COMPASS

Therapeutic Notes on the Management of Asthma

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Contents

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Introduction and background

There is currently no universally accepted definition of the term 'asthma'. This is in part due to an overlap of symptoms with other diseases such as chronic obstructive pulmonary disease (COPD), but it is also due to the probable existence of more than one underlying pathophysiological process. There are, for example, wide variations in age of onset, symptoms, triggers, association with allergic disease, and the type of inflammatory cell infiltrate seen in patients diagnosed with asthma.[1]

The airways are hyper-responsive and constrict easily in response to a wide range of stimuli. Narrowing of the airways is usually reversible (either spontaneously or with medication), leading to intermittent symptoms. In some people with chronic asthma, the inflammation may lead to irreversible airflow obstruction.[2]

How common is asthma?

- 5.2 million people in the UK have asthma.[3]
- In Northern Ireland, 60.6 per 1000 people have asthma.
- More than 4.1 million GP consultations for asthma occur each year.[3]
- In early childhood, asthma is more common in boys than in girls, but by adulthood, the sex ratio is reversed. The mechanism for this is not clear.[5,6]
- Approximately 60% of adults with asthma in the UK are women.[3]

What are the symptoms of asthma?

Patients will typically have symptoms of:

- wheeze
- cough (particularly at night or in the early morning)
- breathlessness
- chest tightness
- sputum production.[1]

Are diagnostic tests helpful in asthma diagnosis?

The diagnosis of asthma is based on the recognition of a characteristic pattern of symptoms and signs and the absence of an alternative explanation for them.[7] Various tests can be used to support a diagnosis, but there is no single test that can definitively diagnose asthma.[8]

Diagnostic tests

A number of tests are available to determine the likelihood of asthma. These include measuring airflow obstruction (spirometry and peak flow) and assessment of reversibility with bronchodilators. Spirometry is the preferred initial test to assess the presence and severity of airflow obstruction in adults.[7]
Normal results do not however exclude asthma and abnormal results do not always mean it is asthma, as they could be indicators of other respiratory diseases or spurious readings.[8]

The value of FeNO tests

Testing for airway inflammation is increasingly used as a diagnostic strategy in clinical practice. This includes measuring fractional exhaled nitric oxide (FeNO).[8]
FeNO measurements correlate well with a raised sputum eosinophil count.[8] FeNO tests can therefore identify patients who are going to respond to corticosteroid therapy.[7]
This test may be useful in patients with an intermediate probability of asthma, although there is some uncertainty about both the sensitivity and specificity of FeNO, particularly as to whether it can distinguish general atopy from asthma.[7,8]

What is Asthma-COPD overlap syndrome (ACOS)?

Asthma-COPD overlap syndrome (ACOS) is not a disease entity but a term applied to patients with clinical features of both asthma and chronic obstructive pulmonary disease (COPD).[85] ACOS is characterised by persistent airflow limitation.[9]

Why is it important to consider ACOS?

Distinguishing asthma from COPD can be problematic, particularly in smokers and older adults. Many older patients presenting with chronic respiratory symptoms are found to have chronic airflow limitation (i.e. not completely reversible after bronchodilation).[9]
ACOS is associated with a greater morbidity than asthma or COPD alone. [85] Further research into ACOS is required. Preliminary advice in publications is to treat with a combination of LABA (COPD treatment) and ICS (asthma treatment).[85]

When to refer patients with ACOS to a specialist?

Assessment and initial treatment may be commenced in primary care.
Referral may be considered in the following situations:

- Persistent symptoms and/or attacks despite treatment.
- Diagnostic uncertainty.
- Atypical or additional symptoms that suggest an additional pulmonary diagnosis.
- When chronic airways disease is suspected, but syndromic features of both asthma and COPD are few.
- Co-morbidities that may interfere with the assessment and management of the airways disease.[9]

A Stepwise approach

Guidance on the management of asthma has been published by the British Thoracic Society (BTS) in collaboration with the Scottish Intercollegiate Guidelines Network (SIGN). The familiar stepwise approach to asthma management is maintained in the latest BTS / SIGN guidance update (2014).[7]

There are some changes to this guidance, which incorporate recommendations from the National Review of Asthma Deaths, 'Why asthma still kills'.[32]

What does asthma control look like?

The aim of asthma management is control of the disease. Complete control of asthma is defined as:[7]

- No daytime symptoms
- No night-time awakening due to asthma
- No need for rescue medication
- No asthma attacks
- No limitations on activity including exercise
- Normal lung function (in practical terms FEV_1 and/ or PEF>80% predicted or best)
- Minimal side effects from medication.

Why a stepped approach?

A stepwise approach aims to abolish symptoms as soon as possible and to optimise peak flow by starting treatment at the level most likely to achieve this.
Patients should:

1. Start treatment at the step most appropriate to the initial severity of their asthma
2. Achieve early control
3. Maintain it by stepping up treatment as necessary and stepping down treatment when control is good.[7]

Prescribing Points

► Before initiating a new drug therapy, practitioners should:

- Check adherence with existing therapies
- Check inhaler technique
- Eliminate trigger factors [7]

►To check adherence:

- ALWAYS review prescription records in the previous 6 to12 months and
- NEVER increase asthma medication without review of prescription filling and discussion with the patient

