GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Use for HIV-1 Post-Exposure Prophylaxis

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) for HIV-1 post-exposure prophylaxis (PEP). This document includes content from, or references to, clinical practice guidelines, and inclusion should not be interpreted as a treatment recommendation or an endorsement of the guidelines by Gilead Sciences, Inc.

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.

Summary

Product Labeling[1]

BIC/FTC/TAF is not indicated for use for HIV-1 PEP.

BIC/FTC/TAF is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥14 kg:

- with no ARV treatment history or
- with an ARV treatment history and not virologically suppressed, with no known or suspected substitutions associated with resistance to the integrase strand inhibitor class, FTC, or TFV, or
- to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable ARV regimen with no known or suspected substitutions associated with resistance to BIC or TFV.

Clinical Data on BIC/FTC/TAF Use for PEP

- In a prospective, open-label cohort study that evaluated the adherence, effectiveness, and tolerability of BIC/FTC/TAF or TDF/FTC + DTG as HIV PEP (N=179), 97.8% (90/92) in the BIC/FTC/TAF group and 86.2% (75/87) in the TDF/FTC + DTG group completed 28 days of PEP (*P*=0.009). No HIV seroconversions occurred through follow-up Week 12. ADRs were reported in 15.2% of participants in the BIC/FTC/TAF group and in 10.3% of participants in the TDF/FTC + DTG group; all were Grade 1 to 2 in severity.[2]
- In a randomized controlled trial that evaluated the tolerability and adherence to 28 days of BIC/FTC/TAF as HIV PEP with text message support vs standard of care (N=119), 90/102 participants (88%) with available data completed ≥28 days of PEP. No HIV seroconversions occurred among the 66 participants tested at Week 12. AEs associated with BIC/FTC/TAF were mostly mild, and the most common AEs included fatigue (20%), nausea (12%), diarrhea (8%), and headache (8%).[3]
- In a single-arm, open-label trial that evaluated the safety, tolerability, and adherence to BIC/FTC/TAF for prophylaxis following potential HIV-1 exposure (N=112), 96.4% of

participants completed the 28-day PEP regimen, with 98.9% adherence. There were no HIV seroconversions through 24 weeks. AEs attributed to BIC/FTC/TAF were mild and included headache (n=2), diarrhea (n=2), and nausea (n=1).[4]

- In a non-randomized, open-label trial that evaluated the safety, tolerability, and acceptability of BIC/FTC/TAF for prophylaxis following potential exposure to HIV-1 (N=52), 90.4% of participants completed the 28-day course of BIC/FTC/TAF with no HIV seroconversions when tested at Week 4 or at the 3-month interview. Most AEs were Grade 1 and included vomiting (15.4%), fatigue (9.6%), and diarrhea (7.7%).[5]

Clinical Data on BIC/FTC/TAF Use for PEP

Prospective Cohort Study of BIC/FTC/TAF vs TDF/FTC + DTG as HIV PEP[2]

Study design and demographics

A prospective, single-center, open-label cohort study evaluated the adherence, effectiveness, and tolerability of BIC/FTC/TAF and TDF/FTC + DTG as HIV PEP (N=179) initiated within 72 hours of screening in adults without HIV following a potential HIV exposure. Participants with HBV were excluded. Treatment was assigned based on participant choice. The primary endpoint was completion of the 28 days of PEP. Secondary endpoints included adherence and HIV seroconversion at Weeks 4 and 12. Baseline demographics are provided in Table 1.

Table 1. Select Baseline Demographics and Characteristics (Gan et al)[2]

Key Demographics and Characteristics		BIC/FTC/TAF (n=92)	TDF/FTC + DTG (n=87)
Age, median (IQR), years		27.5 (25–34)	31 (26–37)
Male, n (%)		80 (86.9)	78 (89.7)
Type of exposure, n (%)	Vaginal intercourse	71 (77.2)	66 (75.9)
	Anal sex	17 (18.5)	18 (20.7)
	Oral sex	4 (4.3)	3 (3.4)
Time from exposure, median (IQR), hours		17 (12–33.2)	17 (12–34)
<24 hours, n (%)		58 (63)	59 (67.8)
24–47.9 hours, n (%)		26 (28.3)	14 (16.1)
48–72 hours, n (%)		8 (8.7)	14 (16.1)
Previously used PEP, n (%)		4 (4.3)	2 (2.3)

