clinical cases DDIs

Date of report 03 Feb 2020

Reported case interaction between **Cobicistat** and **Ranolazine**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Jan. 1, 2014

End date
Ongoing

Victim
Ranolazine

Daily Dose
1000 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Nov. 1, 2018

End date
Jan. 31, 2019

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir (with Ritonavir or Cobicistat)
Emtricitabine/Tenofovir-AF

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

Aspirin 81 mg once daily (5 years), cilostazol 50 once daily (5 years), clopidogrel 75 mg once daily (5 years), atorvastatin 40 mg once daily (5 years), tiotropium 18 ug once daily (2 years), ondansetron 8 mg twice daily (<2months), pantoprazole 40 mg once daily (<2months), tramadol 50 mg once daily (1 year), ranolazine 500 mg twice daily (2 months)

Clinical case description

Gender

Male

Age

64

eGFR (mL/min)

>60

Liver function impairment

No

Description

In early January 2019, a 64 year old man was admitted to the hospital with left-sided chest pain, dizziness and near syncope. The patient also reported persistent and severe episodes of nausea, vomiting, dyspepsia and anorexia for the past 2 months. Electrocadiography revealed first-degree atrioventricular block (AV). During the hospitalization, the pharmacist identified the drug-drug interaction between ranolazine and darunavir/cobicistat which led to the interruption of ranolazine. The patient's chest pain, nausea and dizziness resolved in a couple of days after stopping ranolazine. Gastrointestinal and AV block events are known

side effects of ranolazine. In the present case, these side effects occurred likely due to cobicistat inhibition of ranolazine metabolism leading to an increased exposure. This case has been published by Dougherty JA et al. Ann Pharmacother 2019; 53:966-7.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

8 - Probable

Editorial Comment

Ranolazine levels have been shown to be significantly increased by ketoconazole another strong CYP4A4 inhibitor (Jerling M et al. J Clin Pharmacol 2005). Ranolazine product label contra-indicated the coadministration with strong CYP3A4 inhibitors.

University of Liverpool Recommendation

- These drugs should not be coadministered

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