STEPPING UP? Check adherence, technique and trigger factors

TABLE ONE	SIGN / BTS Stepwise approach for adults & children over 5 years [7,113]
STEP 1 **Mild intermittent asthma**	Prescribe an inhaled short-acting β_2 agonist (such as salbutamol or terbutaline) as short term reliever therapy for all patients with symptomatic asthma.
STEP 2 **Regular preventer therapy**	Inhaled corticosteroids (ICS) should be considered for patients with any of the following asthma-related features: • asthma attack in the last two years* • using inhaled β_2 agonists three times a week or more • symptomatic three times a week or more • waking one night a week Start patients at a dose of ICS appropriate to the severity of disease: • Usually start at 400 micrograms BDP per day or equivalent in adults and 200 micrograms BDP per day or equivalent in children • In children under 5 years, higher doses may be required if there are problems in obtaining consistent drug delivery • Titrate the dose of ICS to the lowest dose at which effective control of asthma is maintained. * the term 'asthma attack' has replaced 'asthma exacerbation' in the SIGN / BTS 2014 guideline—to be more understandable and give a clearer indication of the need to action
STEP 3 **Initial add-on therapy**	The first choice as add-on therapy to ICS in adults and children (5-12 years) is an inhaled long-acting β_2 agonist (LABA). • A LABA should be considered before going above a dose of 400 micrograms BDP or equivalent per day, and certainly before going above 800 micrograms BDP or equivalent . • The first choice as add-on therapy to ICS in children under 5 years old is a leukotriene receptor antagonist. The response to the add-on therapy should be evaluated: • If there is no response to inhaled LABA, **stop** the LABA and increase the dose of ICS to 800 micrograms BDP/day (adults) or equivalent or 400 micrograms BDP/day (children) or equivalent if not already on this dose. • If there is a response to LABA, but control remains suboptimal, continue with the LABA and increase the dose of ICS to 800 micrograms/day (adults) or equivalent or 400 micrograms/day or equivalent (children 5–12 years).
STEP 4 **Addition of fourth drug**	If control is still poor despite moderate dose of ICS and add-on therapy, consider: • Increasing ICS to 2000 micrograms BDP/day (adults) or 800 micrograms BDP/day (children 5-12 years) or equivalent • Leukotriene receptor antagonists • Theophyllines • Slow release β_2 agonist tablets (caution in patients already on LABA). • (Tiotropium) There are no controlled trials that indicate which of these is the best option, although the potential for side effects is greater with theophyllines and β_2 agonist tablets. The response to the add-on therapy should be evaluated: • If a trial of an add-on treatment is ineffective, stop the drug (or in the case of increased dose of ICS, reduce to the original dose).
	Before proceeding to step 5, refer patients with inadequately controlled asthma, especially children, to specialist care.
STEP 5 **Continuous / frequent use of oral steroids**	For the small number of patients who are not controlled at step 4, use daily steroid tablets. These should be used in the lowest dose that provides adequate control. Patients should be counselled about potential side-effects and all other alternative treatments must be considered.

STEPPING DOWN? Reduce ICS slowly, aim to use the lowest effective dose, review after 12 weeks

Medications used to manage chronic asthma

Medications to treat asthma can be classified as controllers or relievers. **Controllers** are medications taken daily on a long-term basis to keep asthma under clinical control, chiefly through their anti-inflammatory effects. They include inhaled and oral corticosteroids, leukotriene receptor antagonists, long-acting β_2-agonists in combination with inhaled steroids and sustained-release theophylline. Inhaled corticosteroids are the most effective controller medications currently available. **Relievers** are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve its symptoms. They include short-acting beta-2-agonists, inhaled anticholinergics, immediate-release theophylline, and short-acting oral beta-2-agonists.[1]

STEP ONE: *Inhaled reliever therapy when required*

Inhaled short-acting β_2-agonists

For the majority of patients in Step ONE, an inhaled, short-acting β_2-agonist is the recommended reliever treatment.[1,10,19] Short-acting β_2-agonists administered by inhalation are the most effective therapy for rapid reversal of airflow obstruction and prompt relief of asthmatic symptoms. Most widely used is the short-acting β_2-agonist, salbutamol. Because a regular schedule of administration four times a day does not improve outcomes, as compared with "as-needed" administration,[20] the short-acting β_2-agonists are recommended for use only as needed.

Overuse of short-acting β_2-agonists is a marker of uncontrolled asthma and has been associated with increased deaths due to asthma.[21] This will be discussed in more detail in the section 'National Review of Asthma Deaths.'

Prescribing Point – Short-acting beta agonists

► If a patient orders more than 12 short acting bronchodilator inhaler devices a year, they should be identified and have their asthma assessed urgently and measures taken to improve asthma control if this is poor.[7]

STEP TWO: *Introduction of regular preventer therapy*

Inhaled corticosteroids

Inhaled corticosteroids (ICS) are effective (but non-specific) anti-inflammatory agents and, in patients of all ages, appear to be the most effective agents for controlling asthma symptoms, improving lung function, improving quality of life, preventing acute attacks and reducing asthma mortality.[10,13,26-33] However, they do not cure asthma, and when they are discontinued, deterioration of clinical control follows within weeks to months in a proportion of patients.[34]

Beclomethasone equivalence

In previous guidelines, doses of inhaled corticosteroids (ICS) were referenced against beclometasone dipropionate (BDP) given via chlorofluorocarbon metered dose inhalers (CFC-MDIs). BDP-CFC is no longer available, so the new reference ICS is the BDP hydrofluoroalkane (BDP-HFA) product. This is available at the same dosage as BDP-CFC.

NB: some BDP-HFA products are more potent and therefore all should be prescribed by brand.[7] **TABLE TWO** provides ICS dose equivalence to BDP.

Qvar® dose equivalence

Qvar® is not equipotent to other CFC-free beclometasone inhalers. Qvar® is approximately 2 to 2.5 times more potent than Clenil Modulite® because it generates an aerosol of smaller particles, achieving greater penetration and lung deposition than CFC-MDIs. Therefore, prescribers wishing to prescribe beclometasone MDI should prescribe by brand name.

Is there any evidence comparing the inhaled corticosteroids?

Comparative evidence is lacking. Studies comparing inhaled corticosteroids are limited by their study design in that:

- normal volunteers and asthma patients differ in their absorption of ICS
- studies are often non-blinded due to difficulty in obtaining competitor's delivery devices.[7]

The current evidence suggests that the inhaled corticosteroids do not differ in efficacy or safety.[7]

ICS dose doubling during an asthma attack?

