Biktarvy® (BIC/FTC/TAF) Crushing, Dissolving, or Splitting of Tablets

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) and the crushing, dissolving, or splitting of tablets.

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]

In adults and pediatric patients weighing ≥25 kg with an estimated CrCl ≥30 mL/min, or virologically suppressed adults with an estimated CrCl <15 mL/min who are receiving chronic hemodialysis, the recommended dosage of BIC/FTC/TAF is one tablet containing 50 mg of BIC, 200 mg of FTC, and 25 mg of TAF taken orally once daily with or without food.

In pediatric patients weighing ≥14 kg to <25 kg with an estimated CrCl ≥30 mL/min, the recommended dosage of BIC/FTC/TAF is one tablet containing 30 mg of BIC, 120 mg of FTC, and 15 mg of TAF taken orally once daily with or without food. For children unable to swallow a whole tablet, the tablet can be split and each part taken separately as long as all parts are ingested within approximately 10 minutes.

In regard to the individual components of BIC/FTC/TAF, BIC has a solubility of 0.1 mg/mL in water at 20°C, FTC has a solubility of approximately 112 mg/mL in water at 25°C, and TAF has a solubility of 4.7 mg/mL in water at 20°C.

Real-World Data on Crushing or Dissolving BIC/FTC/TAF

A retrospective, multicenter study assessed whether crushed or dissolved BIC/FTC/TAF was effective at maintaining or achieving virologic suppression in hospitalized PWH who required an enteral route of medication administration (N=19). Within 1 year of receiving ≥1 week of crushed or dissolved BIC/FTC/TAF, 17 patients (89%) were virologically suppressed, and no treatment-emergent resistance was reported.[2]

PK Data on Crushing or Dissolving BIC/FTC/TAF

A phase 1 crossover study evaluated the bioavailability of crushed or dissolved BIC/FTC/TAF compared with solid BIC/FTC/TAF in HIV-negative, healthy adult volunteers (N=18). After fasting, volunteers received BIC/FTC/TAF dissolved in water, crushed in applesauce, and as a solid tablet in random sequence.[3]

- Dissolved BIC/FTC/TAF was considered equivalent to the solid tablet for all PK parameters evaluated, with the exception of the C_{max} for TAF.
- The $AUC_{0-\infty}$ for the crushed tablet was equivalent to that of the solid tablet for BIC and FTC, but not TAF. The C_{max} for the crushed tablet was not equivalent to that of the solid tablet for FTC or TAF but was equivalent for BIC.
- Twenty-eight percent of volunteers (5/18) experienced ≥1 AE, and no AEs led to BIC/FTC/TAF discontinuation.

Case Reports on Crushing or Dissolving BIC/FTC/TAF

Case reports involving the use of crushed or dissolved BIC/FTC/TAF are summarized below.[4-9]

Real-World Data on Crushing or Dissolving BIC/FTC/TAF

Retrospective Study in PWH[2]

Study design and demographics

A retrospective cohort study assessed whether crushed or dissolved BIC/FTC/TAF was effective at maintaining or achieving virologic suppression in hospitalized PWH who required an enteral route of medication administration (N=19). The analysis included patients who had received crushed or dissolved BIC/FTC/TAF at Massachusetts General Hospital or Brigham and Women's Hospital between February 2018 and December 2023 for ≥1 week and had a VL assessment within 1 year of treatment. The primary endpoint was virologic suppression (VL <200 copies/mL) within 1 year of treatment. Secondary endpoints included treatment-emergent resistance and changes in ART regimens.

Table 1. Baseline Demographics and Disease Characteristics (Mercure et al)[2]

Key Demographics and Characteristics	BIC/FTC/TAF (N=19)
Age, median (IQR), years	54 (47.5–66.5)
Male, n (%)	16 (84)
Virologically suppressed or had an undetectable VL, n (%)	11 (58)
Resistance at baseline,[a] n (%)	8 (42)
Administered crushed/dissolved BIC/FTC/TAF, n (%)	8 (42)/ 2 (11)

Abbreviations: INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor; NRTI=nucleos(t)ide reverse transcriptase inhibitor; PI=protease inhibitor.
[a]NRTI, n=5 (26%); NNRTI, n=4 (21%); PI, n=4 (21%); INSTI, n=0.

Results

The median (IQR) duration of treatment with crushed or dissolved BIC/FTC/TAF was 19 (7.5–64) days. At least one dose was missed in 6 patients (32%). Within 1 year of receiving crushed or dissolved BIC/FTC/TAF, 17 patients (89%) maintained or achieved virologically suppression, including 6 of the 8 patients with detectable VLs at hospital admission; the 2 patients who did not achieve virologic suppression had marked reductions in VLs. No treatment-emergent resistance was reported, and 2 patients had changes to their ART regimen during hospitalization: to limit DDIs with rifampin for tuberculosis treatment and to address ongoing DDI concerns in the setting of central nervous system escape

(each, n=1). Three patients continued to receive crushed or dissolved BIC/FTC/TAF after discharge.

