COMPASS

Therapeutic Notes on the Management of Asthma

June 2018

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Glossary	
Broncho-dilator variability test	A test to determine if there is an improvement in FEV_1 after administration of bronchodilator
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
MART	Maintenance and reliever therapy
MDI	Metered dose inhaler
PEF variability	Peak flow variability (calculated as the difference between the maximum and minimum peak flow in a day. A value of >20% is characteristic of asthma)
QOL	Quality of life
RCT	Randomised controlled trial
PEF	Peak expiratory flow
SABA	Short-acting beta-$_2$ agonist

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.[1]

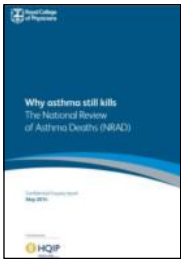
How common is asthma?

- 5.4 million people in the UK have asthma.[2]
- In Northern Ireland, 182,000 people (1 in 10) are currently receiving treatment for asthma (36,000 children and 146,000 adults).[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]

Guidelines on asthma

Since 2003, the British Thoracic Society (BTS) in collaboration with the Scottish Intercollegiate Guidelines Network (SIGN) have published guidance on the management of asthma.
In November 2017, NICE published guidance on diagnosis, monitoring and chronic asthma management.[4]
Although both BTS/SIGN and NICE have looked at the same evidence base when producing their guidelines, NICE have included a health economic evaluation in their guideline development. This has created some differences in their recommendations on how to diagnose and manage people with asthma.
This COMPASS therapeutic note will seek to highlight the similarities and differences between the two guidelines and help guide what this means in primary care practice.

National Review of Asthma Deaths



'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 from NRAD report

Stark findings were reported in relation to the use of NHS services, medical and professional care, prescribing and medicines use, and patient factors such as 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 within the 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 from NRAD report:

The report highlighted four key messages:

1. Every hospital and GP practice should have a designated, named clinician for asthma services.
2. 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.
3. 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.
4. 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 ONE**.[33]
Refer to Medicines Management Newsletter Supplement January 2015 for further details on action points for GPs, practice nurses and community pharmacists

TABLE ONE: 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.

Asthma Diagnosis

No one symptom, sign or test is diagnostic of asthma. Furthermore, the predictive value of tests is influenced by the context, the reference test used, and the thresholds that are applied.[4,7,8]

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.[1,7]

Are diagnostic tests helpful in asthma diagnosis?

According to **BTS/SIGN, the diagnosis of asthma is a clinical one**; tests influence the probability of asthma but do not prove a diagnosis.[7] With this is mind, BTS/SIGN recommend a structured clinical assessment as the first step to determine the probability of asthma. For those people with a high probability of asthma, a trial of drug therapy may be initiated. For those with an intermediate probability of asthma, objective tests should be used.[7]

NICE place a greater emphasis on the use of objective tests in the diagnosis of asthma, advising that **asthma should not be diagnosed on symptoms alone**.[4]

What diagnostic tests are available?

A number of tests are available to determine the likelihood of asthma.

Airway inflammation measures:

Measuring airway inflammation / likely response of corticosteroids.

- Fractional exhaled nitric oxide (FeNO) — FeNO measurements correlate well with a raised sputum eosinophil count.[4] FeNO is therefore a useful assessment of airway inflammation / likely response of corticosteroids. There is however some uncertainty about both the sensitivity and specificity of FeNO, particularly as to whether it can distinguish general atopy from asthma.[4,7]

Lung function tests:

Measuring airflow obstruction (spirometry and peak flow) and assessment of reversibility with bronchodilators.

- Spirometry — not useful in ruling out asthma because sensitivity is low.[8]
- Peak expiratory flow variability
- Bronchodilator variability

Airway hyperreactivity measures:

To provoke bronchoconstriction (airway narrowing) - people with asthma will react to lower doses of challenge test than someone without airway hyperactivity.

- Direct bronchial challenge test with histamine or methacholine.

What do the guidelines recommend?