Although recommended in previous guidelines, **doubling the dose of ICS at the time of an attack is of unproven value** and therefore is no longer recommended.[7]

Studies have shown that in patients who are on a low dose of regular ICS (i.e. 200 BDP), a five-fold increase in the ICS dose led to a decrease in the severity of asthma attacks. However, this cannot be extrapolated to patients taking moderate or high regular doses of ICS.[7] It is thought that inhaled corticosteroids reach a plateau in their dose-response relationship, where increasing the dose further will only benefit patients who have not yet reached their plateau dose.[16]

Prescribing points – Inhaled corticosteroids

► At high doses of ICS via pMDI a spacer should be used.[7]

► Adult patients requiring doses of ICS ≥1000 micrograms BDP equivalent should be given a steroid card.[7]

Table TWO: Equivalence to beclometasone dipropionate (BDP) and current licensed age indications (as per BTS / SIGN Guideline on the management of asthma 2014) [7]				
		UK licence covers		
Inhaled corticosteroid	**BDP equivalent dose**	**> 12 years**	**5 – 12 years**	**< 5 years**
Beclometasone dipropionate				
Aerosol inhaler (prescribe by brand name)				
Non-proprietary	400 micrograms	See individual preparation SPC		
Clenil modulite®	400 micrograms	√	√	√
Qvar®	200 micrograms	√	x	x
Fostair®	200 micrograms	Over age 18	x	x
Dry powder inhaler				
Asmabec Clickhaler®	400 micrograms	√	Over age 6	x
Budesonide				
Dry powder inhaler				
Easyhaler®, Novolizer®	400 micrograms	√	Over age 6	x
Turbohaler® preparations	400 micrograms	See individual preparation SPC		
Ciclesonide				
Aerosol inhaler	200 to 300 micrograms	√	x	x
Fluticasone propionate				
Aerosol inhaler				
Flixotide®, Flutiform® and Seretide®	200 micrograms	See individual preparation SPC		
Dry powder inhaler				
Flixotide® and Seretide®	200 micrograms	See individual preparation SPC		
Fluticasone furoate				
Dry powder inhaler				
Relvar▼®	* see later	√	x	x
Mometasone furoate				
Dry powder inhaler				
Twisthaler®	200 micrograms	√	x	x
NB: Dosage equivalents are approximate and dose delivered will depend on other factors such as inhaler technique				

Long-acting β_2-agonists
Addition of a long-acting β_2-agonist (LABA) is the preferred treatment when a medium dose of inhaled corticosteroids alone fails to achieve control of asthma. Addition of a LABA to a daily regimen of inhaled corticosteroids improves symptom scores, decreases nocturnal asthma, improves lung function and decreases the use of short-acting inhaled β_2-agonists. It also reduces the number of attacks experienced and achieves clinical control of asthma in more patients more rapidly, and at a lower dose of inhaled corticosteroids than inhaled corticosteroids alone.[96, 99,100, 101-107]

Why are LABAs not recommended in children under 5 years of age?

There is limited evidence for all types of treatment for asthma in children younger than 5 years compared with older children and adults. The first choice as add-on therapy to ICS in children under five years of age is a leukotriene receptor antagonist.[7] Montelukast is the only LTRA that is licensed for use in children 2–5 years of age.[2]

What are the differences between LABAs?

Features distinguishing the LABAs licensed for asthma are both practical and theoretical.[108] The onset of action of formoterol occurs within 5 minutes, whereas salmeterol has a slower onset of action (15 to 20 minutes).[109,110] The more rapid onset of action of formoterol makes it suitable for symptom relief as well as symptom prevention.[111] Formoterol is a full agonist in its action at the beta-receptor, whereas salmeterol is a partial agonist (and partial antagonist). The clinical significance of these differences are however uncertain.[76]
Vilanterol is a relatively new LABA and is only available in a combination inhaler with fluticasone furoate (Relvar® Ellipta®▼).[1]

Safety issues: long-acting-β_2 agonist monotherapy
► LABA should only be started in patients who are **already on ICS**.
► LABA should be prescribed only in combination with ICS in a LABA/ICS combination inhaler. LABA monotherapy has been associated in controlled trials with increased mortality and is without a licence or guideline endorsement.
► Do not start anyone with acutely deteriorating asthma on a LABA.
► Anyone starting treatment with a LABA should be advised to report any deterioration in symptoms.
► Closely monitor anyone started on a LABA, especially during the first three months of treatment.
► Advise anyone who has been prescribed salmeterol that they should not use it to relieve an acute asthma attack.[15, 32]

What are the advantages of using an inhaler that contains both a steroid and a LABA?

Fixed dose ICS/LABA combination inhalers:[7,9]

- Are convenient for patients.
- Improve adherence to drug treatment, as fewer inhalations and devices are needed.[78,79]
- Ensures that the LABA is always accompanied by a corticosteroid.
- Can overcome the potential for over-reliance on bronchodilator therapy at the expense of ICS.

Relvar®▼ dose equivalence

Relvar®▼ is a combination inhaler containing a new ICS (fluticasone furoate) and a new LABA (vilanterol). It is available in two strengths, 92 micrograms and 184 micrograms fluticasone furoate, both with 22 micrograms of vilanterol. **Note: fluticasone furoate is more potent than fluticasone propionate**: fluticasone furoate 92 micrograms once a day is approximately equivalent to fluticasone propionate 250 micrograms twice a day and fluticasone furoate 184 micrograms once a day is approximately equivalent to fluticasone propionate 500 micrograms twice a day.[62]

Fostair® dose equivalence

The beclometasone is an extra fine particle and therefore is more potent than traditional beclometasone dipropionate CFC-free inhalers. When 'stepping up' patients from other beclometasone dipropionate inhalers, Fostair® 100/6 can be prescribed for patients already using beclometasone dipropionate 250 micrograms in another CFC-free inhaler; the dose of Fostair® should be adjusted according to response.[31]

Prescribing Points – Combination ICS / LABA inhalers
► With such a range of combination inhalers on the market, it might be useful as a Practice to select a small number of inhalers that you are familiar with and are able to discuss with patients.

Maintenance and reliever therapy (MART)

The use of budesonide/formoterol in a single inhaler as rescue medication instead of a short-acting β_2 agonist, in addition to its regular use as controller therapy has been shown to be an effective treatment regime.[7] Symbicort® (budesonide / formoterol), DuoResp® (budesonide / formoterol) and Fostair® (beclomethasone / formoterol) now all have a MART license. MART may be considered for adult patients at:

- Step 3 and are poorly controlled or
- Step 2 above BDP 400 micrograms / day and poorly controlled.

