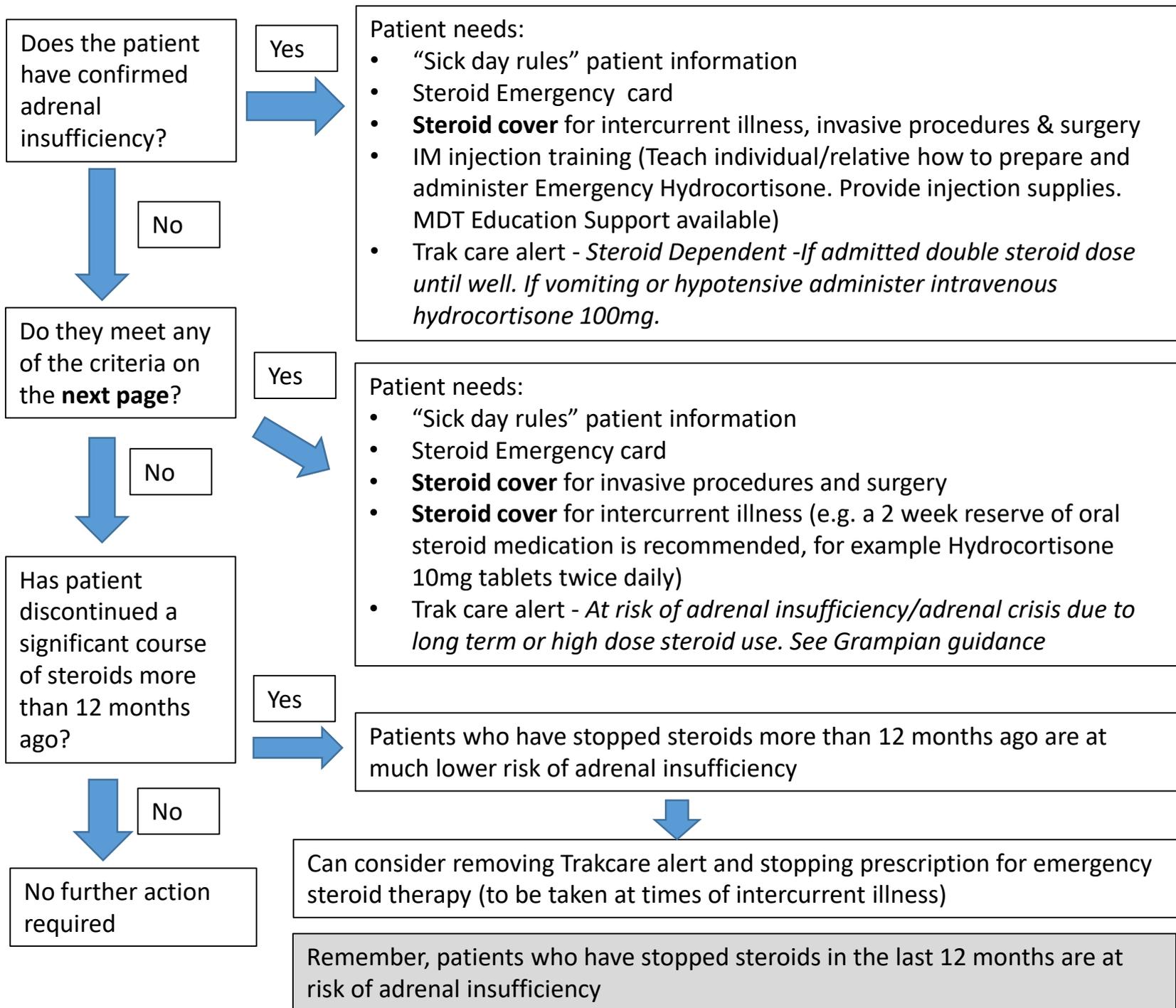


# Is my patient at risk of adrenal insufficiency?

A guide for healthcare professionals involved in the prescription and maintenance of steroid therapy to adult patients



Route of steroid administration	Table Number	Route of steroid administration	Table Number
Oral	Tables 1 & 2	Topical	Table 4
Inhaled	Table 3	Rectal	Table 5

This protocol is for adult patients. Further information (including for paediatric patients) can be found at <https://www.endocrinology.org/adrenal-crisis>

For an assessment of adrenal insufficiency (generally performed in patients not receiving steroid therapy) please see "Assessment of adrenal function using morning cortisol" document

## HAS YOUR PATIENT TAKEN A SIGNIFICANT COURSE OF STEROIDS?

If they meet any of the below criteria then give “sick day rules” advice **IN ADDITION** to steroid emergency card **AND** steroid cover for intercurrent illness, invasive procedures and surgery (i.e. ensure supply of oral rescue steroids is available).