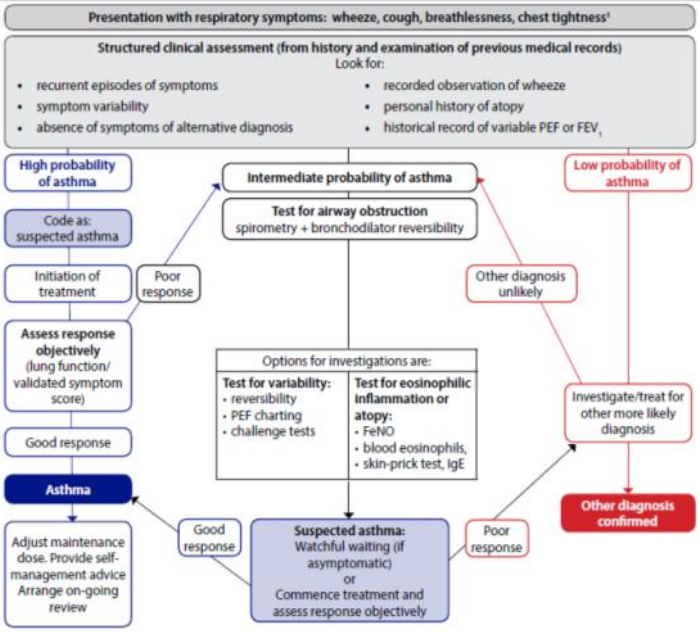
Both BTS/SIGN and NICE recommend spirometry as an initial test to assess the presence and severity of airflow obstruction in adults.[4,7]

NICE recommend that FeNO is also used as soon as is possible when considering a diagnosis of asthma.[4] BTS/SIGN only list FeNO as a potentially useful test in people with an intermediate probability of asthma.[7,8]

Peak flow is recommended by BTS/SIGN as an initial test in primary care. NICE advise the use of peak flow monitoring to check on variability if there is uncertainty with the diagnosis.

If there is still uncertainty, NICE advise that referral for histamine / methacholine challenge is recommended.[4,121]

BTS/SIGN 2016 Diagnostic algorithm



Asthma COPD Overlap Syndrome

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.

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 is required to guide therapeutic choices in this group of patients. Preliminary advice in publications is to treat with a combination of LABA and ICS to minimise the effects of uncontrolled asthma.[85,129]

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]

Non-pharmacological treatment

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.

There are however some non-pharmacological strategies that can improve asthma symptoms. 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.[7]

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 to 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]

Overview of pharmacological therapies

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, tiotropium 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 β_2-agonists, formoterol in a MART regimen, inhaled short-acting anticholinergics, immediate-release theophylline, and short-acting oral β_2-agonists.[1]

What is the aim of asthma management?

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.

Approach to management

1. Start treatment at the level most appropriate to initial severity.
2. Achieve early control.
3. Maintain control by:
   - increasing treatment as necessary
   - decreasing treatment when control is good.[7]

What's new with the BTS/SIGN guideline?

The 2016 update to the BTS/SIGN guideline saw a number of changes from previous versions:

- The stepped approach remains, but the **numbering of the steps has been removed**. Instead, BTS/SIGN provide verbal descriptions at each stage of treatment in order to describe more clearly the sequence of treatment. See page 11 for BTS/SIGN algorithm.
- Another significant change is the **removal of short-acting beta-2 agonists (SABA) on an "as required" basis as first line management**. Instead, regular low dose inhaled corticosteroid (ICS) should be initiated in all patients, except those with very occasional short-lived wheeze.[7,8] This change is in response to findings from the NRAD report that many people with asthma who died were only treated with a SABA.[7,8] ICS is essential, to reduce the inflammation that is the cornerstone of asthma, while treatment with a SABA only provides symptomatic treatment.

What are the main differences between the BTS/SIGN and NICE guidelines?

One of the most significant differences in the management of asthma is the recommendation to use a leukotriene receptor antagonist (LTRA) as first choice add-on therapy for people whose asthma is not well controlled by a low dose ICS (rather than long acting beta agonist (LABA)).[4,7] This will be discussed in further detail in the section '*Add-on therapies'.*

Inhaled short-acting β_2-agonists

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. **They should rarely be used on their own**.[7] Furthermore, overuse of short-acting β_2-agonists is a marker of uncontrolled asthma and has been associated with increased deaths due to asthma.[21]

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]

Formoterol in Maintenance and reliever therapy (MART)

Formoterol may be used as a reliever medicine as part of a MART regimen — see page 9 for further details.

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]

What are the differences between ICS with respect to steroid potency?

- Beclometasone (BDP) and budesonide are approximately equivalent in clinical practice.[7] However, there may be variations with different delivery devices.
- Fluticasone propionate provides equal clinical activity to BDP and budesonide at half the dosage.[7]
- It is difficult to establish the exact equipotent dose of fluticasone furoate.[7] However, the manufacturer's SPC states that in people with asthma, fluticasone furoate 100 micrograms once daily is approximately equivalent to fluticasone propionate 250 micrograms twice daily, and fluticasone furoate 200 micrograms once daily is approximately equivalent to fluticasone propionate 500 micrograms twice daily.

