British Thoracic Society

NHS Steroid Emergency Card and National Patient Safety Alert: what this means for your patients

‘High Dose ICS - for the few and not the many…’

15.07.2021

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Implications for Practicing Clinicians

- High dose ICS and adrenal insufficiency
- High dose ICS for the few and not the many
- Identify and manage high dose ICS – in the context of NatPSA
- Summary

High dose ICS and adrenal insufficiency

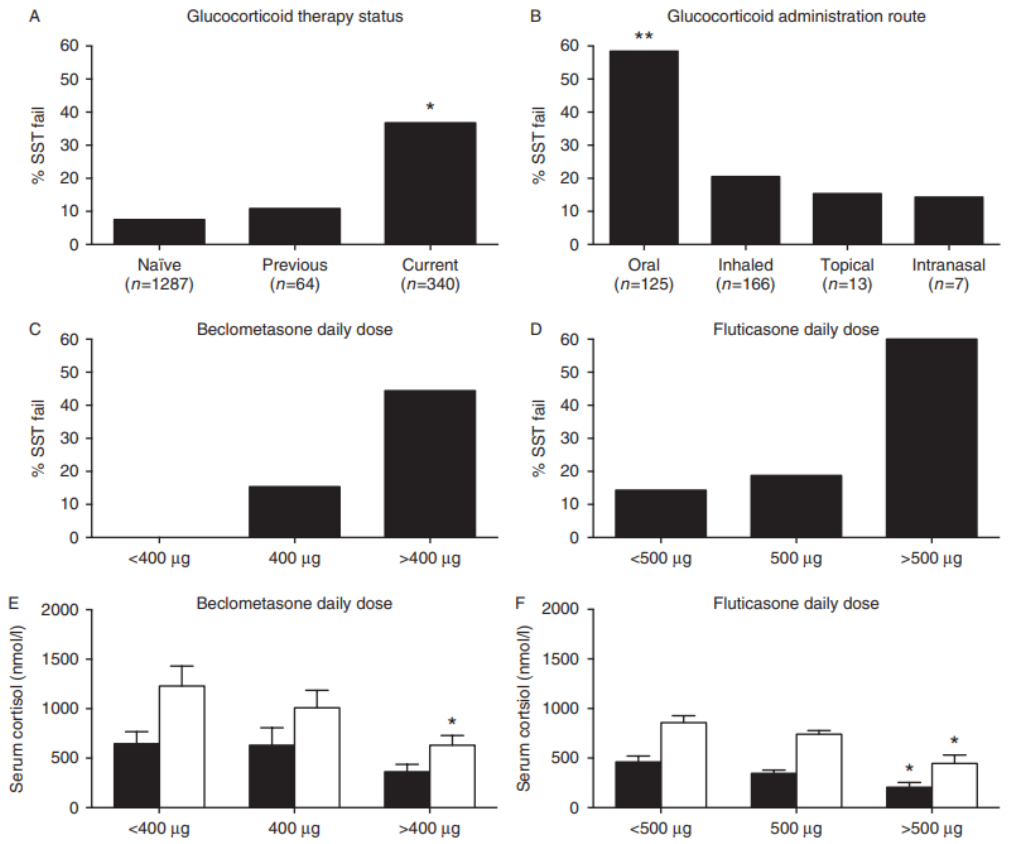
Table 3 Association between mean daily dose of inhaled corticosteroid and adrenal insufficiency

Mean daily dose of ICS (µg)	Cases (n = 154) N	Cases (n = 154) %	Controls (n = 870)* N	Controls (n = 870)* %	OR (95% CI)	OR adjusted for OCS (95% CI)†
0	132	85.7	830	95.4	Reference	Reference
<600	6	3.9	21	2.4	1.6 (0.6 to 4.1)	0.6 (0.2 to 2.3)
600.1–1200	10	6.5	15	1.7	4.6 (1.9 to 10.2)	2.5 (1.0 to 6.2)
>1200.1	6	3.9	3	0.3	13.3 (13.3 to 53.9)	3.7 (0.7 to 19.2)
p value for trend					<0.001	0.036

ICS, inhaled corticosteroid; OCS, oral corticosteroid.
*One missing data point.
†Adjusted for number of courses of oral corticosteroids per year.

