GILEAD | Medical Information

# Truvada® (FTC/TDF) Crushing or Splitting of Tablets

This document is in response to your request for information regarding Truvada® (emtricitabine/tenofovir disoproxil fumarate [FTC/TDF]) and the crushing 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/truvada/truvada_pi.**

## Product Labeling[1]

There is no information in the FTC/TDF product label about the crushing or splitting of FTC/TDF; therefore, it is not recommended that FTC/TDF be administered as a crushed or split tablet. The decision to administer FTC/TDF as a crushed or split tablet is at the discretion of the prescribing or dispensing health care professional.

For the individual components of FTC/TDF, FTC and TDF have a solubility of approximately 112 mg/mL and 13.4 mg/mL, respectively, in water at 25°C.

## Available Data on Crushing or Splitting FTC/TDF

### Gilead Data

FTC/TDF tablets are not enteric coated and do not possess a sustained-release mechanism. However, the stability of FTC and TDF in liquids is unknown. Currently, there are no studies evaluating the PK (eg, oral bioavailability) of a crushed FTC/TDF tablet dispersed in a liquid medium (eg, milk, water, juice) compared with a whole tablet.

Similarly, splitting FTC/TDF tablets has not been studied and is not recommended. There are no studies evaluating the PK of a split FTC/TDF tablet versus a whole tablet.

### Non-Gilead Data

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published up to December 16, 2025, using the search terms Truvada, emtricitabine, tenofovir disoproxil fumarate, and cutting, crushing, splitting tablets and related search terms. The information presented below was found.

#### Case reports

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.[2]

### *Rowe et al, 2022*[3]

A 43-year-old male with newly diagnosed HIV was hospitalized due to changes in his neurological state, failure to thrive, and hypotension. His initial viral load was 769,704 c/mL, and his CD4 count was 36 cells/mcL. On Day 8, he was started on daily oral BIC/FTC/TAF. On Day 28, after he received 14 of the 20 scheduled doses of BIC/FTC/TAF, his viral load was 5887 c/mL. The next day, the patient was reintubated with a diagnosis of bilateral pneumothorax and received BIC/FTC/TAF via nasogastric tube for 7 days until a PEG tube was placed on Day 38. He then started receiving crushed BIC/FTC/TAF diluted in 30 mL of water administered via the PEG tube with continuous tube feeds. By Day 65, the patient had received 37 consecutive doses of BIC/FTC/TAF, and his viral load was 8047 c/mL. On Day 67, his ART regimen was switched to DTG twice daily + DRV/r daily + FTC/TDF daily, and tube feedings were changed from continuous to intermittent boluses to avoid potential drug-drug interactions. DTG and FTC/TDF were crushed, while DRV/r was given as a liquid formulation. A resistance panel showed E157Q and V118I mutations. On Day 92, his viral load was 1071 c/mL; DRV/r was discontinued, and the DTG dose was decreased to once daily. His viral load decreased to 979 c/mL after an additional 9 weeks of DTG + FTC/TDF. He was discharged on Day 161, and oral BIC/FTC/TAF was restarted once the PEG tube was removed 2 months later. His viral load was 429 c/mL at 68 days following discharge. The patient achieved virological suppression and remained suppressed with no AEs or complaints at the 1-year follow-up.

### *Lalley-Chareczko et al, 2017*[4]

A 22-year-old, White MSM was prescribed FTC/TDF for HIV-1 pre-exposure prophylaxis. Because the patient was unable to swallow whole tablets, he was instructed by the pharmacy to crush the FTC/TDF tablet, mix it with 100 mL of juice or water, and drink the mixture immediately. At a follow-up visit, the patient stated that he chewed the FTC/TDF tablets rather than crushing and mixing them with liquid. Urine samples were collected monthly, and plasma TFV was measured at Weeks 24 and 48. These samples confirmed protective levels of medication (urine tenofovir concentrations were >1000 ng/mL throughout the 48-week period; plasma TFV concentrations were >10 ng/mL for both samples). The patient's SCr level and eGFR remained within normal limits throughout the 48 weeks of monitoring. The reported AEs of dizziness, fatigue, and nausea were considered related to FTC/TDF by the study investigator and resolved after 3 days without intervention.

