clinical cases DDIs

Date of report 17 Mar 2026

Reported case interaction between **Dolutegravir** and **Metformin**

Drugs suspected to be involved in the DDI

Perpetrator
Dolutegravir

Daily Dose
50 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
May 16, 2023

End date
Ongoing

Victim
Metformin

Daily Dose
2000 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Dec. 1, 2020

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir/Cobicistat/Emtricitabine/Tenofovir-AF
Dolutegravir

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

Metformin 1000 mg BID; empaglifozin 12.5mg BID; gliclazide 120 mg daily; rosuvastatin 20 mg daily.

Clinical case description

Gender

Male

Age

60

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 60-year-old man diagnosed with HIV infection in 2014 initiated antiretroviral therapy (ART) the same year with oral cabotegravir plus abacavir/lamivudine, and was subsequently switched to long-acting intramuscular rilpivirine plus cabotegravir. In October 2017, ART was changed to tenofovir alafenamide/emtricitabine/darunavir/cobicistat due to virological failure, without selection of resistance-associated mutations. In May 2023, ART was intensified with the addition of dolutegravir due to persistent low-level viremia.

The patient had also been diagnosed with type 2 diabetes mellitus in 2010 and had a body mass index (BMI) ranging between 29 and 31 kg/m^2. In July 2011, high-dose metformin (850 mg every 8 hours) was required due to poor glycemic control. Since December 2020, he has been receiving

metformin 1000 mg every 12 hours in combination with other antidiabetic agents. No metformin-related adverse effects have been reported.
Dolutegravir inhibits the OCT2 transporter, and coadministration with metformin can increase metformin exposure, potentially leading to adverse events, particularly in patients with impaired renal function. Therefore, a daily metformin dose above 1000 mg is generally not recommended when used in combination with dolutegravir. However, metformin exposure may be reduced in individuals with overweight or obesity due to an increased volume of distribution.
In this case, the presence of overweight/obesity together with preserved renal function may have contributed to the absence of metformin-related toxicity despite the use of high metformin doses in combination with dolutegravir.

Clinical Outcome

No unwanted outcome

Editorial Comment

Coadministration of metformin with dolutegravir increases metformin exposure in a dose-dependent manner. When administered with once-daily dolutegravir, metformin C_max and AUC increase by 66% and 79%, respectively, while coadministration with twice-daily dolutegravir results in increases of 111% and 145%. Therefore, dose adjustment of metformin should be considered when initiating or

discontinuing dolutegravir in order to maintain adequate glycaemic control.
The US prescribing information recommends limiting the total daily dose of metformin to 1000 mg when used in combination with dolutegravir. However, this recommendation may not be optimal for all patients. In individuals with obesity, metformin exposure may be reduced due to an increased volume of distribution. Indeed, in a study of obese women living with HIV (mean BMI 45.6 kg/m^2), coadministration of metformin (1000 mg) and dolutegravir (50 mg once daily) resulted in metformin and dolutegravir concentrations approximately 50% lower than those observed in non-obese healthy volunteers. This suggests that dose restriction to 1000 mg daily may lead to subtherapeutic exposure in this population.
Close monitoring of renal function is recommended during coadministration, along with monitoring of blood glucose when initiating or discontinuing dolutegravir. As metformin is primarily eliminated via the kidneys, patients with moderate renal impairment may be at increased risk of lactic acidosis due to elevated metformin concentrations.

University of Liverpool Recommendation

■ Potential interaction - may require close monitoring, alteration of drug dosage or timing of administration

For more information click here

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