

Beaumont Potential Dexamethasone Direct Xa Inhibitor Drug Interaction: Avoid Concurrent Use

Dexamethasone is reported to be a combined P-glycoprotein and strong CYP 3A4 inducer.¹ Some variability exists however in the characterization of the induction potential of dexamethasone. All DOACs are substrates for P-glycoprotein. Human data which support dexamethasone as a P-glycoprotein inducer however is limited. Apixaban and rivaroxaban undergo CYP3A4 metabolism, 25% and 18% respectively. When dexamethasone is used in combination with a direct Xa inhibitor, (apixaban, rivaroxaban) there is a potential for reduced anticoagulant drug concentration and increased risk of thrombosis. The prescribing information for both apixaban and rivaroxaban recommend the avoidance of concurrent use with combined P-glycoprotein and strong CYP3A4 inducers. Considering this, the recommendation is to avoid concurrent use of dexamethasone with apixaban/rivaroxaban when possible. The majority of concurrent use is expected in COVID patients with a time limited exposure to dexamethasone.

Details of the Potential Interaction:

- Only a small portion of the rivaroxaban and apixaban are metabolized by CYP 3A4 however the level of P-gp induction with dexamethasone in humans has not been characterized.
- In equipotent doses dexamethasone has 6 times the anti-inflammatory properties of methylprednisolone (0.75mg dexamethasone = 4mg methylprednisolone)
- The onset of enzyme induction is estimated to be 4-5 days and the offset is related the half-life of the steroid. Dexamethasone is long acting (36-72 hrs) therefore full offset will be delayed
- Although all steroids are thought to have some capability of inducing CYP3A4, the magnitude appears less with steroids other than dexamethasone. In addition, other steroids are not known inducers of P-glycoprotein.

Recommended Approach to Manage Drug Interaction:

1. Change anticoagulant to enoxaparin or heparin infusion for the duration of dexamethasone therapy.
2. If apixaban/rivaroxaban needs to be continued it is recommended to consider switching the patient's steroid.
3. This interaction CANNOT be managed by increasing the dose of the apixaban/rivaroxaban.

Steroid Conversion Table²

Steroid	Route	Equivalent Dose (mg)	Duration of Action
Betamethasone	IV	0.75	Long (36-72 Hours)
Cortisone	PO	25	Short (8-12 Hours)
Dexamethasone (Decadron)	IV or PO	0.75	Long (36-72 Hours)
Hydrocortisone	IV or PO	20	Short (8-12 Hours)
Methylprednisolone	IV or PO	4	Medium (8-12 Hours)
Prednisolone	PO	5	Medium (12-36 Hours)
Prednisone	PO	5	Medium (12-36 Hours)
Triamcinolone	IV	4	Medium (12-36 Hours)

References:

1. Steffel J, Verhamme P, Potpara TS et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin-K antagonist oral anticoagulants in patients with atrial fibrillation, Eur Heart J 2018;39:1330-93.
2. Hayes, Bryan, and Nadia Awad. "Steroid Conversion Calculator." *MDCalc*, www.mdcalc.com/steroid-conversion-calculator.