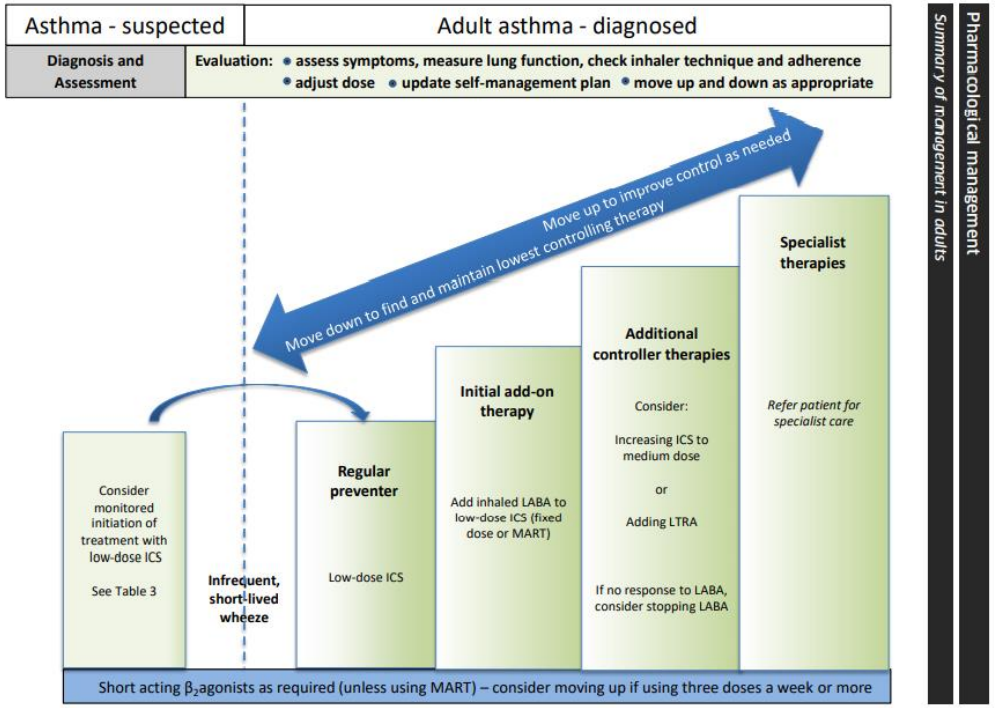
Mortimer KJ et al, Thorax 2006

- High dose ICS are associated with adrenal insufficiency ± adrenal insufficiency related adverse events.
- FP particularly problematic
- Precise number/nature of cases of harm in patients on ICS alone from the National Reporting and Learning system review that triggered NatPSA unclear.



Woods PC et al, European Journal of Endocrinology 2015

Indications for ICS use in asthma and COPD



BTS/SIGN guidelines (2019)

FACTORS TO CONSIDER WHEN INITIATING ICS TREATMENT

Factors to consider when initiating ICS treatment in combination with one or two long-acting bronchodilators (note the scenario is different when considering ICS withdrawal):

· STRONG SUPPORT ·	· CONSIDER USE ·	· AGAINST USE ·
• History of hospitalization(s) for exacerbations of COPD#	• 1 moderate exacerbation of COPD per year#	• Repeated pneumonia events
• ≥ 2 moderate exacerbations of COPD per year#	• Blood eosinophils 100-300 cells/μL	• Blood eosinophils <100 cells/μL
• Blood eosinophils >300 cells/μL		• History of mycobacterial infection
• History of, or concomitant, asthma		