Fine particle inhalers

The beclomethasone in Qvar® (BDP) and Fostair® (BDP plus formoterol) is an extra fine particle, achieving greater penetration and lung deposition than CFC-MDIs, and therefore is more potent than traditional BDP CFC-free inhalers.

- Qvar® is approximately 2 to 2.5 times more potent than Clenil Modulite®.
- 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]

Due to difficulties in making comparisons between ICS inhalers, with respect to potency, both the 2016 BTS/SIGN update and the new NICE guidance, have moved to categorisation of ICS by dose (into low, medium and high dose) — see **TABLE TWO**.

Is there any evidence comparing the inhaled corticosteroids?

Comparative evidence is lacking. Studies comparing ICS 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 in asthma the inhaled corticosteroids do not differ in efficacy or safety.[7]

Adverse effects with ICS

As with all effective medicines, the benefits of 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?

ICS are absorbed from the lung, accounting for some degree of systemic bioavailability. The risk of systemic adverse effects from an ICS 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]

TABLE TWO: Categorisation of inhaled corticosteroids by dose (adults)

Product	Dose		
	Low dose	Medium dose	High dose
pressurised Metered Dose Inhalers (pMDI)			
Alvesco®	80–160 micrograms per day as a single dose	240–320 micrograms per day as a single dose or in 2 divided doses	400–640 micrograms per day in 2 divided doses
Beclometasone dipropionate Non-proprietary	200–400 micrograms per day in 2 divided doses	600–800 micrograms per day in 2 divided doses	1,000–2,000 micrograms per day in 2 divided doses
Clenil Modulite®	200–400 micrograms per day in 2 divided doses	600–800 micrograms per day in 2 divided doses	1,000–2,000 micrograms per day in 2 divided doses
Flixotide Evohaler®	100–250 micrograms per day in 2 divided doses	300–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses
Flutiform®	100–250 micrograms per day in 2 divided doses	300–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses
Fostair® (extra fine)	100–200 micrograms per day in 2 divided doses	300–400 micrograms per day in 2 divided doses	500–800 micrograms per day in 2 divided doses
Seretide Evohaler®	100–250 micrograms per day in 2 divided doses	300–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses
Qvar® (extrafine) Qvar® autohaler Qvar® Easi-breathe	100–200 micrograms per day in 2 divided doses	300–400 micrograms per day in 2 divided doses	500–800 micrograms per day in 2 divided doses
Dry Powder Inhalers (DPI)			
Asmabec®	200–400 micrograms per day in 2 divided doses	600–800 micrograms per day in 2 divided doses	1,000–2,000 micrograms per day in 2 divided doses
Asmanex Twisthaler®	200 micrograms per day as a single dose a day	400 micrograms per day in 2 divided doses	Up to 800 micrograms per day in 2 divided doses
Budelin Novolizer®	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses
DuoResp Spiromax®	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses
Easyhaler® - Beclometasone	200–400 micrograms per day in 2 divided doses	600–800 micrograms per day in 2 divided doses	1,000–2,000 micrograms per day in 2 divided doses
Easyhaler® - Budesonide	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses
Flixotide Accuhaler®	100–250 micrograms per day in 2 divided doses	300–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses
Fostair NEXThaler®	100–200 micrograms per day in 2 divided doses	300–400 micrograms per day in 2 divided doses	500–800 micrograms per day in 2 divided doses
Pulmicort Turbohaler®	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses
Relvar Elipta®		100 micrograms as a single daily dose	200 micrograms as a single daily dose
Seretide Accuhaler®	100–250 micrograms per day in 2 divided doses	300–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses
Symbicort Turbohaler®	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses

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

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

High Dose Inhaled Corticosteroid Safety Cards

► For patients on a high dose of ICS, provide them with a 'High Dose Inhaled Corticosteroid Safety Card'. This supports communication of the risks associated with treatment, and specific written advice to consider corticosteroid replacement during an episode of stress such as intercurrent illness.

► High Dose Inhaled Corticosteroid Safety Cards are available from BSO by emailing: pharmacystationeryorders@hscni.net.

Are there any new safety concerns with ICS?

MHRA/CHM advice (August 2017) Corticosteroids: rare risk of central serous chorioretinopathy with local as well as systemic administration

Central serous chorioretinopathy is a retinal disorder that has been linked to the systemic use of corticosteroids. Recently, it has also been reported after local administration of corticosteroids via inhaled and intranasal, epidural, intra-articular, topical dermal, and periocular routes. The MHRA recommends that patients should be advised to report any blurred vision or other visual disturbances with corticosteroid treatment; consider referral to an ophthalmologist for evaluation of possible causes if a patient presents with vision problems.[124]

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 'High Dose Inhaled Corticosteroid Card'.[7]

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

In children, high doses of ICS (> 400 micrograms/day BDP / > 200 micrograms/day 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]

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]

Should the ICS dose be increased during an asthma attack?

