



Date of report 03 Feb 2025

Reported case interaction between  
**Raltegravir** and **Hypericum  
perforatum**

**Drugs suspected to be involved in the DDI**

**Raltegravir**

Daily Dose  
800 (mg)

Dose adjustment performed  
No

Administration Route  
Oral

Start date  
Unknown

End date  
Ongoing

Perpetrator

**Hypericum  
perforatum**

Daily Dose  
900 (mg)

Dose adjustment performed  
No

Administration Route  
Oral

Start date  
Unknown

End date  
Unknown

## Complete list of drugs taken by the patient

Antiretroviral treatment

Raltegravir  
Emtricitabine/Tenofovir-DF

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

St. John's wort (*Hypericum perforatum*) 300 mg three times daily (300 mg TID).

## Clinical case description

Gender  
Female

Age  
27

eGFR (mL/min)  
>60

Liver function impairment  
No

Description

This case involves a 27-year-old Caucasian female patient with no liver or kidney impairment. Since 2019, she has been on her current antiretroviral therapy (cART), consisting of raltegravir (400 mg BID), emtricitabine, and tenofovir disoproxil fumarate (200/300 mg QD). Since initiating cART, she has maintained an undetectable viral load, with a CD4 T-cell count above 800 cells/mm<sup>3</sup>.

In 2023, she became pregnant and delivered at 38 weeks of gestation. Postpartum, she developed depression and was prescribed St. John's Wort (*Hypericum perforatum*) at 300 mg

three times daily (TID). As advised, she took St. John's Wort concomitantly with raltegravir for three months.

Although St. John's Wort can induce UGT1A1 and potentially reduce raltegravir exposure, the patient's HIV RNA remained undetectable, suggesting that raltegravir concentrations remained within the therapeutic range and that no clinically significant drug-drug interaction occurred.

## Clinical Outcome

**No unwanted outcome**

## Editorial Comment

According to the European product label for raltegravir, St. John's Wort may be used with twice-daily or once-daily raltegravir at the recommended doses. However, St. John's Wort is a pregnane X receptor (PXR) agonist, which can induce UGT1A1 and potentially reduce raltegravir exposure. Additionally, in vivo and in vitro studies have shown that St. John's Wort activates PXR, which regulates enzymes of the cytochrome P450 system, including CYP3A4, as well as P-glycoprotein (P-gp), a key transporter involved in drug metabolism, including raltegravir. Therefore, monitoring the response to antiviral therapy is recommended.

In a phase I, open-label, non-randomized, single-sequence study, a low-hyperforin St. John's Wort extract (hyperforin content below 1 mg/day) was investigated in healthy volunteers. No pharmacokinetic interactions were observed for CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP3A4, or P-glycoprotein substrates. These findings suggest that low-

hyperforin preparations of St. John's Wort have a lower risk of drug-drug interactions compared with high-hyperforin formulations.

## University of Liverpool Recommendation

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

For more information [click here](#)