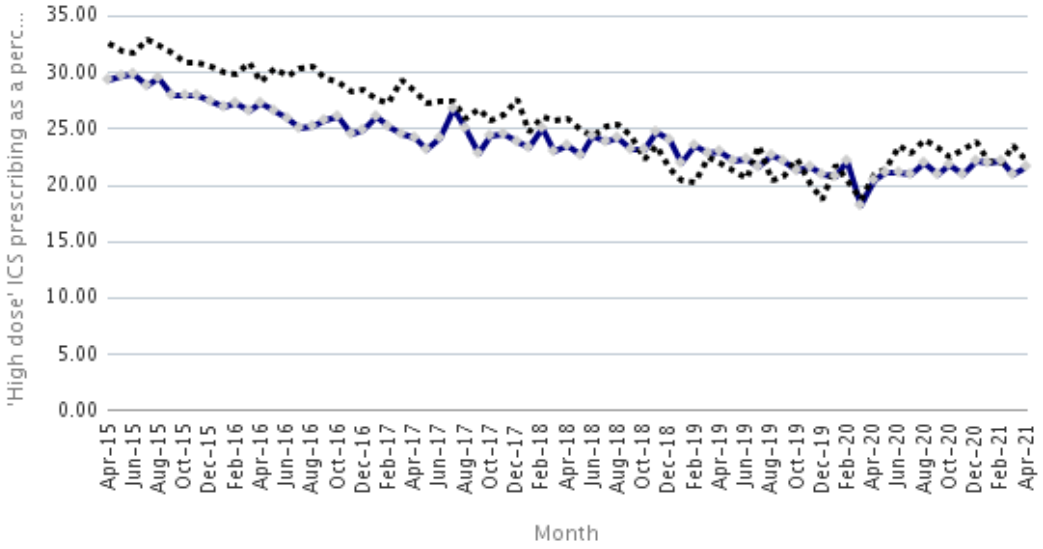
GOLD guidelines (2020)

What is high dose ICS (a few examples)

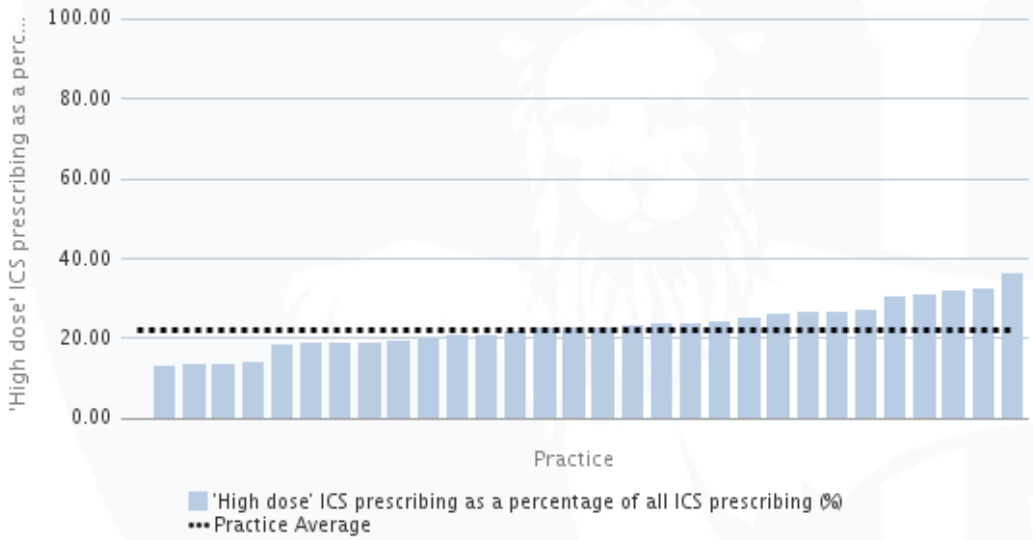
ICS, ICS/LABA	High Dose ICS Equivalent	Asthma	COPD
QVAR pMDI **> 400**	100 mcg, 4 puffs, bid (800 mcg)	Specialist therapy	n/a
Ciclesonide **> 320**	160 mcg, 2 puffs, bid (640 mcg)	Specialist therapy	n/a
DuoResp Spiromax	320/9, 2 puffs, bid (1280 mcg)	Specialist therapy	unlicensed
Pulmicort/Symbicort turbohaler **> 800**	400 mcg, 2 puffs, bid (1600 mcg)	Specialist therapy	unlicensed
Flixotide Accuhaler, AirFlusal, Seretide DPI/MDI, Sirdupla **> 500**	500 mcg bid (1000 mcg)	Specialist therapy	*Yes- Airflusal or Seretide*
Fostair pMDI or NEXThaler **> 400**	200/6 mcg, 2 puffs, bid (800 mcg)	Specialist therapy	unlicensed
Relvar Ellipta **> 92**	184/22 one puff, once daily (184 mcg)	Specialist therapy	unlicensed
Triple therapy combinations	various	*Not high dose ICS*	*Not high dose ICS*

