Date of report 29 Jun 2023

# Reported case interaction between **Cobicistat** and **Budesonide**

## Drugs suspected to be involved in the DDI

Perpetrator
**Cobicistat**

Daily Dose
150 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Victim
**Budesonide**

Daily Dose
200 (mcg)

Dose adjustment performed
No

Administration Route
Inhaled

Start date
Unknown

End date
Unknown

## Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat
Raltegravir

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

No other drugs

## Clinical case description

Gender

Male

Age

45

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 45-year old man co-infected by HIV/HCV underwent bariatric surgery (BMI: 50.9 kg/m2) in May 2021. Four months after the surgery, the patient was diagnosed with asthma and was started on inhaled budenoside (200 ug per day) which was later changed to fluticasone (92 ug) 10 months after the surgery. At the 12 month postoperative visit, the patient reported proximal muscle weakness , progressive asthenia, an suboptimal weight loss despite compliance to the nutritional plan. Physical examination revealed moon facies, a slight facila plethora, dorsocervical fat accumulation and abdominal distention with large striae. Laboratory values showed impaired glucose metabolism and hypokaliemia. The patient was on treatment with darunavir/cobicistat (800/150 mg QD) plus raltegravir (1200 mg QD) since 2019 for the HIV infection. A Cushing Syndrome was suspected and

subsequently confirmed by a low cortisol level; negative overnight 1 mg dexamethasone suppression test; low basal morning serum cortisol level and an inadequate response to adrenal stimulation test. The Cushing's Syndrome has been attributed to the inhibition of budenoside/fluticasone metabolism by darunavir/cobicistat. Thus, darunavir/cobcistat was stopped and replaced by dolutegravir plus doravirine. The inhaled corticosteroids were switched to beclomethasone and the glucocorticoid substitutive therapy with prednisolone (2.5 mg per day) was introduced. Two weeks later, the patient showed signs of clinical improvement with less asthenia and muscle weakness.
The case was published by Silva B et al. in Cureus 15(1): e34367, 2023

## Clinical Outcome

## Toxicity

## Drug Interaction Probability Scale (DIPS)

Score

**7 - Probable**

## Editorial Comment

In this clinical case, a well-known interaction is described, that of certain steroids with cobicistat (and also ritonavir). Potent CYP3A4 inhibitors cause an increase in glucocorticoids that are metabolized through CYP450, such as fluticasone or

budesonide, irrespective of the steroids administration route. This entails a risk of Cushing's syndrome or even Addison's syndrome due to adrenal insufficiency.

Just because an interaction is well described, it does not diminish the value of its communication, as it is convenient to periodically recall interactions with frequently used drugs, especially if they are administered through routes other than oral, which are sometimes considered less prone to interaction, such as the inhaled route or intranasal drops, for example. It is also important to remember those interactions that can have serious consequences for the patient if they are not detected and acted upon accordingly.

In patients receiving boosted darunavir and requiring corticosteroids, it is recommended to use beclomethasone, which is not metabolized by CYP450 but is hydrolysed via esterase enzymes to the active metabolite. However, the active metabolite is subsequently converted to inactive metabolites via CYP3A4/5. Thus, cobicistat/ritonavir can increase the active metabolite, although this increase has shown no impact on adrenal function. However, it is recommended to use the lowest possible dose and monitor for side effects when using beclomethasone and boosted darunavir.

In this clinical case, the antiretroviral treatment was changed (from darunavir/cobicistat and raltegravir to dolutegravir and doravirine), and the inhaled corticosteroid was also changed from fluticasone to beclomethasone. This is somewhat surprising because it is necessary to change one of the two medications (either the ART or the inhalers), but not both, since there are no significant interactions between dolutegravir or doravirine and budesonide/fluticasone (nor with beclomethasone). However, it is important to have an option for an inhaled corticosteroid that can be administered concomitantly with boosted darunavir, because in some

patients it is not possible to discontinue the boosted protease inhibitor due to previous failures/presence of resistance mutations.

## University of Liverpool Recommendation

- These drugs should not be coadministered

For more information click here

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