

Guidance for Healthcare Professionals on Inhaled Corticosteroids in Adults

The side effect profile of an ICS

- Inhaled corticosteroids (ICS) are prescribed in asthma to improve control, reduce exacerbations and risk of death, and in those with severe to very severe COPD, to reduce the frequency of exacerbations. The benefits of an ICS outweigh the risks when used in clinically effective doses, however, long-term high doses (≥ 1000 micrograms beclometasone dipropionate (BDP) equivalent/day) may cause systemic side effects.
- The systemic side effects of corticosteroids are well known. High doses of ICS are associated with clinically detectable adrenal suppression (*Arch Intern Med* 1999;**159**:941-55), increased risk of non-fatal pneumonia in patients with COPD (*Arch Intern Med* 2009;**169**:219-29), increased risk of type II diabetes (*Am J Med* 2010;**123**:10016), and may increase the risk of fractures (*Thorax* 2011;**66**:699-708) and tuberculosis (*Chest* 2014;**145**(6):1286-1297). It is recommended that all patients on high doses of ICS are made aware of the risks and given an ICS safety warning card. This card should be completed by a healthcare professional for each individual patient prior to issue.
- At equipotent doses, the safety profiles of all ICS are similar. Budesonide and ciclesonide are approximately equipotent with BDP, while fluticasone propionate (FP), mometasone and ultrafine particle BDP-HFA inhalers (Qvar® and Fostair®) are twice as potent as standard BDP inhalers. Equivalence data for fluticasone furoate is not currently available.

In patients with Asthma:

- Once a patient has persistently good control (e.g. for 3 months), consider stepping down to the lowest dose of ICS that maintains symptom control.
- There is limited evidence that increasing an ICS dose above 800 micrograms BDP equivalent/day improves asthma control, even in acute exacerbations (Cochrane Review CD007524). MHRA guidance suggests that a total daily dose of 500-1000 micrograms of fluticasone propionate should only be prescribed for moderate to severe asthma, with doses above this, only prescribed by an asthma specialist, when additional benefit is expected or demonstrated, or by the ability to reduce oral corticosteroid use (<http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con007456.pdf>).

In patients with COPD:

- In severe COPD ($FEV_1 < 50\%$), an ICS+LABA may reduce the frequency of exacerbations. Clinical trials in severe COPD and ≥ 2 exacerbations/year, suggest that twice daily inhalation of Symbicort (budesonide/formoterol) 400/12 (*ERJ* 2003;**22**:912-19, *ERJ* 2003;**21**:74-81), Fostair (beclometasone HFA/formoterol) 200 micrograms (*Respir Med* 2010;**104**:1858-68) and Seretide (FP/salmeterol) 500 Accuhaler (*NEJM* 2007;**356**:775-89) are equally effective in reducing the frequency of exacerbations. Patients taking Seretide will need an ICS card whereas those prescribed Symbicort, DuoResp and Fostair may not.

Before increasing an ICS (or any therapy) the following are recommended:

1. **Check adherence** to therapy. Very few patients take their medicines as directed all the time. Sub-optimal inhaler technique or not taking the medicines regularly as directed are common, but often fixable causes of treatment failure. Always ask the patient to describe *how* they take their medicines in a non-judgmental way – the purpose is to discover if you should change therapy or discuss how to take current therapy more effectively.
2. **Improve ICS delivery** to the lungs. This may be more effective than increasing the dose, so inhaler technique must be checked and optimized regularly. Using a metered dose inhaler (MDI) with a spacer device improves lung deposition (*Br J Clin Pharmacol* 1998;**46**:45-8, *Clin Pharmacokinet* 2004;**43**:349-60) and in aiding co-ordination, reduces oropharyngeal deposition and local side effects (eg hoarseness or sore throat).
3. **Encourage people to stop smoking.** Provide stop smoking therapy for people with COPD and asthma who smoke. In COPD, intervening early reduces mortality (*Ann Intern Med*. 2005;**142**:233-239) and improves health status (*Thorax*. 2010;**65**:711-8). In asthma, stopping smoking may avoid the need for stepping up ICS dose when poorly controlled (*Thorax* 2005;**60**:282-287).

Doses of inhaled corticosteroids in adults that require an inhaled corticosteroid card

	Total Daily Dose of Inhaled Corticosteroid		
	Low dose No ICS card required	Intermediate dose Consider an ICS card	High dose ICS card is required
Beclomethasone dipropionate			
<i>Aerosol Inhaler (prescribe by brand name)</i>			
Non-proprietary	<800 micrograms	800-1000 micrograms	≥1000 micrograms
Clenil modulite	<800 micrograms	800-1000 micrograms	≥1000 micrograms
Qvar (BDP HFA)	<400 micrograms	400-500 micrograms	≥500 micrograms
Fostair (BDP HFA)	<400 micrograms	400-500 micrograms	≥500 micrograms
<i>Dry Powder Inhaler</i>			
Asmabec Clickhaler	<800 micrograms	800-1000 micrograms	≥1000 micrograms
Budesonide			
<i>Dry Powder Inhaler</i>			
Easyhaler, Novolizer	<800 micrograms	800-1000 micrograms	≥1000 micrograms
Turbohaler (Pulmicort, Symbicort)	<800 micrograms	800-1000 micrograms	≥1000 micrograms
Spiromax (DuoResp)	<640 micrograms	640-800 micrograms	>800 micrograms
Ciclesonide			
<i>Aerosol Inhaler Alvesco</i>	≤240 micrograms	320 micrograms	≥480 micrograms
Fluticasone propionate (FP)			
<i>Aerosol Inhaler</i>			
Flixotide, Flutiform, Seretide Sirdupla, Non-proprietary	<400 micrograms	400-500 micrograms	≥500 micrograms
<i>Dry Powder Inhaler</i>			
Flixotide, Seretide, AirFluSal	<400 micrograms	400-500 micrograms	≥500 micrograms
Fluticasone furoate (FF)*			
<i>Dry Powder Inhaler Relvar[▼]</i>		Literature not available*	
Mometasone furoate			
<i>Dry Powder Inhaler Asmanex</i>	220 micrograms	440 micrograms	≥880 micrograms

*Fluticasone furoate 92 micrograms once daily is approximately equivalent to fluticasone propionate 250 micrograms twice daily (<https://www.medicines.org.uk/emc/medicine/28496>). This could be interpreted as being equivalent to 1000 micrograms of beclomethasone dipropionate, but caution is advised as direct comparator studies have not been published.

- Dosage equivalents are approximate and dose delivered will depend on other factors such as inhaler technique
- Encourage patients to use appropriate breathing techniques according to inhaler device e.g.: “Slow and Steady” for an aerosol inhaler, “Quick and Deep” for a dry powder inhaler
- If a patient is using nasal corticosteroids and an ICS, they should be assessed individually. For example, for a patient taking nasal corticosteroids and 800-1000 micrograms of BDP equivalent/day, a corticosteroid safety card is recommended.
- Before prescribing, patients should always have their therapy reviewed for continued appropriateness and if necessary, issued an ICS card.