National and regional variations in high dose ICS prescribing

East Leicestershire and Rutland CCG

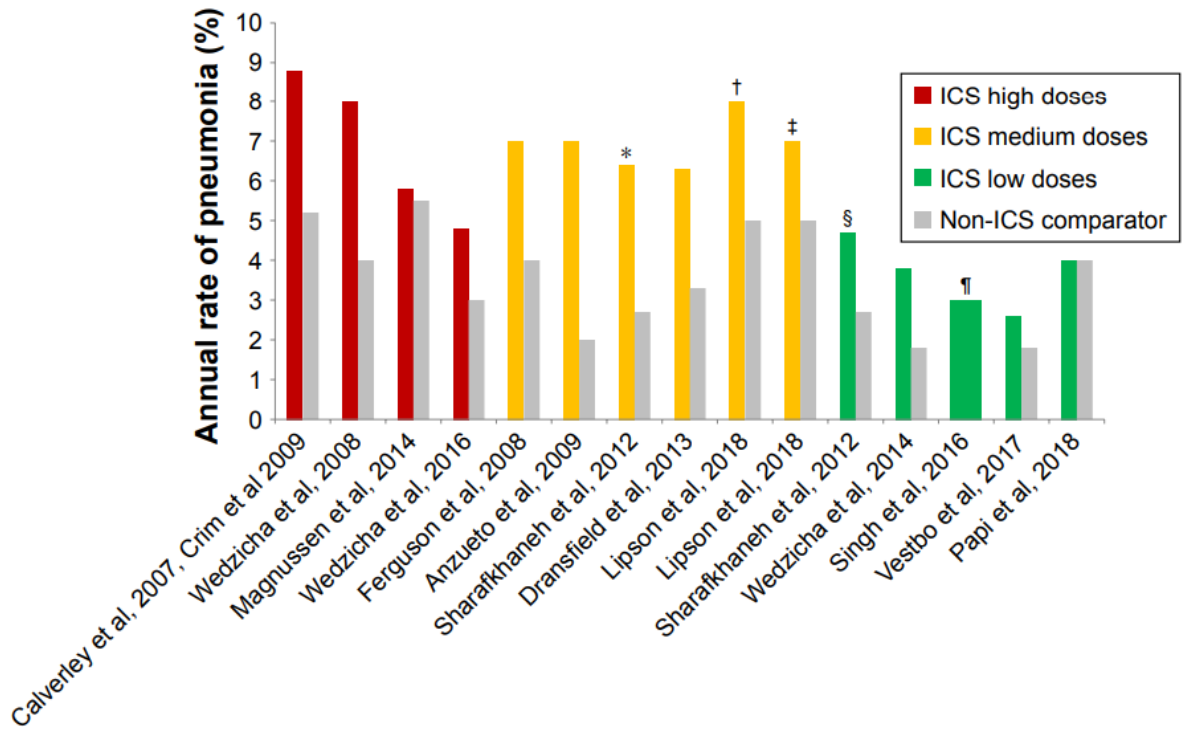


East Leicestershire and Rutland CCG



ePACT2 data – High dose ICS prescribing (Courtesy of Professor Anna Murphy)

High dose ICS & COPD



- Unlicensed for the majority of ICS formulations in COPD
- Higher load of airway bacteria
- Higher pneumonia risk
- Increased risk of mycobacterial infection

Izquierdo JL *et al*, International Journal of COPD (2018)

