

Long-term use medications and FTC/TDF PrEP

Revised December 2022

This is a summary of **key long-term use medications** to be avoided or used with caution with **emtricitabine/tenofovir-DF (FTC/TDF)** when used as PrEP. Full details and interactions with additional comedications can be found at www.hiv-druginteractions.org.

The renal safety of on-demand and daily dosed FTC/TDF PrEP was shown to be good in the ARNS-PREVENIR study (Liegeon G *et al. J Antimicrob Chemother*, 2022, epub ahead of print).

	Advice	Comment
Analgesics		
Aspirin	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Celecoxib	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Diclofenac	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Ibuprofen	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Mefenamic acid	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Meloxicam	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Naproxen	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Nimesulide	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Piroxicam	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Antiarrhythmics		
Amiodarone	Caution	Increased TDF absorption. Monitor for TDF side effects.
Quinidine	Caution	Increased TDF absorption. Monitor for TDF side effects.
Anticonvulsants		
Topiramate	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Antidepressants		
Lithium	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Antidiabetic		
Canagliflozin	Avoid	Risk of bone toxicity.
Antifungals		
Amphotericin B	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Fluconazole	Caution	Increased TDF absorption. Monitor for TDF side effects.
Flucytosine	Caution	Monitor haematological parameters
Itraconazole	Caution	Increased TDF absorption. Monitor for TDF side effects.
Ketoconazole	Caution	Increased TDF absorption. Monitor for TDF side effects.
Posaconazole	Caution	Increased TDF absorption. Monitor for TDF side effects.
Voriconazole	Caution	Increased TDF absorption. Monitor for TDF side effects.
Antiprotozoals		
Eflornithine	Caution	Monitor renal function.
Meglumine antimoniate	Caution	Monitor renal function.
Pentamidine	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Pyrimethamine	Caution	Monitor renal function.
Antivirals		
Aciclovir	Caution	Monitor renal function.
Adefovir	Contra-indicated	Risk of tubular necrosis. Contraindicated.
Cidofovir	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Famciclovir	Caution	Monitor renal function.
Foscarnet	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Ganciclovir	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Valaciclovir	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.

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	Advice	Comment
Calcium Channel Blockers		
Verapamil	Caution	Increased TDF absorption. Monitor for TDF side effects.
Cytotoxics		
Capecitabine	Caution	Monitor for side effects of cytotoxic agent.
Carboplatin	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Cisplatin	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Dacarbazine	Caution	Monitor renal function and haematological parameters.
Ifosfamide	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Lenalidomide	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Methotrexate	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Oxaliplatin	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Hepatitis C DAAs		
Ledipasvir/Sofosbuvir	Caution	Increased TDF absorption. Monitor for TDF side effects.
Sofosbuvir/Velpatasvir	Caution	Increased TDF absorption. Monitor for TDF side effects.
Sofosbuvir/Velpatasvir/Voxilaprevir	Caution	Increased TDF absorption. Monitor for TDF side effects.
Herbals/Supplements/Vitamins		
Cubeb pepper (Piper cubeba)	Caution	Increased TDF absorption. Monitor for TDF side effects.
Green tea extracts (Camellia sinensis)	Caution	Effect on TDF is unclear.
Liquorice (Glycyrrhiza glabra)	Caution	Increased TDF absorption. Monitor for TDF side effects.
Turmeric (Curcuma longa)	Caution	Effect on TDF is unclear.
Hypertension / Heart Failure Agents		
Furosemide	Caution	Monitor renal function.
Hydralazine	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Ranolazine	Caution	Increased TDF absorption. Monitor for TDF side effects.
Sacubitril	Caution	Monitor renal function.
Immune Modulators		
Hydroxyurea (Hydroxycarbamide)	Avoid	Risk of pancreatitis and hepatitis.
Interferon alpha	Avoid	Risk of hepatic decompensation.
Interleukin 2 (Aldesleukin)	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Peginterferon alfa-2a Peginterferon alfa-2b	Avoid	Risk of hepatic decompensation.
Immunosuppressants		
Ciclosporin	Caution	Increased TDF absorption. Monitor for TDF side effects.
Mycophenolate	Caution	Monitor renal function.
Sirolimus	Caution	Monitor renal function.
Tacrolimus	Caution	Monitor renal function.
Other		
Acetazolamide	Caution	Monitor renal function.
Penicillamine	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.
Probenecid	Caution	Monitor renal function.
Pyridostigmine	Caution	Monitor renal function.
Zoledronic acid	Avoid	Risk of nephrotoxicity with TDF. Monitor renal function.

