clinical cases DDIs

Date of report 16 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
Jan. 1, 2011

End date
May 19, 2025

Perpetrator
Diclofenac

Daily Dose
50 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
May 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

Fixed-dose combination of diclofenac and vitamin B12

Clinical case description

Gender

Male

Age

46

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 46-year-old male was diagnosed with HIV in 2011, with a history of chronic hepatitis B coinfection. He initiated antiretroviral therapy (ART) with emtricitabine/tenofovir disoproxil fumarate/efavirenz (FTC/TDF/EFV), achieving sustained virological suppression and good immunological recovery.

In April 2025, routine laboratory monitoring revealed impaired renal function: serum creatinine was 3.29 mg/dL, creatinine clearance was 29 mL/min, with associated glucosuria, proteinuria (176 mg/dL), and an elevated urine albumin-to-creatinine ratio of 0.352 (normal <0.03). Upon clinical review, the patient disclosed daily use of a fixed-dose combination of diclofenac and vitamin B12 for chronic low back pain under investigation.

Given the suspicion of TDF-related nephrotoxicity due to a drug-drug interaction with diclofenac (which may impair renal

elimination of tenofovir and increase the risk of nephrotoxicity), ART was temporarily switched to lamivudine/dolutegravir (3TC/DTG), resulting in partial improvement of renal function. Subsequently, the regimen was modified to FTC/tenofovir alafenamide/dolutegravir (FTC/TAF/DTG) to ensure continued HBV suppression.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

3 - Possible

Editorial Comment

Diclofenac is a potent inhibitor of the renal transporter MRP4, which contributes to the secretion of tenofovir into the urine for elimination. Inhibition of MRP4 by diclofenac means that tenofovir remains inside the tubular cell, increasing the risk of tubular toxicity. Diclofenac should be avoided with tenofovir disoproxil fumarate (TDF); however, coadministration is possible with tenofovir alafenamide (TAF), as TAF results in systemic tenofovir levels approximately 90% lower than TDF, thereby significantly reducing the risk of nephrotoxicity.
Other NSAIDs may be safer than diclofenac, but they should also be used with caution, especially for long-term use, in

patients with pre-existing renal impairment, in those with low body weight, or when co-administered with other drugs that may increase tenofovir exposure.
It is important to note that NSAIDs are often available over the counter, so frequent review of concomitant medications is recommended.
References:

- Kohler JJ, Hosseini SH, Green E, Abuin A, Ludaway T, Russ R, Santoianni R, Lewis W. Tenofovir renal proximal tubular toxicity is regulated by OAT1 and MRP4 transporters. Lab Invest. 2011 Jun;91(6):852-8.
- Bickel M, Khaykin P, Stephan C, et al. Acute kidney injury caused by tenofovir disoproxil fumarate and diclofenac co-administration. HIV Med. 2013;14(10):633-8.

University of Liverpool Recommendation

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

For more information click here

Personal information from the specialist

Name
Ezequiel

Surname
Cordova

Institution
Hospital Cosme Argerich

Country
AR

Other authors

Name
Ezequiel

Surname
Cordova

Institution
Hospital Cosme Argerich (Argentina)

Name
Vanesa

Surname
Dadon

Institution
Hospital Cosme Argerich (Argentina)