High dose ICS for the few and not the many

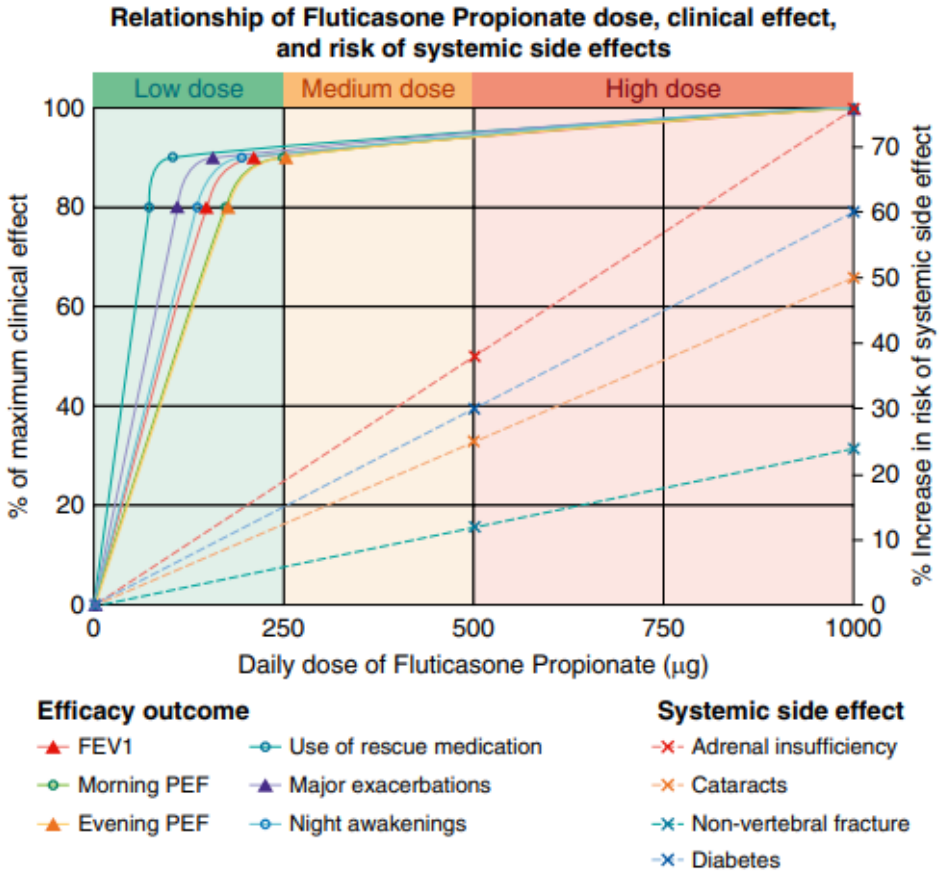
Inhaled Corticosteroid	Dose (μg/d) Low	Medium	High	Bioequivalence*
Beclomethasone dipropionate (CFC)	200–500	>500–1,000	>1,000	1.0
Beclomethasone dipropionate (HFA)	100–200	>200–400	>400	2.5
Budesonide (DPI)	200–400	>400–800	>800	1.25
Ciclesonide (HFA)	80–160	>160–320	>320	3.125
Fluticasone propionate (HFA)	100–250	>250–500	>500	2.0
Fluticasone furoate (DPI)	100	NA	200	5.0
Mometasone furoate	110–220	>220–440	>440	2.25

Definition of abbreviations: CFC = chlorofluorocarbon propellant; DPI = dry powder inhaler; HFA = hydrofluoroalkane propellant; NA = not applicable.
*Bioequivalence compared with beclomethasone dipropionate, derived from the stated "high dose."

Doses of Fluticasone Propionate at Which 80% and 90% of Maximum Effect Are Achieved, as Derived from a Negative Exponential Model

Outcome Measure	80% of Maximum Effect Achieved	90% of Maximum Effect Achieved
FEV_1	146	209
Morning PEF	172	247
Evening PEF	175	251
Use of rescue medication	71	102
Major exacerbations	108	155
Night awakenings	135	193

Data derived from Holt S *et al*, BMJ (2001)



Beasley R et al, AJRCCM (2019)

Practical implementation NatPSA - Identify high dose ICS

Patients who require to be issued a Steroid Emergency Card

University Hospitals of Leicester NHS
NHS Trust

ORAL glucocorticoids

Medicine	Dose (on or above for total daily dose) 4 weeks or longer	Short course 1 week or longer but has been on longer course or mOCS during year
Beclometasone	625microgram	5mg
Betamethasone	750micrograms	6mg
Budesonide	1.5mg	12mg
Deflazacort	6mg	48mg
Dexamethasone	500microgram	4mg
Hydrocortisone	15mg	120mg
Methylprednisolone	4mg	32mg
Prednisone	5mg	40mg
Prednisolone	5mg	40mg

In addition the following:
- Respiratory patients who receive repeat rescue packs of steroids (3 or more)
- Dexamethasone
  - used as an antiemetic in repeat cycles for chemotherapy
  - a long high dose use as part of ARDS regimen for severe Covid-19 infection

