287 (20)	157 (144–171)	167 (162–173)
C_{max}, ng/mL	280 (61)	27 (21)	217 (48)	18 (22)	128 (109–151)	151 (145–158)
C_T, ng/mL	—	17 (22)	—	10 (23)	—	174 (168–180)

TAF/TFV, Mean (% CV)	BIC/FTC/TAF + LDV/SOF (n=30)		BIC/FTC/TAF 75/200/25 mg (n=30)		GMR (90% CI)	
	TAF	TFV	TAF	TFV	TAF	TFV
AUC_T, h·ng/mL	430 (29)	475 (21)	343 (34)	284 (21)	127 (119–134)	167 (160–174)
C_{max}, ng/mL	305 (46)	26 (20)	262 (50)	18 (20)	117 (100–138)	143 (137–150)
C_T, ng/mL	—	17 (24)	—	9 (21)	—	181 (173–190)

[a]AUC from time 0 to last measurable concentration.

Table 3. Effect of BIC/FTC/TAF on HCV DAAs (Garrison et al)[4]

LDV, Mean (% CV)	BIC/FTC/TAF + LDV/SOF (n=30)		LDV/SOF (n=30)		GMR (90% CI)	
AUC_T, h·ng/mL	10,200 (35)		11,500 (29)		87 (83–92)	
C_{max}, ng/mL	567 (31)		656 (25)		85 (81–90)	
C_T, ng/mL	365 (39)		401 (34)		90 (84–96)	
VEL, Mean (% CV)	**BIC/FTC/TAF + SOF/VEL/VOX (n=30)**		**SOF/VEL/VOX (n=30)**		**GMR (90% CI)**	
AUC_T, h·ng/mL	7710 (36)		8050 (34)		96 (90–102)	
C_{max}, ng/mL	898 (32)		937 (30)		96 (91–101)	
C_T, ng/mL	138 (53)		144 (47)		94 (88–101)	
VOX, Mean (% CV)	**BIC/FTC/TAF + SOF/VEL/VOX (n=30)**		**SOF/VEL/VOX (n=30)**		**GMR (90% CI)**	
AUC_T, h·ng/mL	4460 (66)		4820 (61)		91 (80–103)	
C_{max}, ng/mL	880 (69)		929 (56)		90 (76–106)	
C_T, ng/mL	28 (71)		28 (57)		97 (88–106)	
SOF/GS-331007, Mean (% CV)	**BIC/FTC/TAF + LDV/SOF (n=30)**		**LDV/SOF (n=30)**		**GMR (90% CI)**	
	SOF	GS-331007	SOF	GS-331007	SOF	GS-331007
AUC_T, h·ng/mL	3170 (24)	11,600 (17)	2970 (25)	10,400 (15)	107 (101–113)	111 (108–114)
C_{max}, ng/mL	1910 (37)	904 (18)	1700 (38)	822 (18)	111 (101–124)	110 (107–113)
C_T, ng/mL	—	316 (21)	—	308 (18)	—	102 (99–106)
SOF/GS-331007, Mean (% CV)	**BIC/FTC/TAF + SOF/VEL/VOX (n=30)**		**SOF/VEL/VOX (n=30)**		**GMR (90% CI)**	
	SOF	GS-331007	SOF	GS-331007	SOF	GS-331007
AUC_T, h·ng/mL	3450 (28)	11,200 (16)	3130 (23)	10,800 (17)	109 (102–115)	103 (100–106)
C_{max}, ng/mL	1870 (48)	852 (16)	1570 (33)	832 (17)	114 (104–125)	103 (100–106)
C_T, ng/mL	—	308 (21)	—	303 (20)	—	101 (98–105)

Safety

Twenty-eight percent of healthy volunteers (17/60) included in the two studies reported AEs. There were no Grade 3 or 4 or serious AEs reported with BIC/FTC/TAF and LDV/SOF or SOF/VEL/VOX coadministration, and no participant discontinued treatment due to AEs. The only AE commonly reported (≥5%) in both studies was headache (10%, 6/60 healthy volunteers). Grade 3 hematuria was reported in 2 healthy volunteers with confirmed menses. All other laboratory abnormalities were Grade 1 or 2.

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Lutz JD, Kirby BJ, Shao Y, Gao Y, Quirk E, Mathias A. No Clinically Relevant Effect of Patient Demographic or Disease Covariates on the Exposures of Bictegravir and Tenofovir Alafenamide Following Administration of a B/F/TAF Single-Tablet Regimen to HIV-1–Infected Patients [Poster P262]. Paper presented at: HIV Drug Therapy/Glasgow 2018; 28-31 October, 2018; Glasgow, UK.
3. Johnson M, Taylor S, Wei X, Collins SE, Martin H. Hepatic Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide [Presentation]. Paper presented at: 25th Annual Conference of the British HIV Association; 02-05 April, 2019; Bournemouth, UK.
4. Garrison KL, Humeniuk R, West SK, et al. Lack of Clinically Relevant Drug Interactions Between Bictegravir/Emtricitabine/Tenofovir Alafenamide and Ledipasvir/Sofosbuvir or Sofosbuvir/Velpatasvir/Voxilaprevir [Poster P264]. Paper presented at: HIV Drug Therapy/Glasgow 2018; 28-31 October, 2018; Glasgow, UK.

Abbreviations

AE=adverse event
AUC_T=area under the concentration-time curve over the dosing interval
BIC=bictegravir
C_{max}=maximum plasma concentration
C_T=concentration at the end of the dosing interval
CV=coefficient of variation
DAA=direct-acting antiviral
FTC=emtricitabine
GMR=geometric least-squares mean ratio
GS-331007=predominant circulating nucleoside metabolite of SOF
LDV=ledipasvir
PK=pharmacokinetic(s)
PWH=people with HIV
TAF=tenofovir alafenamide
TFV=tenofovir
SOF=sofosbuvir
VEL=velpatasvir
VOX=voxilaprevir

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Biktarvy, Epclusa, Harvoni, and Vosevi US Prescribing Information available at: www.gilead.com/~/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi; www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi; www.gilead.com/-/media/files/pdfs/medicines/liver-disease/harvoni/harvoni_pi; www.gilead.com/-/media/files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi; www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vosevi/vosevi_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 🖱 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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