Resource: ART Drug-Drug Interactions

August 2024

Table 10: Doravirine (DOR) Interactions (also see drug package inserts)

Class or Drug	Mechanism of Action	Clinical Comments
Strong inducers or inhibitors of CYP3A [Deeks 2018]	DOR is a CYP3A substrate, and as such, drugs that affect its metabolism affect its concentrations.	• Avoid concomitant use if possible. • Dose adjustments of DOR are not recommended. • Consider alternative concomitant agents.
Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	Coadministration may significantly reduce ARV concentrations through induction of CYP450 system.	• Coadministration is not recommended; use alternative anticonvulsant. • If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. • Perform TDM if use cannot be avoided.
Rifabutin, rifampin, rifapentine	• **Rifabutin:** CYP3A induction is expected to decrease DOR levels. • **Rifampin, rifapentine:** CYP3A induction reduces DOR bioavailability.	• **Rifabutin:** When used concomitantly, increase DOR to 100 mg twice per day. • **Rifampin, rifapentine:** – Concomitant use is contraindicated. – After stopping rifampin or rifapentine, wait 4 weeks before starting DOR.
Mpox treatments [a]	**Tecovirimat** is weak inducer of CYP3A and weak inhibitor of CYP2C8 and CYP2C19; use may potentially increase or decrease plasma concentrations of other medications.	**Tecovirimat** may reduce NNRTI levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary.
ADHD medications	**Modafinil:** CYP3A4 induction may reduce NNRTI levels.	**Modafinil:** Avoid concurrent use due to potential loss of virologic response.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ARV, antiretroviral agents; AUC, area under the curve; CYP, cytochrome P450; NNRTI, non-nucleoside reverse transcriptase inhibitor; TDM, therapeutic drug monitoring; VIGIV, vaccinia immune globulin intravenous.

Note:

a. No data are currently available on effects related to concurrent use of tecovirimat and HIV medications. However, midazolam AUC was reduced by 32% with concomitant tecovirimat use, and some experts recommend caution due to the mild CYP3A4 induction associated with tecovirimat. Among them is University of Liverpool HIV Drug Interactions, which makes the following dosing change recommendations, although they are not based on any clinical data: Increase dose to 100 mg twice daily for the duration of tecovirimat treatment and for 2 weeks after tecovirimat is stopped.

No significant interactions/no dose adjustments necessary (see guideline section Drug-Drug Interactions by Common Medication Class)**:** Common oral antibiotics; antihypertensive medications; anticoagulants; antiplatelet medications; statins; antidiabetic medications; polyvalent cations; asthma and allergy medications; long-acting beta agonists; inhaled and injected corticosteroids; antidepressants; benzodiazepines; sleep medications; antipsychotics; nonopioid pain medications; opioid analgesics and tramadol; hormonal contraceptives; erectile and sexual dysfunction agents; alpha-adrenergic antagonists for benign prostatic hyperplasia; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; methadone, buprenorphine, naloxone, and naltrexone; immunosuppressants; COVID-19 therapeutics; gender-affirming hormones.

Reference

Deeks ED. Doravirine: first global approval. *Drugs* 2018;78(15):1643-50. [PMID: 30341683] https://pubmed.ncbi.nlm.nih.gov/30341683