Prescribing Points – MART
► The total regular dose of daily ICS is not decreased.
► Patients taking rescue budesonide / formoterol ≥ once a day on a regular basis should have their treatment reviewed.
► Careful education of patients on this regimen is required.[7]

STEP FOUR: Persistent poor control

If control is still poor despite moderate dose of ICS and add-on therapy, consider:

- Increasing ICS to 2000 micrograms BDP/day (adults) or 800 micrograms BDP/day (children 5-12 years) or equivalent
- Leukotriene receptor antagonists
- Theophyllines
- Slow release β_2 agonist tablets (caution in patients already on LABA).
- Tiotropium (**new to step 4**)

What is the place in therapy of leukotriene receptor antagonists (LTRAs)?

Clinical studies have demonstrated that leukotriene receptor antagonists (montelukast and zafirlukast) (LTRAs) have a small and variable bronchodilator effect, reduce symptoms (including cough), improve lung function, and reduce airway inflammation and asthma attacks.
However, they are less effective than inhaled corticosteroids when used alone as controller medication. When used as add-on therapy, LTRAs may reduce the dose of inhaled corticosteroids required by patients with moderate to severe asthma and may improve asthma control in patients whose asthma is not controlled with inhaled corticosteroids. However, LTRAs are less effective than LABAs as add-on therapy.[7,18-30]

Note: leukotriene receptor antagonists are an option for treatment at STEP 3 of the pathway for adults and children over 5 years where a LABA has been tried but is ineffective.[116]

If leukotriene antagonists are used then a short trial (e.g. for 28 days) is advisable to identify those patients who will respond to this therapy class. If there is no evidence of therapeutic benefit after the month trial then the drug should be stopped.[119,120]

Practice Point – Leukotriene receptor antagonists

▶ Prescribe montelukast or zafirlukast for a short trial of 28 days and review response, i.e. do not automatically put on repeat.

▶ You may wish to consider carrying out an audit on patients receiving montelukast or zafirlukast to ensure that they are also using inhaler therapy.

What is the place in therapy for tiotropium in asthma management?

Tiotropium in the Spiriva® Respimat® device (i.e. not the Handihaler®) now has a license for asthma. It is licensed as an add-on maintenance bronchodilator treatment in adults with asthma receiving maintenance treatment with the combination of inhaled corticosteroid (≥800µg budesonide/day or equivalent) and long acting β_2 agonist, and who have experienced one or more severe exacerbations in the previous year.[17] This is in line with step 4 of the BTS / SIGN asthma guideline.

What is the evidence for tiotropium in asthma?

Evidence to support the license came from two RCTs that evaluated tiotropium (Spiriva® Respimat®) in adults with poorly controlled asthma and persistent airflow obstruction who were already treated with an ICS + LABA. Tiotropium improved peak and trough forced FEV_1 and lengthened the time to first severe attack compared with placebo. Differences between add-on therapy with tiotropium and placebo in patient-assessed asthma control and QOL were small and did not meet the threshold for the minimal clinically important difference. No RCTs comparing tiotropium with other active treatments or in people with asthma without persistent airflow obstruction are available.
Tiotropium is therefore likely to be of most benefit to patients with asthma who have a more severe disease and a pattern of illness and physiology more similar to that seen in COPD.[17]

STEP FIVE: Continuous / frequent courses of oral corticosteroids

For the small number of patients who are not controlled at STEP 4, daily steroid tablets may be used. These should be used in the lowest dose that provides adequate control. Patients should be counselled about potential side-effects (see 'Inhaled and oral corticosteroids – the safety issues'). All other alternative treatments must be considered.[7]

Other treatment options at STEP FIVE

What is omalizumab?

Omalizumab (Xolair®) is a recombinant humanised monoclonal antibody that inhibits the binding of IgE to receptors on the surface of mast cells and basophils.[117,118] It prevents the release of pro-inflammatory mediators and reduces allergen-induced airway reactions. Omalizumab is administered by subcutaneous injection every 2 to 4 weeks and the dose is based on the patient's body weight and blood IgE level.

What is the place in therapy of omalizumab?

Omalizumab is a red list medication. It should only be initiated in specialist centres with experience of evaluation and management of patients with severe and difficult asthma.[7] It may be used in patients on high-dose ICS and long-acting β_2 agonists who have impaired lung function, are symptomatic with frequent asthma attacks, and have allergy as an important cause of their asthma.[7]

Choice of inhaler device

In adults, a pMDI ± spacer is as effective as any other hand-held inhaler, but patients may prefer some types of DPI.[7] In children aged 5 to 12 years, a pMDI + spacer is as effective as any other hand-held inhaler.[7] See **TABLE THREE** for suitable inhaler delivery devices for children. There is no evidence to dictate an order in which devices should be prescribed for patients who cannot use a pMDI. Therefore the most important points to consider are patient preference and local cost.[7]
Prescribing mixed inhaler types may cause confusion and lead to errors in using the different inhalers. Therefore, using the same type of device to deliver preventer and reliever treatments may improve outcomes.[7]

TABLE THREE: Age requirements for correct use of inhaler delivery devices [2]

Delivery system	Minimum age
pMDI	> 5 years
pMDI with spacer	> 4 years
pMDI with spacer and mask	4 years or younger
Breath-actuated metered-dose inhaler	> 5 years
Dry-powder inhaler	5 years or older

Inhaler device technique

Inhalers should only be prescribed after patients have received training in the use of the device and have demonstrated satisfactory technique.[7]
It is important that inhaler technique is checked regularly as poor technique, even after training, is very common.[2] Any difficulties should either be corrected or the patient offered another device.[57]

Useful resources for inhaler technique
Asthma UK have produced a series of videos on how to use the different inhaler devices available: http://www.asthma.org.uk/Sites/healthcare-professionals/pages/inhaler-demos

PrescQIPP have produced 'inhaler technique assessment tools'. They are designed to be used by healthcare professionals to support inhaler technique assessments in patients and cover nine types of inhaler device on the market https://www.prescqipp.info/resources/viewcategory/317-inhaler-technique-assessment-tools.

Should inhalers be prescribed generically?