Patients taking oral prednisolone 5mg or above (or equivalent dose of other oral glucocorticoids ) for more than 4 weeks, **and for 12 months after stopping oral steroids** (see Table 1)

Patients receiving intra-articular or intramuscular glucocorticoid injections **who also use glucocorticoids by another route** (e.g. inhaled steroids, oral steroids etc.)

Concomitant use of CYP3A4 enzyme inhibitors (table 6) and glucocorticoids (any route of administration except small amounts of topical mild or moderate potency glucocorticoid which should be assessed on a case-by-case basis)

Patients with respiratory disease such as COPD and asthma on high dose inhaled steroids receiving repeated courses of oral steroids (**3 or more courses over the past 6 months**).

3 or more short courses of high-dose oral glucocorticoids within the last 12 months, and for 12 months after stopping (see Table 2).

3 or more intra-articular/intramuscular glucocorticoid injections within the last 12 months, and for 12 months after stopping.

Repeated courses of dexamethasone as an antiemetic in oncology regimens, and for 12 months after stopping (**the Steroid Emergency Card should be given on first cycle of dexamethasone**) when future cycles are anticipated.

Prolonged courses of dexamethasone (>10 days) for the treatment of severe Covid-19.

Inhaled steroids >1000mcg/day beclomethasone or >500mcg/day fluticasone (or equivalent dose of another glucocorticoid), and for 12 months after stopping (see Table 3).

Patients taking inhaled corticosteroids at doses described in right hand column of Table 3 and **ANY** other form of glucocorticoid treatment (including potent/very potent topical glucocorticoids, intra-articular injection, regular nasal glucocorticoids).

Topical high-dose (>= 200g/ week) potent or very potent glucocorticoids used across a large area of skin for 4 weeks or more, or factors increasing absorption assessed on a case-by-case basis, and for 12 months after stopping (see Table 4).

Potent or very potent topical glucocorticoids applied to the rectal or genital areas and used at high dose (more than 30g per month) for more than 4 weeks, and for 12 months after stopping (see Table 5).

There is no need for the above patients to be issued with an emergency hydrocortisone injection kit unless there is specific clinical concern.

# What is a significant course of steroids?

**Table 1: Long-term oral glucocorticoids (i.e. 4 weeks or longer)**

Beclometasone	625 microgram per day or more
Betamethasone	750 microgram per day or more
Budesonide	1.5mg per day or more
Deflazacort	6mg per day or more
Dexamethasone	500 microgram per day or more
Hydrocortisone	15mg per day or more
Methylprednisolone	4mg per day or more
Prednisolone	5mg per day or more

The detailed guidance regarding exogenous steroid therapy and risk of adrenal insufficiency is available [here](#)

Lists are in alphabetical order

**Table 2: Short-term oral glucocorticoids (one week course or longer AND has been on long-term course within the last year or has regular need for repeated courses)**

Beclometasone	5mg
Betamethasone	6mg per day or more
Budesonide	12mg
Deflazacort	48mg per day or more
Dexamethasone	4mg per day or more
Hydrocortisone	120mg per day or more
Methylprednisolone	32mg per day or more
Prednisolone	40mg per day or more

**Intra-articular glucocorticoid injections:**

A single intra-articular glucocorticoid injection is unlikely to permanently suppress the HPA axis, but if a patient has major surgery, trauma or intercurrent illness within 28 days of having an intra-articular glucocorticoid steroid injection, then they may be at risk of AI.

If a patient is receiving repeated intra-articular glucocorticoid injections, they should be considered at risk of HPA axis suppression. If they are also on an additional steroid, for example a moderately high-dose of inhaled glucocorticoid (see Table 4), then permanent HPA axis suppression can occur and further assessment should be considered.

