clinical cases DDIs

Date of report 23 Sep 2025

Reported case interaction between **Tenofovir-DF** and **Diclofenac**

Drugs suspected to be involved in the DDI

Victim
Tenofovir-DF

Daily Dose
300 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Oct. 5, 2011

End date
April 1, 2025

Perpetrator
Diclofenac

Daily Dose
Unknown

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
April 1, 2025

Complete list of drugs taken by the patient

Antiretroviral treatment

Efavirenz/Emtricitabine/Tenofovir-DF

Complete list of all comedications taken by the patient, included that involved in the DDI

Diclofenac (oral)
Diclofebac (intramuscular)

Clinical case description

Gender

Male

Age

47

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 47-year-old man with HIV infection diagnosed in 2011 and chronic HBV coinfection had been on long-term antiretroviral therapy (ART) with efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF), with excellent adherence and no complications. His HIV RNA remained consistently suppressed (<50 copies/mL), CD4 counts were stable (most recently 1003 cells/µL in October 2024), and renal function had been normal.
In 2024, he developed chronic lumbar pain secondary to a herniated disc and began self-medicating with diclofenac (oral and intramuscular, including diclofenac–B12 combinations) without medical supervision, which he used chronically.
In April 2025, laboratory tests revealed acute kidney injury (AKI), with serum creatinine 3.29 mg/dL, glucosuria, proteinuria, and reduced creatinine clearance (16 mL/min). At

that time, he was still on EFV/FTC/TDF and diclofenac. Both diclofenac and TDF were discontinued, and ART was switched to dolutegravir/lamivudine (DTG/3TC). Follow-up showed partial renal recovery, with creatinine decreasing to 2.34 mg/dL and creatinine clearance improving to 28 mL/min by July 2025. Nevertheless, chronic kidney disease persisted.
To maintain HBV treatment and reduce the risk of further nephrotoxicity, ART was subsequently changed to dolutegravir/tenofovir alafenamide/emtricitabine (DTG/TAF/FTC). No HBV reactivation was observed.
This clinical course supports a drug–drug interaction between TDF and diclofenac, as the patient had tolerated TDF for more than a decade without renal impairment, and the onset of AKI coincided with chronic diclofenac exposure. The persistence of renal damage despite drug withdrawal is consistent with previously reported cases of NSAID-potentiated TDF nephrotoxicity.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

5 - Probable

Editorial Comment

This case highlights the risk of nephrotoxicity associated with the coadministration of tenofovir disoproxil fumarate (TDF) and nonsteroidal anti-inflammatory drugs (NSAIDs), particularly diclofenac. The patient tolerated TDF for over a decade without renal impairment, but the onset of acute kidney injury (AKI) coincided with chronic diclofenac use, and renal function only partially recovered after drug withdrawal. Diclofenac is a strong inhibitor of the renal transporter MRP4, which contributes to the active tubular secretion and elimination of tenofovir. Inhibition of this pathway can markedly increase the risk of nephrotoxicity, especially with TDF, which achieves higher systemic and renal tubular concentrations of tenofovir compared to tenofovir alafenamide (TAF). Because TAF leads to ~90% lower plasma tenofovir exposure than TDF, the risk of clinically significant nephrotoxicity is substantially reduced with TAF.
This case underscores the importance of considering transporter-mediated drug–drug interactions in clinical practice. In patients receiving long-term TDF, concomitant use of NSAIDs such as diclofenac should be avoided or closely monitored. Switching to TAF-based therapy may mitigate nephrotoxicity risk while preserving HBV activity in individuals with HIV and HBV.

University of Liverpool Recommendation

■ Potential interaction - may require close monitoring, alteration of drug dosage or timing of administration

For more information click here

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