Eye drops	Unlikely to suppress HPA axis but consider if used with other routes
Intra-articular	A single dose unlikely to suppress HPA axis permanently but consider if repeated injections
Rectal	30g per month or more for over 4 week Those containing significant amounts of glucocorticoids Budesonide enema 2mg per dose Budesonide rectal foam 2mg per dose Prednisolone rectal solution 20mg per dose Prednisolone suppositories 5mg per dose

INHALED Glucocorticoids

Medicine	Doses greater than (per day)	Inhaled dose when a nasal glucocorticoid is also used
Beclometasone (Clenil, Easyhaler, Soprobec)	1000 microgram	800-1000 micrograms
Beclometasone (Qvar, Kelhale, Fostair)	500 micrograms	400-500 micrograms
Budesonide	800 micrograms	400-800 micrograms
Ciclesonide	320 micrograms	160-320 micrograms
Fluticasone proprionate	500 micrograms	400-500 micrograms
Fluticasone fuorate	184 micrograms	92-184 micrograms
Mometasone	800 micrograms	400-800 micrograms

Check if using combination inhalers or MART regimen

TOPICAL glucocorticoid creams and ointments

Those using potent or very potent glucocorticoid on extensive areas for 4 weeks or more

Potent	Very potent
Beclomethasone dipropionate 0.025% Betamethasone valerate 0.1% or higher Diflucortolone valerate 0.1% Fluocinonide 0.05% Fluocinolone acetonide 0.025% Fluticasone propionate 0.05% Hydrocortisone butyrate 0.1% Mometasone 0.1% Triamcinolone acetonide 0.1%	Clobetasol propionate 0.05% or higher Diflucortolone valerate 0.3%

Consider when treating patients on high dose inhaled steroids (see above)

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- Adjust down ICS dose equivalence If on concurrent topical CS by up to 50%
- Patient on Fostair 100/6 two actuation twice a day for asthma, starts Avamys (Fluticasone Fuorate) 27.5mcg/nostril OD for CRS - is on high dose topic CS and needs a steroid card..

McKechnie E, UHL specialist pharmacist

Practical implementation - Clinical review

- Clinically indicated
- Review & optimise inhaler technique
- Other reasons for poor symptom control
- Adherence e.g. prescription refils
- Consider measuring FeNO to guide decisions
- Consider ICS step down after optimising the above

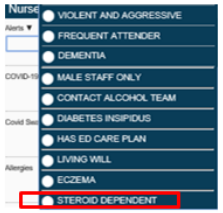
CYP3A4 enzyme inhibitors & HPA suppression

- Be aware of HPA suppression in patients on ***any dose*** of glucocorticoid and use of the following drugs

- Anti fungal e.g. itraconazole and voriconazole
- Long tern macrolide antibiotics
- Protease inhibitors (HIV) e.g. Ritonavir, Saquinavir

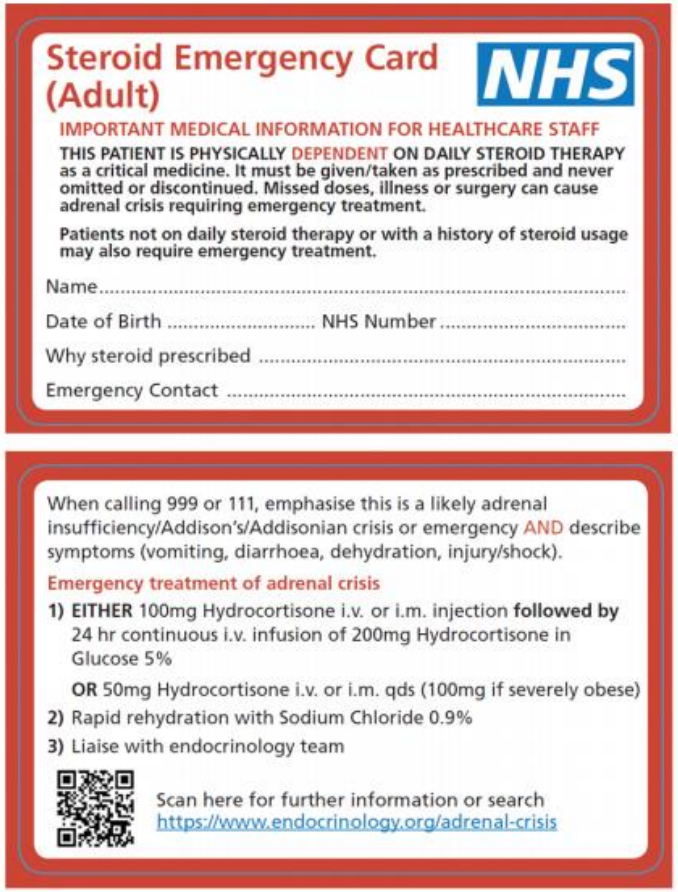
- **All** of these patients should receive a steroid emergency card

