Stribild® (E/C/F/TDF) 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 Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate [E/C/F/TDF]).

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/stribild/stribild_pi.

Product Labeling[1]

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

Description

The solubility in water of the individual components of E/C/F/TDF varies across the active ingredients.

- EVG has a solubility of <0.3 µg/mL in water at 20°C.
- COBI has 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.
- TDF has a solubility of 13.4 mg/mL in water at 25°C.

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

Gilead Data

Crushing E/C/F/TDF tablets and adding into a liquid medium has not been studied by Gilead Sciences, Inc. and is not recommended. Currently, there are no studies evaluating the PKs (eg, oral bioavailability) of a crushed E/C/F/TDF tablet dispersed into a liquid medium (eg, milk, water, juice) compared with those of a whole tablet.

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

Non-Gilead Data

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and January 26, 2026, using the search terms Stribild, elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate, cutting, crushing, splitting tablets, and related search terms. The information presented below was found.

Phase 1 PK study of crushed E/C/F/TDF[2]

Study design and demographics

An open-label, crossover, phase 1 study was conducted to assess the bioequivalence of crushed E/C/F/TDF compared with whole tablet E/C/F/TDF administered with breakfast or enteral nutrition. A total of 24 healthy volunteers were randomly assigned to receive a variety of treatment sequences: 1) reference treatment as a single dose of E/C/F/TDF whole tablet with breakfast (350 kcal), 2) single dose of crushed and suspended E/C/F/TDF tablet with breakfast (350 kcal), and 3) single dose of crushed and suspended E/C/F/TDF tablet with enteral nutrition (350 mL containing 350 kcal). There was a 7-day washout period between each treatment. Blood samples were collected before dosing and at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10, 12, 24, and 32 hours after administration of study medication. Key baseline demographics are presented in Table 1.

Table 1. Baseline Demographics (Jongbloed-de Hoon et al)[2]

Key Demographics	Total **(N=24)**
Age, median (range), years	37 (20–54)
Male, n (%)	12 (50)
White race, n (%)	23 (96)
BMI, median (range), kg/m^2	23.8 (19–29)

Efficacy results

Crushed and suspended E/C/F/TDF given with enteral nutrition was bioequivalent to a whole E/C/F/TDF tablet given with breakfast (Table 2). Crushed and suspended E/C/F/TDF given with breakfast showed bioequivalence across all components for AUC but not for C_{max} when compared with the reference treatment; thus, overall bioequivalence was not achieved. Per the EMA guidelines, bioequivalence is shown when the 90% CI of the GMR of $AUC_{0\text{-}t}$ and C_{max} falls between 80% and 125%.

Table 2. PK Parameters and Bioequivalence (Jongbloed-de Hoon et al)[2]

Parameter		GMR (90% CI) of Crushed E/C/F/TDF With Breakfast vs Reference Treatment	GMR (90% CI) of Crushed E/C/F/TDF With Enteral Nutrition vs Reference Treatment
EVG	$AUC_{0\text{-}32h}$, h·mg/L	109 (99–120)	104.3 (95–114)
	C_{max}, mg/L	115.8 (105–127)	104.5 (95–115)
COBI	$AUC_{0\text{-}32h}$, h·mg/L	89.4 (82–97)	102.4 (94–111)
	C_{max}, mg/L	83.3 (76–91)	100.9 (92–111)
FTC	$AUC_{0\text{-}32h}$, h·mg/L	99.1 (95–103)	100.6 (97–105)
	C_{max}, mg/L	89.9 (83–97)	97.6 (91–105)
TFV	$AUC_{0\text{-}32h}$, h·mg/L	96.7 (91–103)	100.7 (95–107)
	C_{max}, mg/L	81 (71–92)	94.2 (83–107)

Abbreviations: $AUC_{0\text{-}32h}$=AUC from time 0 to 32 hours; COBI=cobicistat; EVG=elvitegravir; FTC=emtricitabine; TFV=tenofovir.

Safety

A total of 89 AEs were reported, 28 of which were considered to be unrelated to study medication. Seven reports of bad taste after intake of crushed E/C/F/TDF tablet were considered related to study drug. The AEs of diarrhea (n=1) and elevated amylase (n=1) were considered to probably be related to study drug; both resolved after the study was completed. No serious AEs were reported.

Table 3. Common AEs Reported in >1 Healthy Volunteer (Jongbloed-de Hoon et al)[2]

AE,[a] n	Volunteers	Events
Headache	12	18
Bad taste after intake of crushed tablet	7	7
Nausea	6	9
Tiredness	3	4
Elevated amylase level	3	3
Stomachache	3	3
Bloated feeling	2	2
Elevated creatine kinase level	2	2
Vomiting	2	2

[a]All AEs were considered to be Grade 1 or 2.

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.[3]

Crushed E/C/F/TDF mixed in juice[4]

A 42-year-old woman with newly diagnosed HIV (HIV RNA of 1,830,000 c/mL at baseline) and difficulty swallowing whole tablets self-administered crushed E/C/F/TDF mixed in juice with and without honey. Virologic suppression was achieved at 7 months (viral load, 25 c/mL) and maintained through the last follow-up visit at 10 months (viral load, <20 c/mL) after initiation of crushed E/C/F/TDF. Progressive improvement in CD4 cell count was also observed from baseline (4 cells/mm^3) through 10 months (360 cells/mm^3) of treatment. A weight gain of 11 kg was noted, but no other AEs or intolerances were reported.

References

1. Enclosed. Gilead Sciences Inc, STRIBILD® (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Jongbloed-de Hoon M, Colbers A, Velthoven-Graafland K, et al. Pharmacokinetics of Crushed Elvitegravir Combination Tablet Given With or Without Enteral Nutrition [Accepted]. *J Acquir Immune Defic Syndr.* 2017.
3. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC Res Notes.* 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
4. Fulco PP, Ayala-Sims VA. Sustained virological response after taking crushed elvitegravir-cobicistat-emtricitabine-tenofovir tablets. *Am J Health Syst Pharm.* 2014;71(10):784, 786. http://www.ncbi.nlm.nih.gov/pubmed/24780482

Abbreviations

AE=adverse event
AUC=area under the concentration-time curve
AUC_{0-t}=area under the concentration-time curve from time 0 to the last measurable concentration
CD4=cluster of differentiation 4
c/mL=copies/mL
C_{max}=maximum concentration
E/C/F/TDF=elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
GMR=geometric mean ratio
PK=pharmacokinetic(s)

Product Label

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