clinical cases DDIs

Date of report 07 Jul 2026

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
Dec. 18, 2019

End date
Feb. 12, 2026

Victim
Budesonide

Daily Dose
400 (mcg)

Dose adjustment performed
No

Administration Route
Inhaled

Start date
May 27, 2021

End date
Ongoing

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

Indacaterol/glycopyrronium bromide 85/43 mcg once daily (inhaled)
Ipratropium bromide 60 mcg every 6 hours (inhaled)
Budesonide 200 mcg every 12 hours (inhaled)
Methadone 75 mg (oral)
Enalapril 10 mg once daily (oral)

Clinical case description

Gender

Male

Age

56

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 56-year-old man was diagnosed with HIV infection in 2017. Antiretroviral therapy (ART) was initiated in April 2017 with abacavir/lamivudine/dolutegravir. His nadir CD4 cell count was 109 cells/mm³ (7%), and he had no history of opportunistic infections. Initial virological response to ART was favourable, with subsequent immune recovery.
In 2019, the patient experienced several episodes of low-level viraemia (<200 copies/mL), likely related to poor adherence, with no resistance-associated mutations detected. Consequently, ART was switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide. Since

February 2020, virological suppression has been maintained, and the most recent CD4 cell count was 230 cells/mm³ (20%). The patient had a history of tobacco use until September 2025, as well as previous alcohol misuse and intravenous drug use. Other comorbidities included hypertension, chronic liver disease without evidence of liver dysfunction or portal hypertension, and chronic obstructive pulmonary disease (COPD). Because of recurrent COPD exacerbations, he was receiving maintenance inhaled therapy with indacaterol/glycopyrronium, ipratropium bromide, and budesonide. Despite prolonged coadministration of inhaled budesonide and cobicistat, no corticosteroid-related adverse effects or virological rebound were observed. Nevertheless, to reduce the long-term risk of corticosteroid toxicity and avoid clinically relevant drug–drug interactions, ART was switched to bictegravir/emtricitabine/tenofovir alafenamide.

Clinical Outcome

No unwanted outcome

Editorial Comment

This case highlights the clinically relevant interaction between inhaled budesonide and cobicistat-boosted antiretroviral therapy. Budesonide is extensively metabolized by CYP3A4, and cobicistat, a potent CYP3A4 inhibitor, can substantially increase systemic corticosteroid exposure even after inhaled administration. Consequently, **coadministration is not recommended** because of the

risk of iatrogenic Cushing's syndrome and secondary adrenal suppression. Whenever possible, inhaled beclomethasone, which is less dependent on CYP3A4 metabolism, should be considered, or alternatively an unboosted antiretroviral regimen should be selected, as was done in this case.
The absence of corticosteroid-related adverse effects in this patient should be interpreted with caution. Although the interaction between budesonide and cobicistat is well established, the lack of reported clinical consequences does not exclude its occurrence. Therefore, the absence of documented toxicity in this clinical case should not be interpreted as evidence of absence of a clinically relevant interaction.
An additional potential interaction in this patient involved concomitant methadone therapy. Boosted protease inhibitors may alter methadone plasma concentrations through complex effects on its metabolism, although the overall clinical effect is variable. Clinically, this may result in reduced methadone exposure with withdrawal symptoms or, less commonly, increased opioid-related adverse effects. Therefore, patients receiving methadone together with boosted protease inhibitors should undergo close clinical monitoring, with dose adjustments guided by clinical signs of opioid withdrawal or toxicity.

University of Liverpool Recommendation

- These drugs should not be coadministered

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