# What is a significant course of steroids? - continued

Table 3: Inhaled glucocorticoid doses	If no additional steroid therapy	If using nasal glucocorticoids as well
Beclometasone (as non-proprietary, Clenil, Easihaler, or Soprobeq)	>1000 mcg per day	≥800 mcg per day
Beclometasone (as Qvar, Kelhale or Fostair )	>500 mcg per day	≥400mcg per day
Budesonide	>1000 mcg per day	≥800 mcg per day
Ciclesonide	>480 mcg per day	≥320 mcg per day
Fluticasone propionate	>500 mcg per day	≥400 mcg per day
Fluticasone furoate (as Trelegy and Relvar)	>200 mcg per day	≥100 mcg per day
Mometasone	>800 mcg per day	≥400 mcg per day

**Nasal glucocorticoids**

The guidance suggests an indicative threshold of 1000 micrograms per day. This limit is extremely unlikely to be reached using any of the “over the counter” preparations or available glucocorticoid sprays or drops for allergic rhinitis but may be an issue with prescription drops used to treat nasal polyps.

**Steroid eye drops**

The guidance suggests an indicative threshold of 1000 micrograms per day. This limit is extremely unlikely to be reached using any of the available glucocorticoid eye drops for allergic conjunctivitis. If the patient is only on steroid eye drops, HPA axis suppression is unlikely.

Lists are in alphabetical order

The detailed guidance regarding exogenous steroid therapy and risk of adrenal insufficiency is available [here](#)

## What is a significant course of steroids? - continued

### Topical glucocorticoid creams and ointments

Whilst low dose topical steroids rarely cause adrenal insufficiency, potent and very potent glucocorticoids ( $\geq 200\text{g}$  per week) (listed in table 4), can cause adrenal insufficiency. All other topical glucocorticoids available in the UK are either mild or moderate potency and would not generally thought to be at risk of provoking adrenal insufficiency.

**Table 4: Topical glucocorticoids**

Beclometasone dipropionate 0.025%	potent
Betamethasone dipropionate 0.05% and higher [incl Dalonev, Diprosone, Dovobet, Enstilar, in combination with clotrimazole (incl Lotriderm) and salicylic acid (incl Diprosalic)]	potent
Betamethasone valerate 0.1% and higher [incl Audovate, Betacap, Betesil, Betnovate, Bettamousse, and in combination with clioquinol, fusidic acid (incl Fucibet, Xemacort) or neomycin]	potent
Clobetasol propionate 0.05% and higher [incl. Clarelux, ClobaDerm, Dermovate, Etrivex and in combination with neomycin and nystatin]	Very potent
Diflucortolone valerate 0.1% [incl Nerisone]	Potent
Diflucortolone valerate 0.3% [incl Nerisone Forte]	Very potent
Fluocinonide 0.05% [incl Metosyn]	potent
Fluocinolone acetonide 0.025% [(incl. Synalar) and in combination with clioquinol (incl Synalar C)]	Potent
Fluticasone propionate 0.05% [incl Cutivate]	Potent
Hydrocortisone butyrate 0.1% [incl Locoid]	Potent
Mometasone 0.1% [incl Elocon]	Potent
Triamcinolone acetonide 0.1% [incl Aureocort]	Potent

### Rectal glucocorticoids

There are some reports of rectal glucocorticoids causing adrenal insufficiency when used for inflammatory bowel disease. Table 5 gives an outline of clinically significant glucocorticoid doses in rectal formulations. Using other rectal formulations would be unlikely to lead to HPA suppression.

**Table 5: Rectal treatments which contain significant amounts of glucocorticoid**

Budesonide enema	contains 2mg per dose
Budesonide rectal foam	contains 2mg per dose
Prednisolone rectal solution	contains 20mg per dose
Prednisolone suppositories	contains 5mg per dose

# What is a significant course of steroids? - continued

**Table 6. CYP3A4 enzyme inhibitors increasing cortisol concentration and risk of HPA axis suppression**

Potent Protease inhibitors:	Atazanavir Darunavir Fosamprenavir Ritonavir (+/- lopinavir) Saquinavir Tipranavir
Antifungals:	Itraconazole Ketoconazole Voriconazole Posaconazole
Antibiotics:	Clarithromycin—long term courses only