Dry powder inhalers—prescribe by brand
There are a variety of dry powder inhalers on the market. Dry powder inhalers differ in their method of administration. In order for the patient to be maintained on the inhaler device they have been trained to use, it is essential to specify inhaler device (e.g. Accuhaler®, Turbohaler®), strength and dose when prescribing a dry powder inhaler (i.e. do not prescribe generically). Brand prescribing of dry powder inhalers is now even more important with the arrival of new branded-generic inhalers on the market.

Metered dose inhalers (MDIs) — prescribe generically with the exception of beclomethasone-containing MDIs
Following loss of patent for Seretide Evohaler®, branded generic versions of fluticasone / salmeterol MDIs are emerging on the market. Patients who are trained and competent in using a MDI should be able to use branded generic fluticasone / salmeterol MDIs. However it is important that patients are counselled regarding a change from brand to generic MDI.
Beclometasone-containing MDIs (Qvar®, Clenil Modulite® and Fostair®) are **not interchangeable** and should be prescribed by brand name:

- Qvar® has extra-fine particles and is approximately twice as potent as Clenil Modulite® [114]
- Fostair® has extra-fine particles. Fostair® 100/6 can be prescribed for patients already using beclometasone dipropionate 250 micrograms in another CFC-free inhaler.[31]

Key message on inhaler devices:

- **Dry powder inhalers (DPIs) should be prescribed BY BRAND**
- **Metered dose inhalers (MDIs) should be prescribed GENERICALLY *WITH THE EXCEPTION OF BECLOMETHASONE-CONTAINING INHALERS***

Northern Ireland Formulary

The Northern Ireland Formulary provides guidance on choices of inhalers: http://niformulary.hscni.net. The Formulary recognises the importance of inhaler technique: 'choice of device should be considered on basis of ability to use the inhaler, patient-acceptability and cost.'

Prescribing Points – Choice of inhaler device
► Only prescribe an inhaler after the patient has received training and demonstrated satisfactory response. It is essential that patients are trained and competent in using the inhaler device that is prescribed for them.
► Check inhaler technique at every opportunity.
► MDIs require co-ordination between actuation and inhalation. This can be overcome through use of a spacer device.
► DPIs require sufficient inspiratory flow to deliver medication and so may not be suitable in frail patients.
► If considering a switch to another type inhaler device , switches should only be carried out at a face to face review.
► DPIs should be prescribed by brand. Consider carrying out a search of patient records to find out if any DPIs are prescribed generically, and amend.

Community pharmacists
If a prescription is presented that is written generically for a dry powder inhaler (DPI), the brand should be confirmed with the prescriber.

As with all effective medicines, the benefits of inhaled corticosteroids (ICS) must be balanced against their potential risks. These range from unpleasant local effects (such as oral candidiasis and dysphonia) to less common systemic side-effects, such as adrenal suppression and osteoporosis.[63,64]

Although local side-effects can occur in 1 or 2 of every 100 patients using ICS at standard doses, the risk is greater when higher doses are used.[65] For most patients, dose escalation to high doses produces little additional clinical benefit but increases the risk of side effects.[65,66]

What local adverse effects are associated with use of ICS?

ICS are known to cause various upper airway adverse effects. The most often reported local adverse effects are:

- **Oropharyngeal candidiasis —** this can be minimised by using a large volume spacer device along with a MDI (this reduces oropharyngeal deposition by filtering out larger particles), and by rinsing the mouth with water immediately after ICS use.[67]
- **Hoarseness and dysphonia —** use of a spacer device does not appear to alleviate this.
- **Cough —** this can usually be overcome by changing either the ICS itself or the delivery system.[76]

Although the mechanisms by which ICS cause these local adverse effects are not entirely clear, these adverse effects seem related to deposition of the ICS in the oropharynx and larynx. The rate of local adverse effects may vary by ICS dose, device, and potency.[68-71]

Can inhaled corticosteroids cause systemic adverse effects in adults?

Inhaled corticosteroids are absorbed from the lung, accounting for some degree of systemic bioavailability. The risk of systemic adverse effects from an inhaled corticosteroid depends upon its dose and potency, the delivery system, systemic bioavailability, first-pass metabolism (conversion to inactive metabolites) in the liver, and half-life of the fraction of systemically absorbed drug (from the lung and possibly gut).[72]

Virtually no clinically important, long-term adverse systemic effects are observed among adults taking low-to-medium ICS doses. At high doses (usually > 1000 micrograms BDP per day or equivalent), the risk of systemic adverse effects increases.[73-75]

The systemic side-effects of long-term treatment with high doses of inhaled corticosteroids include:

- Adrenal suppression
- Decreased bone mineral density (BMD)[76,77]
- Cataracts and glaucoma [73,74]
- Easy bruising [78]

What problems are associated with long-term ICS use in children?

In children, high doses of ICS (> 400 micrograms/day / > 200 micrograms/day for fluticasone or equivalent) may be associated with systemic side-effects, including growth failure and adrenal suppression.[7]

The CSM has 'strongly advised that the paediatric licensed doses of all ICS should not be exceeded'.[77]

Use the lowest dose of ICS that will maintain disease control. If adequate control is not achieved, consider using add-on agents rather than increasing the dose of ICS.[7]

While the use of ICS may be associated with adverse effects, with careful ICS dose adjustment, this risk is likely to be outweighed by their ability to reduce the need for multiple bursts of oral corticosteroids.[7]

Prevention of oral steroid side effects

Patients who have been taking oral steroids for longer than three months or who require three or more courses a year will be at increased risk of systemic steroid side effects.[7]

The following should be monitored:

- Blood pressure
- Urine / blood sugar and cholesterol
- Bone mineral density (BMD) should be monitored in children over 5 years and adults *
- Growth in children (height and weight centile)
- Cataracts may be screened for in children.[7]

* When a significant reduction in BMD occurs in adults, treatment with a long-acting bisphosphonate should be offered (see British Osteoporosis Society guidelines, www.nos.org.uk).[7]

Bone mineral density for children is expressed as z-scores. Either a DEXA scan or ultrasound are used locally in paediatric respiratory services.

