Guidance for the Use of Non-oral Steroids with Strong CYP3A4 Inhibitors

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Recommendations for non-oral steroids with strong CYP3A4 inhibitors

		Preferred	Caution required *(only coadminister if necessary)*	Do Not Coadminister	Follow Up
Drugs for HIV					
Any combination containing any of the following: • Atazanavir • Cobicistat • Darunavir • Lopinavir • Ritonavir	*Inhaled*	**Beclometasone**		**Budesonide** **Fluticasone** **Mometasone**	Periodic control of morning cortisol
	Nasal	**Beclometasone**		**Budesonide** **Fluticasone** **Mometasone**	
	Intra-articular or epidural	**Prednisolone** (30% dose reduction required) **Methylprednisolone** (at least 50% dose reduction required)		**Triamcinolone**	
	Topical	**Hydrocortisone**	**Clobetasol** **Betamethasone** **Fluocinolone**		
Any other HIV drug combinations		Check with pharmacist	Check with pharmacist	Check with pharmacist	Check with pharmacist
Drugs for Hepatitis C					
Any DAA combination containing the following: • Paritaprevir/ritonavir	*Inhaled* *Nasal* *Intra-articular or epidural* *Topical*	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Periodic control of morning cortisol
Others					
Any potent CYP3A4 inhibitor (particularly in case of long term treatment) including: • Clarithromycin • Erythromycin • Itraconazole • Ketoconazole • Posaconazole • Voriconazole	*Inhaled* *Nasal* *Intra-articular or epidural* *Topical*	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Same recommendations as for HIV protease inhibitors and pharmacokinetic boosters	Periodic control of morning cortisol

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Management of patients with a suspected steroid-CYP3A4 inhibitor interaction

Is the patient receiving a CYP3A4 inhibitor and concomitant steroid via any route?

Is there potential for a drug-drug interaction with steroid? (Discuss with pharmacist/specialist)

- Unlikely → Careful ongoing clinical monitoring
- Yes →

Inhaled/nasal/topical steroids

Conduct joint review of the steroid first with specialist/endocrine/HIV teams:
- ***Inhaled steroids*** – switch to beclometasone or a steroid-sparing agent
- ***Topical steroids*** – limit exposure, consider switch to steroid sparing agents

If steroid with high interaction risk is unavoidable, discuss with HIV team to remove CYP3A4 inhibitor where possible.

Injectable steroids

Intra-muscular / Intra-articular / Epidural:
- This cannot be removed. Discuss with HIV team to switch CYP3A4 inhibitor.
- If not possible, monitor closely.
- Avoid further injections – consider disease-modifying antirheumatic drugs (DMARDs) in future.

If patient acutely unwell, hypotensive ± hyponatraemic: measure serum cortisol, commence steroid replacement and discuss with endocrine team

Arrange for 9 am cortisol

If 9 am cortisol <450 nmol/L*, arrange for short synachten test (SST)

- If SST normal (peak cortisol >550 nmol/L*), no need for further testing. Monitor closely. → If ongoing exposure to CYP3A4 inhibitor and steroid, return to top of chart and follow.
- If abnormal SST (peak cortisol <550 nmol/L*), start steroid replacement in patients with symptoms of adrenal insufficiency. Asymptomatic patients - discuss with local endocrine team. → Repeat 9 am cortisol and/or the SST every 8 weeks in order to assess for recovery of the hypothalamic-pituitary-adrenal axis. Stop any steroid replacement once 9 am cortisol ≥450 nmol/L* or post SST cortisol >550 nmol/L*.

If 9 am cortisol ≥450 nmol/L*, monitor clinically. No need for further testing unless very high index of suspicion of secondary adrenal insufficiency.

→ If ongoing exposure to CYP3A4 inhibitor and steroid, return to top of chart and follow.

Other steps:
- Patients with secondary adrenal insufficiency – provide information leaflet with steroid sickness rules and advise to attend emergency department if they become unwell
- Complete incident form and inform patient's GP and other relevant specialists

* Depending on local assay

Adapted with permission from Elliot ER et al. Clin Med, 2016, 16: 412-418

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