Practical implementation - Flag tag and alert

Situation	• **Steroid Dependent Alert** can be inserted on Nervecentre (UHL patient management software) • This will be visible in the Alert section of the patient's details on Nervecentre.
Background	• This alert is created to identify patients on long term steroids or who are steroid dependent, to improve patient safety.
Action	• An Alert for **Steroid Dependen**t patient is now added to the alert list on Nervecentre as per the image below.  • Once Steroid Dependent Alert selected, this would create a permanent tag as per the image below.  • All clinical and pharmacy staff should identify steroid dependent patients and update the alert section as above as well as issue **Steroid Emergency Card**.
Recommendations	• For any queries please contact the Clinical Facilitators mailbox: clinicalfacilitator@uhl-tr.nhs.uk or through the helpline: [redacted]

Implementation on primary care systems e.g. EMIS & SystmOne?

Practical implementation - Issue a steroid alert card



Steroid Emergency Card (Adult)

NHS

IMPORTANT MEDICAL INFORMATION FOR HEALTHCARE STAFF

THIS PATIENT IS PHYSICALLY DEPENDENT ON DAILY STEROID THERAPY as a critical medicine. It must be given/taken as prescribed and never omitted or discontinued. Missed doses, illness or surgery can cause adrenal crisis requiring emergency treatment.

Patients not on daily steroid therapy or with a history of steroid usage may also require emergency treatment.

Name.....

Date of Birth ..... NHS Number .....

Why steroid prescribed .....

Emergency Contact .....

When calling 999 or 111, emphasise this is a likely adrenal insufficiency/Addison's/Addisonian crisis or emergency AND describe symptoms (vomiting, diarrhoea, dehydration, injury/shock).

