GILEAD | Medical Information

Viread® (tenofovir disoproxil fumarate) Crushing or Splitting of Tablets

This document is in response to your request for information regarding splitting or crushing Viread® (tenofovir disoproxil fumarate [TDF]) 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/viread/viread_pi.

Product Labeling[1]

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

TDF has a solubility of 13.4 mg/mL in distilled water at 25°C.

TDF is also available as an oral powder. Please refer to the US product labeling for information regarding the preparation and administration of TDF oral powder.

Clinical Data on Crushing or Splitting TDF Tablets

Gilead Data

TDF tablets are not enteric-coated and do not possess a sustained-release mechanism. TDF tablets can be disintegrated in at least 100 mL of water, orange juice, or grape juice with minor stirring and pressure with a spoon.[2] Currently, there are no studies evaluating the PKs (eg, oral bioavailability) of a crushed TDF tablet dispersed into a liquid medium (eg, milk, water, juice) compared with a whole tablet.

Similarly, splitting TDF tablets has not been studied, and it is not recommended. Currently, there are no studies evaluating the PKs of a split tablet versus 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 20, 2025, using the search terms Viread, tenofovir disoproxil fumarate, cutting, crushing, and 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.[3]

Crushed TDF administered via PEG tube in setting of infection[4]

A 44-year-old, Caucasian male with HIV presented with relapsing, life-threatening toxoplasma encephalitis and other recurring opportunistic infections. He was chronically non-adherent to oral ARVs, which resulted in critical illness, suppressed CD4 lymphocyte count, and an elevated HIV RNA viral load. A previous phenotypic resistance test showed resistance to 3TC and all NNRTIs but susceptibility to all available PIs and all other nucleos(t)ide reverse transcriptase inhibitors. A PEG tube was inserted after failed attempts to overcome physiological aversion to taking medication orally and to begin treatment for an opportunistic infection. An ARV regimen of liquid formulations of LPV, low-dose RTV, ABC, TDF, 3TC, and subcutaneous T20 was initiated. The patient used his PEG tube over the entire 15-month follow-up period, and he maintained virological suppression (HIV RNA <50 c/mL).

Crushed TDF administered via PEG tube in setting of oral candidiasis[5]

A 40-year-old, White female presented with late-stage HIV disease, a nadir absolute CD4 lymphocyte count of 10 cells/mm^3, HIV-related wasting, and azole-resistant oral-esophageal candidiasis. The patient failed multiple ARV regimens due to tolerability issues, including difficulty swallowing capsules and taste aversions to liquids, which led to her provider's decision to perform a PEG tube placement for ARV administration. The patient was started on a regimen that included APV; however, a moderate-to-severe, generalized, erythematous, and pruritic maculopapular eruption rash occurred after two attempts at APV initiation. Due to limited treatment options, APV desensitization was performed and administered via a PEG tube. Desensitization was successful and she also started the following medications through the PEG tube: RTV oral solution 100 mg twice daily, a crushed 300 mg tablet of TDF once daily, and 3TC oral solution 300 mg once daily. The regimen was continued for more than 19 months without another rash or other indications of hypersensitivity. For the first 6 months after starting this regimen, the patient responded well with a decline in HIV RNA level and an increase in CD4 cell count. However, she eventually had signs of treatment failure, which resulted in T20 initiation. She responded well to the new treatment agent with a 15-lb weight gain, an increase in CD4 lymphocyte count to 159 cells/mm^3, a decrease in HIV RNA viral load to 11,800 c/mL, and remained free of opportunistic infections.

Crushed TDF administered in pediatric patient via gastrostomy tubes[6]

A study was conducted to evaluate the PKs of NNRTIs and PIs in children with gastrostomy tubes. One patient received TDF as part of their regimen, but PK results specific to TDF or general efficacy outcomes were not available for this patient.

References

1. Enclosed. Gilead Sciences Inc, VIREAD® (tenofovir disoproxil fumarate) tablets, for oral use/ VIREAD® (tenofovir disoproxil fumarate) powder, for oral use. U.S. Prescribing Information. Foster City, CA.
2. Gilead Sciences Inc. Data on File.
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. Leipe J, Hueber AJ, Rech J, Harrer T. Bypassing non-adherence via PEG in a critically ill HIV-1-infected patient. *AIDS Care.* 2008;20(7):863-867.
5. Kohli-Pamnani A, Huynh P, Lobo F. Amprenavir-induced maculopapular exanthem followed by desensitization in a patient with late-stage human immunodeficiency virus. *Ann Allergy Asthma Immunol.* 2006;96(4):620-623.
6. King JR, Yogev R, Aldrovandi G, Chadwick E, Acosta EP. Pharmacokinetics of antiretrovirals administered to HIV-infected children via gastrostomy tube. *HIV Clin Trials.* 2004;5(5):288-293.

Abbreviations

3TC=lamivudine
ABC=abacavir
APV=amprenavir
ARV=antiretroviral
CD4=cluster of differentiation 4
c/mL=copies/mL
LPV=lopinavir
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
PEG=percutaneous endoscopic gastrostomy
PI=protease inhibitor
PK=pharmacokinetic
RTV=ritonavir
T20=enfuvirtide
TDF=tenofovir disoproxil fumarate

Product Label

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