Prescribing Points – Children and ICS

► Monitor growth (height and weight centile) of children with asthma on an annual basis.[7]

► For children treated with ≥800 micrograms BDP per day or equivalent:

- Specific written advice about steroid replacement in the event of a severe intercurrent illness or surgery should be part of the management plan.
- The child should be under the care of a specialist paediatrician for the duration of the treatment.[7]

Steroid warning cards

► Consider giving a 'steroid card' to support communication of the risks associated with treatment, and specific written advice to consider corticosteroid replacement during an episode of stress, such as severe intercurrent illness or an operation, to patients using greater than maximum licensed doses of inhaled corticosteroids.

► Steroid treatment cards are available from BSO by emailing pharmacystationeryorders@hscni.net

Stepping down asthma treatment

Stepping down therapy once asthma is controlled is recommended, but often not implemented, leaving some patients over-treated.[7]

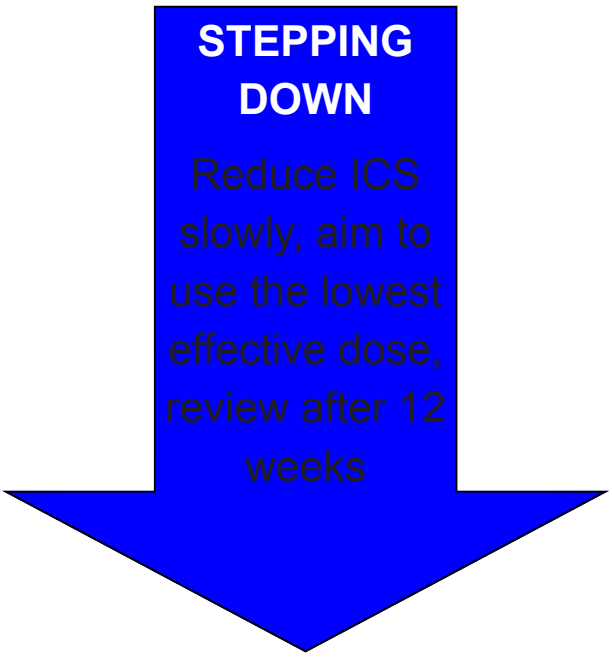
The reduced need for medication once control has been achieved is not fully understood, but may reflect the reversal of some of the consequences of long-term inflammation of the airways. Higher doses of anti-inflammatory medication may be required to achieve this benefit than to maintain it.
Alternatively, the reduced need for medication might simply represent spontaneous improvement as part of the seasonal cyclical natural history of asthma.
Whatever the explanation, in all patients, the minimum controlling dose of treatment must be sought through a process of regular follow-up and staged dose-reductions.[1]

Prescribing Notes: How to step down treatment

- Step down of ICS therapy should be slow, at a 25 to 50% dose reduction every three months, until low dose ICS is achieved (as patients deteriorate at different rates). BTS / SIGN guidance suggests that this is realistic and possible without compromising patient care.
- When on a combination of LABA and ICS, the ICS should be reduced to low dose (as above) before stopping the LABA.[10]
- Ideally the dose of LABA should remain constant during the 'step down' process.
- Patients should be maintained at the lowest possible dose of ICS.[7]
- There should be regular patient review while stepping down — recommended to review after 12 weeks.[113]

When to consider stepping down treatment?

Stepping down treatment should be considered for those patients whose disease has been stable for at least three months.[10]
Regular review and step down of treatment is essential to prevent over-treating.[10]



Non-pharmacological management

There is a common perception amongst patients and carers that there are numerous environmental, dietary and other triggers of asthma and that avoiding these triggers will improve asthma and reduce the requirement for pharmacotherapy.[7] As a result there can be less concordance with recommended pharmacological therapy.[7] Evidence that non-pharmacological therapies are effective in either preventing the development or reducing symptoms in asthma is difficult to find. SIGN/ BTS guidelines have made the following recommendations:

Benefit:

- Smoking cessation
- Breathing exercises
- Weight reduction

No benefit:

- Fish oils
- Antioxidants
- Probiotics
- Physical and chemical methods of reducing house dust mite levels in the home.

Smoking and asthma

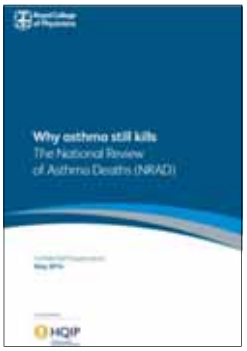
Direct or passive exposure to cigarette smoke adversely affects quality of life, lung function, need for rescue medications for acute episodes of asthma and long-term control with ICS.[11-14] **Parents who smoke should be advised about the dangers for themselves and their children, and offered appropriate support to stop smoking**.[7]

Why should smokers with asthma be encouraged to quit?

Anyone with asthma who smokes should be encouraged to quit for the following reasons:

- People with asthma who smoke have more asthma symptoms than non-smokers with asthma.
- Smokers show a faster decline in FEV_1 over time, and a higher mortality rate after admission with a near fatal asthma attack.
- The response to corticosteroid treatment is impaired in smokers with asthma. This has been shown to be the case with inhaled corticosteroids[81,82] and with short courses of oral corticosteroids.[83]
- Prescribers should be aware that higher doses of inhaled corticosteroids may be needed in patients who are smokers or ex-smokers.[9]

National Review of Asthma Deaths



Why asthma still kills

'Why asthma still kills' is a report following the National Review of Asthma Deaths (NRAD), into the circumstances surrounding deaths from asthma in the UK from 1st February 2012 to 30th January 2013.The report was published in May 2014.
The aim of the project was to understand why people of all ages continue to die from asthma, so that recommendations could be made to prevent deaths from asthma in the future.[32]

Key findings

Stark findings were reported in relation to use of NHS services, medical and professional care, prescribing and medicines use, and patient factors and perception of risk of poor control.[32]

Examples include:

- 45% of people died without seeking or before medical care could be provided
- Only 23% had a personal asthma action plan (PAAP)
- 43% had no asthma review in primary care in last year
- Only 39% were classed as "severe asthma", suggesting that some people were under-treated.
- 39% were prescribed more than 12 SABAs in the year before they died, while 4% were prescribed more than 50 reliever inhalers.[32]

Key messages:

The report highlighted four key messages:

- Every hospital and GP practice should have a designated, named clinician for asthma services.
- Better monitoring of asthma control; where loss of control is identified, immediate action is required including escalation of responsibility to other healthcare professional, treatment change and arrangements for follow-up.
- Better education is needed for doctors, nurses, patients and carers to make them aware of the risks. They need to be able to recognise the warning signs of poor asthma control and know what to do during an attack.
- All patients should be provided with a personal asthma action plan (PAAP), which can help them to identify if their asthma is worsening and tell them how and when to seek help.[32]

'Prescribing and medicines use' points

Among the recommendations in the NRAD report were a number of points in relation to prescribing and medicines use. These points are summarised in **TABLE FOUR**.[33]
Refer to Medicines Management Newsletter Supplement January 2015 for further details on **action points for GPs, practice nurses and community pharmacists**

TABLE FOUR: Key prescribing / medicines issues highlighted in the NRAD

Prescribing / medicines issues	NRAD recommendations
1. Overuse of SABAs	All asthma patients who have been prescribed more than 12 SABA reliever inhalers in the previous 12 months should be invited for urgent review of their asthma control, with the aim of improving their asthma through education and change of treatment if required.[33]
2. Inhaler technique	An assessment of inhaler technique to ensure effectiveness should be routinely undertaken and formally documented at annual review, and also checked by the pharmacist when a new device is dispensed.[33]
3. Non-adherence to ICS	Non-adherence to preventer inhaled corticosteroids is associated with increased risk of poor asthma control and should be continually monitored.[33]
4. Combination inhalers encouraged	Where LABA bronchodilators are prescribed for people with asthma, they should be prescribed with an inhaled corticosteroid in a single combination inhaler.[33]

Community pharmacists

- Community pharmacists are ideally placed to support the recommendations in the NRAD. Through the provision of a medication use review (MUR), pharmacists can discuss patients' adherence to medication and their use of inhalers. This is of particular importance for patients who do not attend for their annual review with their GP.
- Reminder: patients presenting with a prescription for a new inhaler should be shown how to use the inhaler device as part of the dispensing process.

Self-management plans

What are self-management plans?

Self-management plans are structured, documented plans that are developed to support a person to become more involved and empowered in managing their condition.[34]
Self-management plans are recommended for all patients with asthma by SIGN, BTS and NICE.

Why are self-management plans needed?

Due to the often variable nature of asthma, a fixed treatment regimen is not always appropriate.[58] It is important that people with asthma know how to recognise and act on symptoms and signs of deterioration in a timely fashion (as shown in the NRAD).[7]

There is a substantial body of evidence to show that self-management education incorporating written personal asthma action plans (PAAPs) improves health outcomes for people with asthma. They have been found to:

- Reduce emergency use of healthcare resources
- Improve markers of asthma control, e.g. reduced symptoms and days off work, and improved quality of life.[7,35-56]

BTS / SIGN Guideline
All people with asthma (and/or parents or carers) should be offered self-management education which should include a written personalised asthma action plan and be supported by regular professional review.[7]

NICE QUALITY STATEMENT (QS25)
People with asthma receive a written personalised action plan (PAAP).[84]

What are the components of a self-management plan?

1. Patient education
The goal of patient education is to provide suitable information and training so that patients can keep well and adjust treatment according to a medication plan developed with their healthcare professional.[1]
Education should include personalised discussion of issues such as trigger avoidance and achieving a smoke-free environment.[7]

2. Personal asthma action plans (PAAPs)
PAAPs should contain specific advice about recognising loss of asthma control. This can be assessed by symptoms, peak flows or both (symptom-based plans are generally preferable for children).[7]
Two or three action points should be included in the PAAP that state what to do if asthma deteriorates, including (as appropriate to clinical severity):

- Seeking emergency help
- Starting oral steroids (which may include provision of an emergency course of steroid tablets)
- Restarting or temporarily increasing (as opposed to just doubling) ICS.[7]

Written personalised action plans, given as part of structured education, can improve outcomes such as self-efficacy, knowledge and confidence for people with asthma, particularly for people with moderate to severe asthma whose condition is managed in secondary care. For people with asthma who have had a recent acute attack resulting in admission to hospital, written personalised action plans may reduce readmission rates.[84]

Examples of self-management plans can be found on the Asthma UK website (www.asthma.org.uk) or on the HSCB Public Health website (http://www.publichealth.hscni.net/publications/asthma-action-plan).

Implementation of self-management in primary care

Implementation of self-management interventions is challenging in the non-specialist setting. SIGN / BTS have suggested a number of strategies that have been used in effective interventions:

- the use of proactive triggers to ensure routine reviews
- structured protocols for asthma reviews
- support of community pharmacists
- routine mailing of educational resources
- telephone calls to provide ongoing support and advice
- IT-based education and monitoring
- Involvement of community workers to support clinical teams in deprived and/or ethnic minority communities.[7]

Good Practice points (BTS/SIGN)
► A hospital admission represents a window of opportunity to review self-management skills. No patient should leave hospital without a written PAAP.
► An acute consultation offers the opportunity to determine what action the patient has already taken to deal with the asthma attack. Their self-management strategy may be reinforced or refined and the need for consolidation at a routine follow up considered.
► A consultation for an upper respiratory tract infection or other known trigger is an opportunity to rehearse with the patient their self-management in the event of their asthma deteriorating.
► Education should include personalised discussion of issues such as trigger avoidance and achieving a smoke-free environment to support people and their families living with asthma.
► Brief simple education linked to patient goals is most likely to be acceptable to patients.[7]

Patient review

Regular review of people with asthma is associated with reduced absence from school or work, reduced exacerbation rate, improved symptom control and reduced attendance in accident and emergency departments.[84]
Therefore, patients with stable asthma should be reviewed at least once a year in primary care.[7] This is reinforced by the inclusion of asthma review in the General Medical Services (GMS) Quality and Outcomes Framework (QoF)[59] and the NICE Quality Statements for asthma.[84]

Components of a structured review [7]
Components of a structured review for adults include:

- Assessment of symptomatic asthma control using a recognised tool
- Measurement of lung function, assessed by spirometry or by peak expiratory flow
- Review of exacerbations, oral corticosteroid use and time off work or study since last assessment
- Checking inhaler technique
- Assessing adherence (which can be done by reviewing prescription refill frequency)
- Adjustment of treatment (consider stepping up if poor control or stepping down if good control since the last annual review).[84]
- Bronchodilator reliance (which can be assessed by reviewing prescription refill frequency)
- Possession and review of PAAP
- Smoking status
- Assessment of co-morbidities
- Review of diagnosis.