Emergency treatment of adrenal crisis

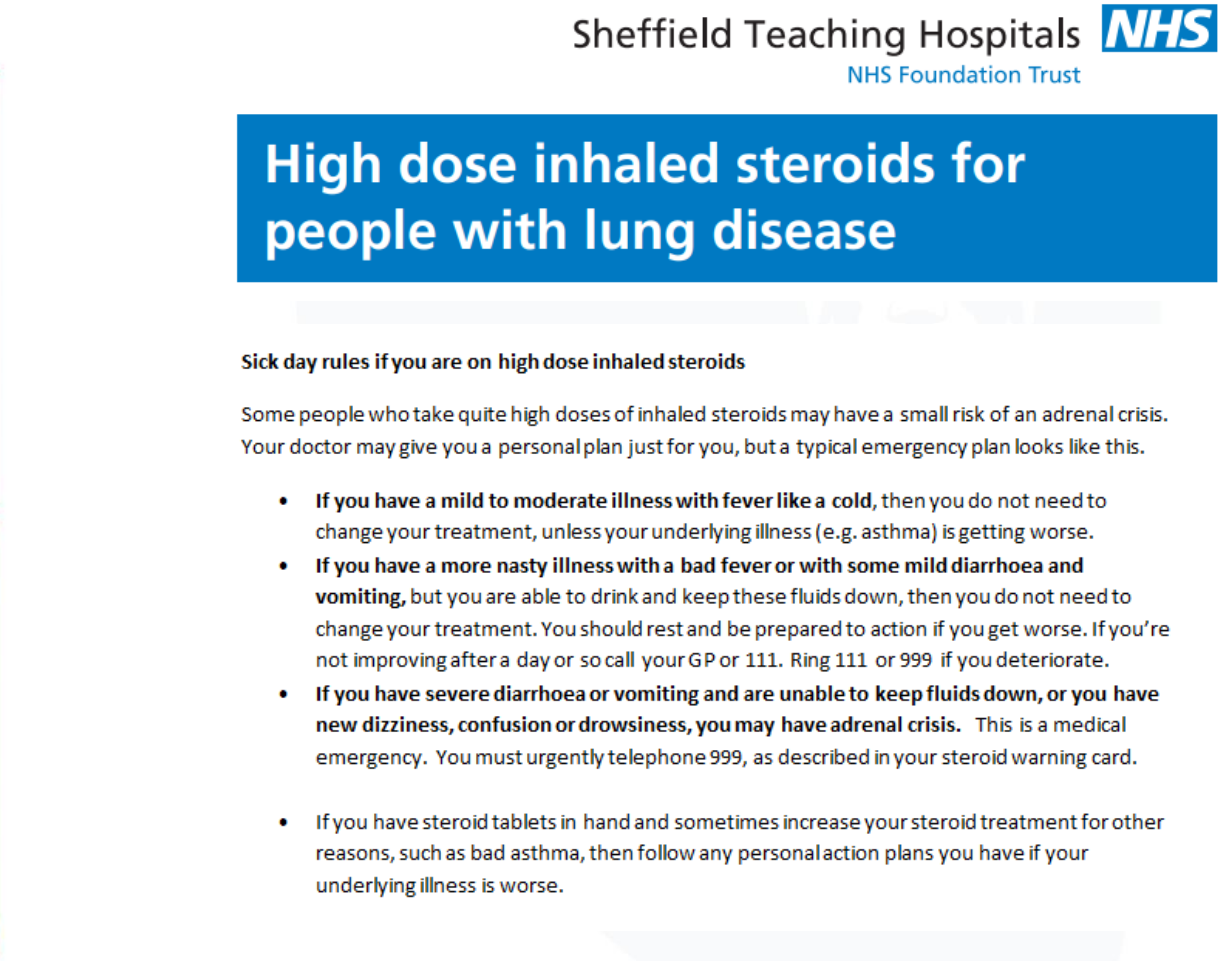
1) **EITHER** 100mg Hydrocortisone i.v. or i.m. injection **followed by** 24 hr continuous i.v. infusion of 200mg Hydrocortisone in Glucose 5%

   OR 50mg Hydrocortisone i.v. or i.m. qds (100mg if severely obese)

2) Rapid rehydration with Sodium Chloride 0.9%

3) Liaise with endocrinology team

Scan here for further information or search https://www.endocrinology.org/adrenal-crisis



Sheffield Teaching Hospitals NHS
NHS Foundation Trust

High dose inhaled steroids for people with lung disease

Sick day rules if you are on high dose inhaled steroids

Some people who take quite high doses of inhaled steroids may have a small risk of an adrenal crisis. Your doctor may give you a personal plan just for you, but a typical emergency plan looks like this.

- **If you have a mild to moderate illness with fever like a cold**, then you do not need to change your treatment, unless your underlying illness (e.g. asthma) is getting worse.
- **If you have a more nasty illness with a bad fever or with some mild diarrhoea and vomiting,** but you are able to drink and keep these fluids down, then you do not need to change your treatment. You should rest and be prepared to action if you get worse. If you're not improving after a day or so call your GP or 111. Ring 111 or 999 if you deteriorate.
- **If you have severe diarrhoea or vomiting and are unable to keep fluids down, or you have new dizziness, confusion or drowsiness, you may have adrenal crisis.** This is a medical emergency. You must urgently telephone 999, as described in your steroid warning card.

- If you have steroid tablets in hand and sometimes increase your steroid treatment for other reasons, such as bad asthma, then follow any personal action plans you have if your underlying illness is worse.

What about mOCS?

- Use established secondary care endocrinology guidelines, patient information and sick day rules

Summary

- **New NatPSA mandates steroid cards in patients on high dose ICS**
- This is an opportunity to review whether high dose ICS are indeed necessary in relevant patient groups e.g. asthma/COPD
- **Where they are necessary after clinical review - appropriate electronic flag tags and steroid card with patient education are needed**
- Identify/examine outliers in prescribing within CCGs via integrated care services?
- Further evidence of high dose ICS related harm due to AI needs to be gathered from local/national surveillance systems