Eight deaths were reported: non-HIV–related infection, n=5; opportunistic infections associated with HIV, n=2; and hemorrhagic stroke, n=1. No deaths were deemed related to the administration of crushed or dissolved BIC/FTC/TAF.

PK Data on Crushing or Dissolving BIC/FTC/TAF

SOLUBIC Study in HIV-Negative Volunteers

Study design and demographics

A phase 1, open-label, single-dose, three-period crossover study evaluated the bioavailability of crushed or dissolved BIC/FTC/TAF compared with that of a solid tablet in HIV-negative, healthy adult volunteers (N=18). After fasting, all healthy volunteers received BIC/FTC/TAF dissolved in water, crushed in applesauce, and as a solid tablet in random sequence separated by a washout period of 14 to 28 days. Plasma concentrations were collected before dosing and through 72 hours following the administration of each dose.[3] The primary endpoints of the study were AUC ($AUC_{0-\infty}$ for BIC and FTC; $AUC_{0\text{-last}}$ for TAF, due to its short $t_{1/2}$) and C_{max} of each of the three components to determine the bioequivalence of the dissolved or crushed tablets with the whole tablet.[3,10] Bioequivalence was met if the 90% CI of the geometric least squares mean ratios of AUC and C_{max} for the dissolved or crushed tablets were within 80% to 125% of the whole tablet. Secondary endpoints included assessments of safety and tolerability. All volunteers were White, and 9 volunteers were female; the median age was 30 years, and the median BMI was 21 kg/m^2.[3]

Results[3]

The AUC for dissolved BIC/FTC/TAF was equivalent to that of the solid tablet for all individual components ($AUC_{0-\infty}$ for BIC and FTC; $AUC_{0\text{-last}}$ for TAF). The C_{max} for dissolved BIC/FTC/TAF was considered equivalent to that of the solid tablet for BIC and FTC, but not for TAF. The $AUC_{0-\infty}$ for the crushed tablet showed equivalence to the solid tablet for BIC and FTC, but not for TAF. The C_{max} for the crushed tablet showed equivalence to the solid tablet for BIC, but not for FTC and TAF (Table 2).

Table 2. PK Parameters of BIC, FTC, and TAF According to Administration Modality (Hocqueloux et al)[3]

Drug	PK Parameter	Solid Tablet	Dissolved Tablet	Crushed Tablet	Dissolved: Solid, % (90% CI)	Crushed: Solid, % (90% CI)
BIC	$AUC_{0-\infty}$, GM (CV), h·mg/L	107.9 (39)	119.4 (31)	115 (36)	111 (100–122)	107 (96–118)
	C_{max}, GM (CV), mg/L	5 (42)	5.2 (62)	5.5 (84)	105 (93–119)	110 (97–124)
	T_{max}, median (range), h	2.3 (0.5–4)	2.5 (0.5–4)	2 (0.5–8)	–	–
	$t_{1/2}$, GM (CV), h	19.1 (20)	18.2 (18)	19.1 (25)	–	–

Drug	PK Parameter	Solid Tablet	Dissolved Tablet	Crushed Tablet	Dissolved: Solid, % (90% CI)	Crushed: Solid, % (90% CI)
FTC	$AUC_{0-\infty}$, GM (CV), h·mg/L	10.5 (18)	10.5 (20)	9.1 (19)	100 (94–105)	86 (82–91)
	C_{max}, GM (CV), mg/L	2 (24)	2 (38)	1.4 (27)	97 (87–108)	70 (63–78)
	T_{max}, median (range), h	1.5 (1–2.5)	1.5 (0.5–2.5)	2 (1–3)	–	–
	$t_{1/2}$, GM (CV), h	14.2 (46)	14.4 (65)	19.2 (45)	–	–
TAF	AUC_{0-last}, GM (CV), h·mg/L	0.053 (98)	0.053 (102)	0.047 (91)	99 (81–120)	84 (69–103)
	C_{max}, GM (CV), mg/L	0.065 (130)	0.062 (133)	0.043 (116)	96 (74–124)	66 (51–85)
	T_{max}, median (range), h	1 (0.5–2)	0.5 (0.5–1)	0.5 (0.5–2)	–	–
	$t_{1/2}$, GM (CV), h	0.415 (180)	0.383 (55)	0.458 (45)	–	–

Abbreviations: CV=coefficient of variation; GM=geometric mean; T_{max}=time at which the maximum concentration is observed.