Results

The rate of PEP completion was 97.8% (90/92) in the BIC/FTC/TAF group and 86.2% (75/87) in the TDF/FTC + DTG group (*P*=0.009), and the adherence rates were 99.6±2.82% and 90.2±25.29%, respectively (*P*=0.003). A multivariable logistic regression model that adjusted for confounding variables found that the only assessed factor associated with incomplete PEP adherence was TDF/FTC + DTG use (adjusted odds ratio, 7.02; 95% CI: 1.82–46.29; *P*<0.05). No HIV seroconversions occurred through follow-up Week 12. ADRs were reported in 15.2% of participants in the BIC/FTC/TAF group and in 10.3% of participants in the TDF/FTC + DTG group; all were Grade 1 to 2 in severity. The most common ADRs were dyslipidemia (5.4%), hepatic function abnormalities (2.2%), increased blood uric acid levels (2.2%), and elevated serum creatinine levels (2.2%) in the

BIC/FTC/TAF group and dyslipidemia and increased blood uric acid levels (each, 3.4%) in the TDF/FTC + DTG group. One participant (1.1%) in the TDF/FTC + DTG group discontinued PEP due to a drug-related ADR of dizziness.

Tolerability and Adherence to BIC/FTC/TAF as HIV PEP[3]

Study design and demographics

A randomized controlled trial evaluated the tolerability and adherence to BIC/FTC/TAF as HIV PEP with text message support vs standard of care in HIV-negative adult participants who initiate PEP within the prior 6 days for sexual exposure. This was a switch study in which participants were randomized to switch to BIC/FTC/TAF to complete the remainder of the 28-day PEP regimen (median 2 days on PEP before switch). HIV status was assessed at baseline, Week 6, and Week 12. Additional outcomes included adherence, assessed via telephone call at Week 4, and AEs, assessed at Week 4 and Week 13 follow-up visits. A total of 120 participants enrolled in the trial; 1 participant was HIV seropositive at baseline and was not included in the analysis. Baseline demographics are listed in Table 2.

Table 2. Select Baseline Demographics and Characteristics (Tan et al)[3]

Key Demographics and Characteristics		BIC/FTC/TAF (N=119)
Age, median (Q1, Q3), years		29.3 (25.8–34.4)
Sexual orientation and gender, n (%)	MSM	97 (81)
	Heterosexual men	16 (13)
	Heterosexual women	7 (6)
Type of condomless exposure,[a] n (%)	Anal insertive	40 (34)
	Anal receptive with ejaculation	36 (30)
	Anal receptive without ejaculation	21 (18)
	Vaginal insertive	15 (13)
	Vaginal receptive with ejaculation	4 (3)
	Vaginal receptive without ejaculation	3 (3)
Previously used PEP, n (%)	0	91 (77)
	1	24 (20)
	2	4 (3)
Initially prescribed PEP regimen, %	DTG + TDF/FTC	106 (89)
	BIC/FTC/TAF	11 (9)
	RAL + TDF/FTC	2 (2)
Time from exposure to PEP initiation, median (Q1, Q3), hours		23 (13, 39)

Abbreviations: MSM=men who have sex with men; Q=quartile; RAL=raltegravir.
[a]Report included the highest-risk type of sexual exposure.

Results

A total of 90 of the 102 participants (88%) with available data reported completing ≥28 days of PEP. No HIV seroconversions occurred among the 66 participants (55%) who were tested at Week 12. By the final visit, 28 participants (23%) had initiated PrEP. AEs associated with the study drug were mostly mild, and the most common AEs included fatigue (20%), nausea (12%), diarrhea (8%), and headache (8%). Only 10% of participants experienced AEs of Grade ≥2 severity, which included diarrhea (3%) and fatigue (2%).

Prospective Study of BIC/FTC/TAF as HIV-1 PEP[4]

Study design and demographics

A prospective, single-arm, open-label, single-site study evaluated the safety, tolerability, and adherence to BIC/FTC/TAF in adult participants (N=112) who initiated prophylaxis within 72 hours of potential HIV-1 exposure. Participants were instructed to take one BIC/FTC/TAF tablet once daily for 28 days. Participants were assessed with laboratory tests at baseline and 2, 4, 12, and 24 weeks; tests included serologies, biochemistry, liver function tests, glucose, and lipids. HIV RNA was tested to exclude participants with acute-stage HIV. Endpoints included HIV diagnosis, completion of PEP, and PEP adherence via self-reports and pill counts.

The mean age of participants was 30 ±8 years and the majority of participants were male (97.3%). The type of HIV exposure included anal sex (51.8%), vaginal intercourse (38.4%) and oral sex (25.9%). The mean time from exposure was 27.5 ± 18.8 hours, with 48.2% of individuals exposed within ≤24 hours (n=54), 40.2% within 25–48 hours (n=45), and 11.6% within 49–72 hours (n=13).

