

Beaumont

Potential Dexamethasone Direct Xa Inhibitor Drug Interaction:

Dexamethasone is reported to be a combined P-glycoprotein and CYP 3A4 inducer.¹ Although characterized as a moderate CYP 3A4 inducer in some literature, the available body of evidence suggests that dexamethasone is a weak CYP 3A4 inducer. Significant inter-patient variability however has been reported in the magnitude of dexamethasone CYP 3A4 induction. Apixaban and rivaroxaban undergo partial CYP3A4 metabolism, 25% and 18% respectively. The onset of CYP 3A4 enzyme induction is estimated to be 4-5 days. De-induction (the offset of enzyme induction) is expected to be delayed after dexamethasone discontinuation secondary to its the long duration of action. Apixaban and rivaroxaban are substrates for P-glycoprotein. Human data which support dexamethasone as a P-glycoprotein inducer is limited.

Small studies suggest that concurrent use of dexamethasone with apixaban or rivaroxaban does not result in a significant reduction in direct Xa inhibitor concentration.² The large inter-patient variability in this interaction leaves the potential for dexamethasone to decrease apixaban or rivaroxaban concentrations thus potentially increasing the risk of thrombosis. Concurrent use thus requires an individualized risk-benefit assessment. Enoxaparin can be considered as an alternate anticoagulant during dexamethasone therapy.

Recommended Approach to Manage Drug Interaction:

1. Consider enoxaparin as an alternate anticoagulant during dexamethasone therapy
2. If apixaban/rivaroxaban needs to be continued consider switching steroid (methylprednisolone is the preferred alternative in COVID-19 patients)
3. DO NOT increase apixaban or rivaroxaban dose to account for the potential reduction in drug concentration in drug concentration

References:

1. Steffel J, Collins R, Antz et al. The 2021 European Heart Rhythm Association Practical Guide on the use of non-vitamin-K antagonist oral anticoagulants in patients with atrial fibrillation, *Europace* 2021;00:1-65.
2. Potere N, Candeloro M, Porreca E et al. Direct oral anticoagulant plasma levels with hospitalized COVID-19 patients treated with dexamethasone, *J Thromb Thrombolysis* 2021, In Press