Genvoya® (E/C/F/TAF) Crushing or Splitting of Tablets

This document is in response to your request for information regarding the crushing or splitting of the oral single-tablet regimen Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide [E/C/F/TAF]).

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/genvoya/genvoya_pi.

Product Labeling[1]

There is no information in the E/C/F/TAF product label about the crushing or splitting of E/C/F/TAF; therefore, it is not recommended that E/C/F/TAF be administered as a crushed or split tablet.

Description

In regard to the individual components of E/C/F/TAF, EVG has a solubility of <0.3 mcg/mL in water at 20°C, COBI 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.

Available Data on Crushing or Splitting E/C/F/TAF

Gilead Data

Crushing E/C/F/TAF tablets and adding to a liquid medium has not been studied and is not recommended. TAF is soluble in water; however, it has a bitter and burnt aromatic flavor profile.[2]

Similarly, splitting E/C/F/TAF tablets has not been studied and is not recommended. Currently, there are no studies evaluating the PK of a split E/C/F/TAF tablet vs a whole tablet.

Non-Gilead Data

A literature search was conducted in Ovid MEDLINE, BIOSIS Previews, and Embase databases for studies published between 1946 and January 07, 2026, using the search terms Genvoya, elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide, and cutting,

crushing, splitting tablets and related search terms. The information presented below was found.

Whole vs dissolved E/C/F/TAF tablets[3]

A within-subject, fixed-order, two-period, open-label bioequivalence study assessed the PK of EVG, FTC, TAF, and TFV components of E/C/F/TAF tablets administered as a whole tablet or a single tablet dissolved in tap water. A total of 12 participants who tested negative for HIV were included in the study. Participants fasted overnight, ate a standardized meal (400 kcal, 20% fat), and received a single-dose whole tablet of E/C/F/TAF at least 30 minutes after starting the meal and not more than 10 minutes after finishing the meal. Plasma PK sampling was conducted prior to dosing and over the next 3 days at 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 8, 10, 14, 24, 48, and 72 hours after the study drug dose was taken. Participants had a safety visit at Day 8, and there was at least a 14-day washout period before beginning the next period. The same sequence and plasma PK sampling schedule were followed in the second period, in which the tablet was dissolved for at least 5 minutes in 60 mL room temperature tap water with gentle stirring. After swallowing the E/C/F/TAF dissolved in water, participants drank another 60 mL of tap water.

Bioequivalence was demonstrated if the 90% CI of the GMRs (dissolved/whole tablets) for $AUC_{0-\infty}$ and C_{max} were between 80 and 125%. When $AUC_{0-\infty}$ and C_{max} levels after taking whole tablets were compared with those after taking dissolved E/C/F/TAF tablets, FTC met the bioequivalence criteria for both $AUC_{0-\infty}$ and C_{max}, TAF did not meet the bioequivalence criteria for either PK parameter, and EVG and TFV only met the bioequivalence criteria for $AUC_{0-\infty}$ (Table 1). The study authors concluded that the differences in bioequivalence were not expected to be clinically significant. No participants complained of an unpleasant taste with the dissolved tablets, and no adverse events were attributed to the study drug.

Table 1. Bioequivalence of E/C/F/TAF Administered Whole vs Dissolved[3]

Drug	PK Parameter	Whole Tablet Mean (CV%)	Dissolved Tablet Mean (CV%)	GMR[a] (90% CI)	Bioequivalence Criteria Met (Yes/No)[b]
EVG	C_{max}, ng/mL	1650 (22.5)	1946 (28)	1.18 (1.03–1.35)	No
	$AUC_{0-\infty}$, ng.h/mL	24,219 (25)	26,948 (22.1)	1.12 (1.04–1.22)	Yes
FTC	C_{max}, ng/mL	2095 (21.2)	1968 (24.4)	0.93 (0.81–1.09)	Yes
	$AUC_{0-\infty}$, ng.h/mL	11,603 (19.8)	10,969 (16.6)	0.95 (0.9–1)	Yes
TAF	C_{max}, ng/mL	186 (43)	171 (42.7)	0.92 (0.68–1.23)	No
	$AUC_{0-\infty}$, ng.h/mL	145 (44.1)	128 (37.5)	0.92 (0.79–1.08)	No
TFV	C_{max}, ng/mL	11 (37.3)	9.5 (24.2)	0.92 (0.77–1.1)	No
	$AUC_{0-\infty}$, ng.h/mL	253 (18.6)	241 (19.1)	0.95 (0.87–1.04)	Yes

[a]GMR is for whole/dissolved tablets.
[b]Yes meant the 90% CI of the GMR was between 80 to 125%. No meant the GMR 90% CI was outside the 80 to 125% boundary.

Case report

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.[4]

Crushed E/C/F/TAF tablets administered via PEG tube[5]

A White adult male with HIV and head and neck squamous cell carcinoma was virologically suppressed (HIV-1 RNA <20 copies/mL) while receiving E/C/F/TAF tablets. After the development of solid and liquid dysphagia, he was administered crushed E/C/F/TAF mixed in 30 mL of water. The mixture was injected via a catheter syringe through a PEG tube followed by the administration of two cans (total of 500 mL) of enteral nutrition. Virologic suppression was maintained through 14 weeks of E/C/F/TAF treatment. The patient died due to diffuse metastatic cancer during Week 15 of treatment with crushed E/C/F/TAF.

References

1. Enclosed. Gilead Sciences Inc, GENVOYA® (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Gilead Sciences Inc. Data on File.
3. Andrade A, Fuchs EJ, Marzinke MA, et al. Evg/Cobi/Ftc/Taf Bioequivalence Comparing Whole Tablets to Tablets Dissolved in Tap Water. *AIDS Res Hum Retroviruses.* 2022.
4. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC research notes.* 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
5. Kaplun O, Psevdos G. Sustained HIV Virologic Suppression with Crushed Combination Tablets Containing Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide. *Am J Health Syst Pharm.* 2019. https://www.ncbi.nlm.nih.gov/pubmed/31287497

Abbreviations

$AUC_{0-\infty}$=area under the concentration-time curve from time 0 to infinity
C_{max}=maximum concentration
E/C/F/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
EVG=elvitegravir
FTC=emtricitabine
GMR=geometric mean ratio
PEG=percutaneous endoscopic gastrostomy
PK=pharmacokinetic(s)
TAF=tenofovir alafenamide
TFV=tenofovir

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Genvoya US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/genvoya/genvoya_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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