clinical cases DDIs

Date of report 30 May 2024

Reported case interaction between **Cobicistat** and **Ergotamine**

Drugs suspected to be involved in the DDI

Perpetrator
Cobicistat

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 1, 2020

End date
Unknown

Victim
Ergotamine

Daily Dose
4 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
June 20, 2021

End date
June 22, 2021

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat/Emtricitabine/Tenofovir-AF

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

Ergotamine, Caffeine

Clinical case description

Gender

Male

Age

46

eGFR (mL/min)

>60

Liver function impairment

No

Description

Clinical Summary: A 46-year-old patient with well-controlled HIV (<50 copies/mL) and a history of anxiety disorder, with no known drug allergies, is currently undergoing antiretroviral therapy with Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide since June 2020.
April 2021 Presentation: In April 2021, the patient experienced a severe headache and sought relief at a pharmacy, where they gave an ergotamine-caffeine combination. Two days later, the patient presented to the emergency department after a night of excessive urination and persistent myalgia in the limbs. Additionally, he reported odynophagia and denied diarrhea, anosmia, and ageusia.
Clinical Examination: The examination revealed a cooperative, afebrile, and hemodynamically stable patient with mild hypotension (108/68 mmHg). The abdomen was

soft and non-tender, and there was no edema in the lower limbs or signs of deep vein thrombosis.

Laboratory Analysis:

Blood analysis to assess for possible rhabdomyolysis showed the following results:

- Creatine Kinase: 103 U/L (Reference Range: 30-200 U/L)
- Potassium: 4.0 mEq/L (Reference Range: 3.3-5.5 mEq/L)
- LDH: 247 U/L (Reference Range: 105-333 U/L)

Since the laboratory values were within normal ranges, rhabdomyolysis was ruled out. The patient was diagnosed with ergotism due to the interaction between ergotamine and cobicistat. Ergotamine is a substrate of CYP3A4, which cobicistat inhibits. The resulting clinical picture was consistent with ergotism explaining the myopathy due to peripheral vasoconstriction, and oliguria.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

5 - Probable

Editorial Comment

Coadministration of ergotamine with potent CYP3A4 inhibitors is contraindicated due to potential for serious and/ or life threatening events such as acute ergot toxicity

characterized by peripheral vasospasm and ischemia of the extremities and other tissues. The present case is very representative of this situation, with the appearance of symptoms suggestive of ergotism after combining darunavir/cobicistat and a preparation of ergotamine and caffeine that the patient obtained from the pharmacy due to a headache. This case highlights a situation that is not uncommon and can become potentially dangerous (and even fatal), which is the occurrence of clinically significant interactions between cobicistat and medicines that can be obtained OTC, such as ergotics (as in this case) or another example could be sildenafil. Although it is not an unknown interaction (there are publications with this interaction, such as Navarro J et al Antivir Ther. 2017;22(1):89-90), it is important to remember to inform the patient of the potential for interactions between cobicistat and many other medications that can be obtained with medical prescription or OTC.

University of Liverpool Recommendation

- These drugs should not be coadministered

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