### *Buscemi, 2016*[5]

A 30-year-old, treatment-naïve, African-American male patient was diagnosed with HIV-1 (CD4 T-lymphocyte count: 466 cells/$mm^3$; viral load: 10,800 c/mL) and received treatment with FTC/TDF and DTG. At baseline, K103S, R211K, L10I, L63Q, I64V, and V771 mutations were recorded. Because the patient had difficulty swallowing, he pulverized FTC/TDF and DTG tablets with a pill crusher, mixed them into applesauce, and immediately swallowed the mixture. Four weeks after therapy initiation, virologic suppression (HIV-1 RNA <20 c/mL) was achieved, and his CD4 T-lymphocyte count was 583 cells/$mm^3$. The patient stated he was adherent to his medication regimen and did not report any AEs.

### *Pintilie, 2016*[6]

A 17-year-old female patient who acquired HIV perinatally was diagnosed with venous sinus thrombosis. The patient had poor adherence to ART (CD4, 248 cells/mcL; viral load, 20,009 c/mL; CD4:8, 0.2), underwent gastrostomy insertion, and received liquid DRV, RTV, and crushed FTC/TDF. The patient briefly achieved virologic suppression (HIV RNA <20 c/mL) within 12 weeks of treatment, but adherence to ART deteriorated despite multidisciplinary efforts. Additional efficacy and safety outcomes were not reported.

### *Lindholm et al, 2013*[7]

A 20-year-old male patient with acute inflammatory demyelinating polyneuropathy was diagnosed with HIV and was treated with FTC/TDF and RAL 2 months after the onset of symptoms (viral load, 100,123 c/mL at treatment initiation). Due to his autonomic neuropathy, the patient experienced severe gastroparesis and intractable nausea and vomiting that resulted in the placement of a jejunostomy tube, which was removed 4 months after the onset of illness. The initial doses of ART were administered via the jejunostomy tube using crushed tablets; the patient was then given crushed ART by mouth, and whole tablets were administered orally when he was able to swallow medications. Fifteen days after treatment initiation, virologic suppression (viral load <20 c/mL) was achieved, and it was maintained for approximately 8 months of treatment. No AEs related to FTC/TDF were reported.

### *Sandkovsky et al, 2012*[8]

A 52-year-old African-American male patient with multidrug-resistant HIV and chronic HBV was treated with FTC/TDF + RAL + ETR. HIV resistance testing showed susceptibility to ETR and RAL, partial susceptibility to TFV, and resistance to FTC. Four months after starting treatment, the patient developed ulcerative esophagitis with perforation and was administered the same regimen using crushed or dispersed tablets. The FTC/TDF tablet was crushed and mixed in 60 mL of warm water. Immediately after preparation, the mixture was injected via a catheter syringe through a gastrostomy tube once daily in the morning. Plasma concentrations of FTC ($C_{max}$=1148 ng/mL) and TFV ($C_{max}$=320 ng/mL) 2 hours after administration of crushed FTC/TDF were comparable to the observed values in other patients with HIV (FTC $C_{max}$=1514 ng/mL; TFV $C_{max}$=367 ng/mL) and healthy volunteers (FTC $C_{max}$=1600 ng/mL; TFV $C_{max}$=252 ng/mL). HIV and HBV viral loads were below the limit of detection after 2 months of oral treatment with ART and remained undetectable during treatment with crushed ART. After 15 months of treatment, the patient died at home due to esophagitis complications. No AEs related to FTC/TDF were reported.

# References

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6. Pintilie H, Raghunanan S, Shlebak A, Everitt A, Foster C. Venous Sinus Thrombosis in a Patient with Perinatally Acquired HIV, a Paediatric Case Report [Abstract P67]. *HIV Medicine.* 2016;17(Suppl 1):36.
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8. Sandkovsky U, Swindells S, Moore R, Acosta EP, Fletcher CV. Acceptable plasma concentrations of raltegravir and etravirine when administered by gastrostomy tube in a patient with advanced multidrug-resistant human immunodeficiency virus infection. *Pharmacotherapy.* 2012;32(2):142-147. http://www.ncbi.nlm.nih.gov/pubmed/22392423

# Abbreviations

AE=adverse event
ART=antiretroviral therapy
BIC=bictegravir
c/mL=copies per mL
CD4=cluster of differentiation 4
$C_{max}$=maximum concentration
DRV=darunavir
DRV/r=darunavir plus ritonavir
DTG=dolutegravir
ETR=etravirine
FTC=emtricitabine
MSM=man who has sex with men
PEG=percutaneous endoscopic gastrostomy
PK=pharmacokinetic(s)
RAL=raltegravir
RTV=ritonavir
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir

## Product Label

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