clinical cases DDIs

Date of report 16 Sep 2025

Reported case interaction between **Dolutegravir** and **Phenobarbital**

Drugs suspected to be involved in the DDI

Victim
Dolutegravir

Daily Dose
50 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
Unknown

End date
Ongoing

Perpetrator
Phenobarbital

Daily Dose
100 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
April 7, 2025

End date
May 29, 2025

Complete list of drugs taken by the patient

Antiretroviral treatment

Dolutegravir/Abacavir/Lamivudine

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

Phenobarbital 100 mg
Pantoprazole 40 mg
Omega-3 Fatty acids 1000 mg
Rosuvastatine/ezetimibe 5/10 mg
Risperidone 0.5 mg
Cholecalciferol 10000 units/week
Macrogol, magnesium citrate, citric acid, calcium citrate, acesulfame K, lemon flavor, potassium chloride, silicon dioxide 1 sachet/day
Insulin: slow (12 units at night)

Clinical case description

Gender

Male

Age

62

eGFR (mL/min)

>60

Liver function impairment

Yes

Child-Pugh

Child-Pugh A

Description

A 62-year-old man was admitted with generalized seizures. His medical history included type 2 diabetes, dyslipidemia, psoriasis, erosive gastritis, liver fibrosis (treated HCV infection with steatosis), and bipolar disorder. HIV infection had been diagnosed 8 years earlier. At admission, he was

receiving abacavir/lamivudine/dolutegravir, with undetectable HIV RNA and a CD4 cell count of 165 cells/mm³. For seizure control, the neurologist prescribed phenobarbital (initially intramuscularly, then orally), with no recurrence of seizures. Due to a prescription error, the dolutegravir dose was not doubled after the introduction of phenobarbital; he therefore received standard once-daily dolutegravir with phenobarbital for approximately two months.
After two months of concomitant treatment, blood tests confirmed undetectable HIV RNA and unexpectedly high dolutegravir trough concentrations (2112 ng/mL). Nevertheless, considering the potential drug–drug interaction, we decided to double the dolutegravir dose for two weeks and, after neurological consultation, to switch phenobarbital to levetiracetam.

Clinical Outcome

No unwanted outcome

Editorial Comment

This case highlights a relevant interaction between dolutegravir (DTG) and phenobarbital. Phenobarbital is a strong inducer of UGT1A1 and CYP3A and, by extrapolation from studies with carbamazepine and rifampicin, is expected to markedly reduce DTG exposure. Guidelines recommend avoiding coadministration or doubling the DTG dose to 50 mg twice daily. In this case, a dosing error led to DTG 50 mg once daily for two months while on phenobarbital, yet trough levels remained high (2112 ng/mL) and HIV RNA

undetectable. This unexpected outcome may be explained by the high inhibitory quotient (Cmin/IC90) of DTG: at 50 mg once daily, plasma exposure is ~19-fold above the protein-adjusted IC90, which may have been sufficient to maintain suppression despite induction. Nevertheless, clinicians should avoid concomitant use of strong inducers, as interindividual variability in DTG exposure could place people at risk of virologic failure. Further clinical data are needed to better define this interaction.

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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