clinical cases DDIs

Date of report 18 Mar 2021

Reported case interaction between **Ritonavir** and **Epleronone**

Drugs suspected to be involved in the DDI

Perpetrator
Ritonavir

Daily Dose
200 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Jan. 1, 2008

End date
Dec. 10, 2018

Victim
Epleronone

Daily Dose
25 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Dec. 3, 2018

End date
Dec. 10, 2018

Complete list of drugs taken by the patient

Antiretroviral treatment

Emtricitabine/Tenofovir-DF
Fosamprenavir (with Ritonavir)
Ritonavir

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

Losartan, carvedilol, aspirin, clopidogrel and atorvastatin

Clinical case description

Gender

Male

Age

48

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 48-year-old HIV-1 positive man who presented an acute myocardial infarction. The patient had been on ART for the last ten years with emtricitabine/tenofovir and ritonavir-boosted fosamprenavir. Eplerenone 25 mg/day was also initiated due to a left ventricular dysfunction. A week after discharge a routine laboratory test revealed severe hyperkalaemia. Due to suspicion of a potential drug–drug interaction, both eplerenone and ARVs were interrupted. Despite daily treatment for hyperkalaemia, serum potassium levels normalized after two weeks, At discharge, antiretroviral treatment was reinitiated with emtricitabine/tenofovir and dolutegravir (DTG) to avoid possible DDIs. Two weeks later, eplerenone was initiated again. No recurrence of the hyperkalaemia was observed up to 12 months of follow-up.

Eplerenone is metabolized by the hepatic P450 cytochrome isoenzyme CYP3A4; therefore, concomitant administration with CYP3A4 inhibitors, like ritonavir, may increase plasma levels of eplerenone and, therefore, the risk of side effects, mainly hyperkalaemia. Cordova E, Garibaldi F, Bono L, Rodriguez C. Severe hyperkalaemia due to a potential drug-drug interaction between eplerenone and antiretrovirals in a HIV-positive patient after a myocardial infarction [published online ahead of print, 2021 Feb 25]. Int J STD AIDS. 2021;956462420987422. doi:10.1177/0956462420987422

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

5 - Probable

Editorial Comment

Coadministration has not been studied and is contraindicated. Eplerenone is metabolized by CYP3A4 and coadministration is expected to substantially increase eplerenone exposure due to inhibition of CYP3A4 and thereby increase the risk of hyperkalaemia. Noteworthy, this patient was also receiving clopidogrel. Co-administration of ritonavir with clopidogrel may result in a decrease in clopidogrel’s active metabolite and to insufficient inhibition of platelet aggregation. As in this

case, changing to an unboosted ART regimen or clopidogrel to prasugrel should be preferred.

University of Liverpool Recommendation

- These drugs should not be coadministered

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