Results

Through 24 weeks, there were no HIV seroconversions. Most participants (96.4%) completed the 28-day PEP regimen, with an adherence rate to all expected doses of 98.9% by self-report and 98.5% by pill count. Two participants did not complete the PEP regimen because the source partner was found to be HIV negative; 1 participant was excluded due to HBV; and 1 participant discontinued due to their own decision. AEs attributed to study drug were mild and included headache (n=2), diarrhea (n=2), and nausea (n=1), all of which resolved on their own without discontinuation of BIC/FTC/TAF. Laboratory abnormalities included Grade 1 elevation of SCr level in 4 participants.

Single-Arm Trial of BIC/FTC/TAF as nPEP[5]

Study design and demographics

A single-site, open-label, single-arm trial evaluated the safety, tolerability, and acceptability of BIC/FTC/TAF for prophylaxis initiated within 72 hours of potential non-occupational exposure to HIV-1. The study enrolled 52 participants without HIV with possible high-risk sexual exposure to HIV-1. Participants were instructed to take one BIC/FTC/TAF tablet once a day for 28 days. Participants were assessed at 2 and 4 weeks and at 3 months. The primary endpoints were nPEP failure, as measured with HIV seroconversion during study participation, and safety and tolerability of BIC/FTC/TAF.

The median age of participants was 37.2 years. Reasons for initiating nPEP included having oral intercourse (57.7%), condomless receptive anal intercourse (51.9%), insertive anal intercourse (42.3%), and insertive or receptive vaginal intercourse (5.8% for each). Over half of participants (55.8%) reported ≥1 potential exposure, and 15.4% reported having unprotected intercourse with a partner known to be HIV positive.

Results

Most participants (90.4%) completed the 28-day BIC/FTC/TAF course with no HIV seroconversions detected when tested at Week 4 or at the 3-month interview.
Five participants were lost to follow-up.

The most commonly reported AEs included nausea with or without vomiting (15.4%), fatigue (9.6%), and diarrhea (7.7%). All AEs were Grade 1, except for a single report of Grade 2 fatigue, which was associated with discontinuation of BIC/FTC/TAF. Laboratory abnormalities were observed in 9 participants: 7 had decreased CrCl, including 4 with Grade 2 decreased CrCl, and 2 had Grade 1 increased transaminases. All laboratory abnormalities returned to normal upon completion of the BIC/FTC/TAF course.

BVY for PEP Clinical Practice Guidelines

The Centers for Disease Control and Prevention clinical practice guidelines of occupational and non-occupational PEP for the prevention of HIV infection in the US can be accessed at: https://www.cdc.gov/hivpartners/php/guidelines/.

Guidelines from the World Health Organization for HIV prevention, testing, treatment, service delivery and monitoring can be accessed at: www.who.int/publications/i/item/9789240031593.

The European AIDS Clinical Society produces guidelines for the management of treatment and prevention of HIV in Europe, which can be accessed at: www.eacsociety.org/guidelines/eacs-guidelines.

Additionally, guidelines from the International Antiviral Society-USA Panel on antiretroviral drugs for the prevention and treatment of HIV in adults can be accessed at: www.iasusa.org/guidelines.

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Gan L, Xie X, Fu Y, et al. Safety and adherence of bictegravir/emtricitabine/tenofovir alafenamide for HIV post-exposure prophylaxis among adults in Guiyang China: a prospective cohort study. *BMC Infect Dis.* 2024;24(1):565.
3. Tan DHS, Persaud R, Qamar A, et al. BIC/FTC/TAF as HIV PEP Was Well-Tolerated With High Adherence and No Seroconversions. [Poster 1134]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 3-6, 2024; Denver, Colorado.
4. Liu A, Xin R, Zhang H, et al. An open-label evaluation of safety and tolerability of coformulated bictegravir/emtricitabine/tenofovir alafenamide for post-exposure prophylaxis following potential exposure to human immunodeficiency virus-1. *Chinese Medical Journal.* 2022;135(22):2725-2729. https://www.ncbi.nlm.nih.gov/pubmed/36719359
5. Mayer K. H, Gelman M, Holmes J, Kraft J, Melbourne K, Mimiaga M. J. Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure. *J Acquir Immune Defic Syndr.* 2022;90(1):27-32.

Abbreviations

ADR=adverse drug reaction
AE=adverse event
ARV=antiretroviral
BIC=bictegravir
DTG=dolutegravir
FTC=emtricitabine
nPEP=non-occupational post-exposure prophylaxis
PEP=post-exposure prophylaxis
PrEP=pre-exposure prophylaxis
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Biktarvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_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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