



Date of report 22 Jun 2020

Reported case interaction between **Dolutegravir** and **Valproate**

Drugs suspected to be involved in the DDI

Victim

Dolutegravir

Daily Dose

50mg (mg)

Dose adjustment performed

Yes

Administration Route

Oral

Start date

Nov. 15, 2019

End date

Ongoing

Perpetrator

Valproate

Daily Dose

3000 (mg)

Dose adjustment performed

No

Administration Route

Oral

Start date
Nov. 6, 2019

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Dolutegravir
Emtricitabine/Tenofovir-DF

Complete list of all comedications taken by the patient, included that involved in the DD
Valproate Alfusozin Ciprofloxacin Colecalciferol Desloratidin Haldol Lora
Quetiapine Multivitamin

Clinical case description

Gender
Male

Age
50

eGFR (mL/min)
>60

Liver function impairment
No

Description

A 50-year old patient with a new HIV infection (CD4 count 10; VL 300.0 to the hospital for respiratory insufficiency due to PJP and Pasteurella infection. The patient was on ART with FTC/TDF and was started on 14 November 2019. The patient also received valproate for a long history mental disorders and drug abuse. The valproate-DTG interaction was considered clinically relevant. Valproate reduces total DTG concentrations due to protein-protein displacement, free DTG fraction increases, leading to therapeutic free DTG concentrations (Bollen P; 20th International Workshop on Clinical Pharmacology of HIV Therapy). DTG plasma trough concentrations were measured in this patient – displayed in Figure 1. We decided to measure free DTG concentrations, because of the extremely low concentrations in 2019. Free DTG fraction did not increase and was thus considered to be subtherapeutic. DTG was given BID instead of QD to increase plasma concentrations from 2019 onwards. DTG trough concentration increased and the free DTG concentration

proposed in vitro EC90 value of unbound dolutegravir (0.9 µg/L). This could be due to the interaction between valproate and DTG might be clinically relevant in some patients. DTG concentrations

Date	Dose	Total DTG	Free DTG
		mg/L	ug/L (% of total)
18-11-2019	1 dd 50mg	0.71	5.8 (0.8)
22-11-2019	1 dd 50mg	0.09	0.58 (0.6)
02-12-2019	2 dd 50mg	0.39	1.47 (0.4)

Viral load data

Date	VL
07-11-2019	300.000 copies/ml
02-12-2019	600 copies/ml
31-01-2020	900 copies/ml

Clinical Outcome

Loss of efficacy

Drug Interaction Probability Scale (DIPS)

Score

2 - Possible

Editorial Comment

University of Liverpool Recommendation

◆ No clinically significant interaction expected

For more information [click here](#)