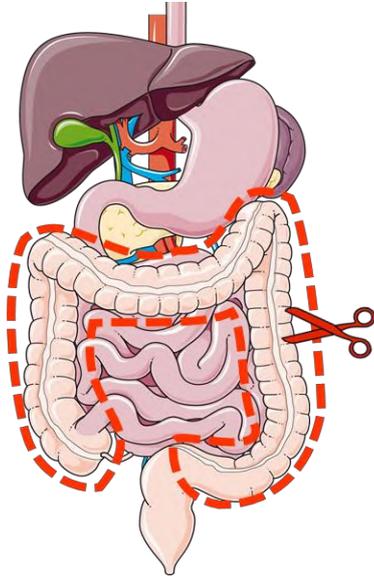
Effect of gastrointestinal surgery/disorders on FTC/TDF PrEP

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Potential pharmacokinetic changes after colonic resection

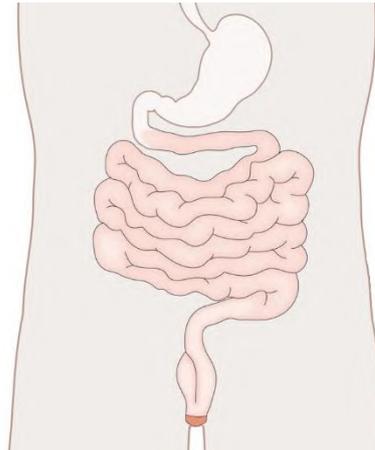
Surgery

Adapted from: www.smart.servier.com

Effect on local delivery of PrEP

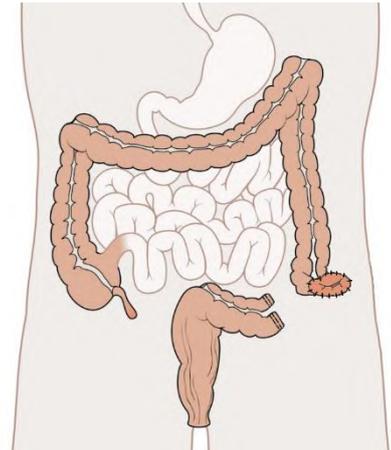
Ileoanal Anastomosis

No effect – pouch functions as new rectum



Colostomy/Ileostomy

No delivery to the rectal stump



- Impact of colonic resection on absorption of ARVs likely to be limited.
- No local delivery of oral PrEP (FTC, tenofovir) to the rectal stump following colostomy/ileostomy. Daily PrEP, rather than event-driven PrEP, is recommended.

Potential pharmacokinetic changes after bariatric surgery and with gastrointestinal disorders

- A case report describes use of the standard FTC/TDF PrEP dose in a man with a total gastrectomy (with Roux and Y anastomosis) which resulted in lower FTC and tenofovir AUC and C_{max} compared with population reference values. Doubling the FTC/TDF dose reversed the lower exposure, in particular for tenofovir. ([Roelofsen EE et al. AIDS. 2020; 34\(13\):1989-1991](#))
- There are also case reports of significantly lower trough plasma tenofovir concentrations (after supervised intake) in four FTC/TDF PrEP users with bariatric surgery or gastrointestinal disorders (sleeve gastrectomy, terminal ileitis, coeliac disease, or chronic diarrhoea). Trough plasma tenofovir concentrations in these users were 21 ± 9.1 ng/ml compared to 138 ± 85 ng/ml in PrEP recipients without gastrointestinal disorders. ([Calcagno A et al. Antimicrob Agents Chemother. 2020; 65\(1\):e01902-20](#))
- When FTC/TDF PrEP is used in patients with gastrointestinal disorders or following gastrointestinal surgery, these patients may require TDM with dose increase if exposure is low.