The authors concluded that in cases where the BIC/FTC/TAF tablet cannot be swallowed in solid form, the tablet should be dissolved in water and taken immediately, rather than crushed. Overall, 28% of volunteers (5/18) experienced ≥1 AE. No AEs led to BIC/FTC/TAF discontinuation. Solid and crushed tablets were rated significantly easier to swallow compared with dissolved tablets (P<0.005), and crushed and dissolved tablets were rated significantly worse than whole tablets in terms of taste (P<0.001).

Case Reports on Crushing or Dissolving BIC/FTC/TAF

There are limitations in the interpretation of case reports. Case reports cannot be generalized. Unlike controlled clinical trials, causality cannot be inferred based on uncontrolled observational data. Additionally, incidence or prevalence cannot be estimated due to the lack of a representative population sample. Other limitations of case reports include the retrospective design and publication bias.[11]

Several case reports have described the administration of crushed or dissolved BIC/FTC/TAF, with durations ranging from 1 to 12 months. In 4 patients, including 1 pediatric patient, HIV-1 VLs remained undetectable after receiving courses of crushed or dissolved tablets. Two other patients with high initial VLs and complex comorbidities achieved virologic suppression after switching from BIC/FTC/TAF to another antiretroviral regimen.[4-9]

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Mercure J, Bey K, Gillett E, Pearson JC, McCluskey SM, Rock AE. Evaluating the Efficacy of Crushed Bictegravir/Emtricitabine/Tenofovir Alafenamide Administered via Tube. *Open Forum Infect Dis.* 2025;12(10):ofaf588.
3. Hocqueloux L, Lefeuvre S, Bois J, et al. Bioavailability of dissolved and crushed single tablets of bictegravir, emtricitabine, tenofovir alafenamide in healthy adults: the SOLUBIC randomized crossover study. *J Antimicrob Chemother.* 2022;78(1):161-168.

4. Roa PE, Bazzi R. Crushed bictegravir/emtricitabine/tenofovir alafenamide in a human immunodeficiency virus-positive patient with pancreatic cancer. *Int J STD AIDS.* 2022;33(1):97-98.
5. Fulco PP. Crushed bictegravir/emtricitabine/tenofovir alafenamide in a human immunodeficiency virus-positive patient with esophageal cancer. *Am J Health Syst Pharm.* 2020;77(7):509-510.
6. Ferrandez JS, Garcia AL, Alonso-Vega GG, Gonzalez AO, Garcia TM. Successful Bictegravir/Emtricitabine/Tenofovir Alafenamide Treatment in a HIV Patient With Swallowing Difficulties. *Ann Pharmacother.* 2020;55(4):556-557.
7. Rowe SM, Clary JC, Drummond M, Derrick C, Sanasi K, Bookstaver PB. Increased viral load in a hospitalized patient on treatment with crushed bictegravir/emtricitabine/tenofovir alafenamide: A case report and review of the literature. *Am J Health Syst Pharm.* 2022;79(16):1330-1336.
8. Lozano AB, Chueca N, de Salazar A, et al. Failure to Biktarvy® and Development of Resistance Mutations in an Antiretroviral Experienced Patient [Journal Pre-Proof]. *Antiviral Res.* 2020. https://www.ncbi.nlm.nih.gov/pubmed/31982483
9. Grant MJ. Dissolved Bictegravir/Emtricitabine/Tenofovir Alafenamide Improves Medication Adherence. *J Pediatr Health Care.* 2025;39(5):811-813.
10. Hocqueloux L, Lefeuvre S, Bois J, et al. Bioavailability of Solid vs. Dissolved vs. Crushed Single-Tablet of Bictegravir / Emtricitabine / Tenofovir Alafenamide in HIV Negative Volunteers: the SOLUBIC Study [Poster]. Paper presented at: 18th European AIDS Conference; 27-30 October, 2021; Online & London, United Kingdom.
11. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC Res Notes.* 2014;7:264.

Abbreviations

AE=adverse event
ART=antiretroviral therapy
AUC=area under the concentration-time curve
$AUC_{0-\infty}$=area under the concentration-time curve from time 0 extrapolated to infinite time
AUC_{0-last}=area under the concentration-time curve from time 0 to the time of the last quantifiable concentration after dosing
BIC=bictegravir
C_{max}=maximum concentration
DDI=drug-drug interaction
FTC=emtricitabine
PK=pharmacokinetic(s)
PWH=people with HIV
$t_{1/2}$=elimination half-life
TAF=tenofovir alafenamide
VL=viral load

Product Label

For the full indication, important safety information, and boxed warning(s), 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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.