Assessment of asthma control

1) Recognised Tools

An assessment of asthma control should use a recognised tool. The available tools include:

- Royal College of Physicians (RCP) 3 questions
- Asthma control questionnaire
- Asthma control test or children's asthma control test
- Mini asthma quality of life questionnaire or paediatric asthma quality of life questionnaire.

For example, the Asthma Control Test™ (**TABLE FIVE**) is simple to use in every day clinical practice.

2) Tests of airway function

These tools are usefully supplemented by one or more tests of airway function, which include:

- Spirometry
- Peak expiratory flow
- Airway responsiveness to change, e.g. indirect challenges such as inhaled mannitol (only available in selected secondary care facilities).
- Exhaled nitric oxide
- Eosinophil differential count in induced sputum.[7,84]

TABLE FIVE: ASTHMA CONTROL TEST™ http://niformulary.hscni.net/Formulary/Adult/PDF/AsthmaControlTest_Web.pdf

Are you in control of your asthma?
Or is your asthma in control of you?
Here's how to find out

Step 1: Read each question carefully, circle your score and write it in the box.

Step 2: Add up each of your five scores to get your total Asthma Control Test™ score.

Step 3: Use the score guide to learn how well you are controlling your asthma

Q1	During the **past 4 weeks**, how often did your asthma prevent you from getting as much done at work, school or home?								Score:
	All of the time	1	Most of the time	2	Some of the time	3	A little of the time	4	None of the time 5
Q2	During the **past 4 weeks**, how often have you had shortness of breath?								Score:
	More than once a day	1	Once a day	2	3-6 times a week	3	1-2 times a week	4	Not at all 5
Q3	During the **past 4 weeks**, how often did your asthma symptoms (wheezing, coughing, chest tightness, shortness of breath) wake you up at night or earlier than usual in the morning?								Score:
	4 or more times a week	1	2-3 nights a week	2	Once a week	3	Once or twice	4	Not at all 5
Q4	During the **past 4 weeks**, how often have you used your reliever inhaler (usually blue)?								Score:
	3 or more times a day	1	1-2 times a day	2	2-3 times a week	3	Once a week or less	4	Not at all 5
Q5	How would you rate your asthma control during the **past 4 weeks?**								Score:
	Not controlled	1	Poorly controlled	2	Somewhat controlled	3	Well controlled	4	Completely controlled 5
									TOTAL SCORE

What does your score mean?

Score 25: WELL DONE Your asthma appears to have been **under control** over the last 4 weeks. However, if you are experiencing any problems with your asthma, you should see your doctor or nurse.	**Score 20 to 24 – ON TARGET** Your asthma appears to have been **reasonably well controlled** during the last 4 weeks. However, if you are experiencing symptoms, your doctor or nurse may be able to help you.	**Score: less than 20 – OFF TARGET** Your asthma may **not have been controlled** during the last 4 weeks. Your doctor or nurse can recommend an asthma action plan to help improve your asthma control.

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Glossary	
DPI	Dry powder inhaler
FEV_1	Forced expiratory volume in 1 second
ICS	Inhaled corticosteroid
LABA	Long-acting beta-$_2$ agonist
LAMA	Long-acting muscarinic antagonist
LTRA	Leukotriene receptor antagonist
MDI	Metered dose inhaler
QOL	Quality of life
RCT	Randomised controlled trial
PEF	Peak expiratory flow
SABA	Short-acting beta-$_2$ agonist

This material was prepared on behalf of the Northern Ireland Health and Social Care Board by:

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Therapeutic Notes on the Management of Asthma

COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 250 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.
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- **Doctors and nurses** should submit their answers at: **www.medicinesni.com**
- **Pharmacists** should submit their answers at: **www.nicpld.org**

1	**In the management of chronic asthma:**			
	a	Dry powder inhalers (DPIs) should be prescribed by brand name.	T	F
	b	Beclomethasone MDIs should be prescribed generically.	T	F
	c	Reducing house dust mite levels in the home has been found to improve symptoms of asthma.	T	F
	d	At the time of an acute exacerbation of their asthma, patients should be counselled to double the dose of their inhaled corticosteroid.	T	F
2	**When stepping down asthma treatment:**			
	a	Patients should be maintained on the minimum dose of ICS that controls their condition.	T	F
	b	Step down of ICS therapy should be slow, at a 25 to 50% dose reduction every three months.	T	F
	c	Stepping down treatment should be considered for those patients whose disease has been stable for at least three months.	T	F
	d	When asthma is controlled with a combination of higher dose ICS and LABA, the preferred approach is to begin by reducing the dose of LABA by approximately 50% while continuing the ICS.	T	F
3	**In relation to adverse effects with inhaled corticosteroids:**			
	a	At high doses of ICS via pMDI a spacer should be used.	T	F
	b	Oropharyngeal candidiasis can be minimised by using a large volume spacer device along with a MDI.	T	F
	c	Virtually no clinically important, long-term adverse systemic effects are observed among adults taking low-to-medium ICS doses.	T	F
	d	Adult patients requiring doses of ICS ≥400 micrograms BDP equivalent should be given a steroid card.	T	F
4	**In relation to long-acting β_2-agonists (LABAs):**			
	a	They are the first choice as add-on therapy to ICS in children under five years of age.	T	F
	b	Do not start anyone with acutely deteriorating asthma on a LABA.	T	F
	c	LABA should only be started in patients who are already on ICS.	T	F
	d	Salmeterol may be used to relieve an acute asthma attack.	T	F
5	**In relation to patient review:**			
	a	It is important that inhaler technique is checked regularly as poor technique, even after training, is very common.	T	F
	b	The Asthma control test is a useful method of assessing asthma control.	T	F
	c	Bronchodilator reliance should be assessed by reviewing prescription refill frequency.	T	F
	d	Where LABA bronchodilators are prescribed for people with asthma, they should be prescribed in a combination inhaler.	T	F