Note: the term 'asthma attack' replaced 'asthma exacerbation' in the SIGN / BTS 2014 guideline in order to be more understandable and to give a clearer indication of the need for action.

Studies have shown that, in patients who are on a low dose of regular ICS (i.e. 200 micrograms of BDP equivalent), 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 ICS 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]

People currently taking a moderate to high dose of ICS (≥400 micrograms daily):

Increasing the ICS dose is ineffective during if patients are already taking a moderate or high dose (i.e. ≥400 micrograms of BDP equivalent daily) - these patients should be advised to move straight to the oral steroid step. Patients may safely hold an emergency supply of prednisolone tablets (for use if their symptoms continue to deteriorate and/or if their peak flow falls to 60% of their best).[7]

People currently taking a low dose of ICS:

For people who are on low doses (e.g. 200 micrograms) of BDP equivalent, they may be advised to increase the dose substantially (e.g. consider quadrupling regular ICS dose) for seven days at the onset of a deterioration. Note: do not exceed the max licensed daily dose.[4,7]

Oral steroids as rescue therapy

Acute attacks of asthma may be treated with short courses of oral steroids, reducing once the attack has been controlled. For example, a standard course could be 40mg prednisolone daily for at least 5 days or until recovery. Courses of less than 3 weeks usually do not require dose tapering.[31]

Counselling points for community pharmacists on spacer devices

These are learning points that were identified when trying to manage asthma attacks.

- Counsel people not to carry or store their or their children's spacer device in a plastic bag as this will cause it to become static (builds up an electrical charge) which reduces the effect of the asthma medicine.
- Counsel people that, if using a spacer device to administer multiple puffs:
  - put one puff of inhaler medicine into the spacer at a time
  - breathe in and out of the mouthpiece five times
  - repeat this for each puff of the inhaler needed.

  Remember: wait 30 seconds between puffs and take out the inhaler and shake it before each one.[3]

Incorporate these points within PAAP

Add-on therapies

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.

What is the first choice add on therapy?

In their new guideline on *Asthma: diagnosis, monitoring and chronic asthma management*, NICE recommend a leukotriene receptor antagonist (LTRA) as the first choice add-on therapy to low dose ICS in patients not controlled on a low dose ICS maintenance therapy.[4]

In their latest update, BTS/SIGN continue to recommend inhaled LABA as first choice add-on therapy to low dose ICS for patients aged 5 years and above.[7]

Why the difference between NICE and BTS/SIGN?

While both NICE and BTS/SIGN evaluated the same evidence base, NICE included health economic modelling in their methodology, i.e. NICE consider both effectiveness and cost-effectiveness. LTRAs are now available generically and as such are substantially cheaper than ICS/LABA.

TABLE THREE: Price comparison add-on therapies

Product		Cost for one month [123]
Montelukast tablets	10mg	£1.02
Clenil Modulite® MDI (beclometasone)	200 micrograms	£16.17
Sirdupla® MDI (salmeterol / fluticasone)	125/25	£26.25
	250/25	£44.61
Seretide® MDI (salmeterol / fluticasone)	125/25	£35.00
	250/25	£59.48

How do LTRAs and LABAs compare in terms of clinical effectiveness?

Head-to-head comparisons of ICS/LABA compared to ICS/LTRA in adults have shown that ICS/LABA is *marginally* more clinically effective than ICS/LTRA (the evidence is inconclusive in children). **BOX ONE** summarises the evidence findings by NICE.

BOX ONE: Summary of ICS low dose + LTRA versus ICS low dose + LABA evidence by NICE

- No clinical difference in terms of severe exacerbations
- No clinical difference in terms of quality of life (AQLQ/ mini AQLQ)
- No clinical difference in terms of quality of life (EQ-5D)
- No clinical difference in terms of asthma control (ACQ)
- No clinical difference in terms of hospitalisations
- No clinical difference in terms of reliever medication use (puffs/day)
- No clinical difference in terms of reliever medication use (puffs/night)
- No clinical difference in terms of reliever medication use (% reliever free nights)
- No clinical difference in terms of reliever medication use (reliever free days during study period)
- No clinical difference in terms of FEV_1 (L)
- Clinical harm in terms of FEV_1 (% predicted)
- No clinical difference in terms of PEF (L/min)
- No clinical difference in terms of infections (all respiratory).

While ICS/LABAs are marginally more effective in controlling all exacerbations, no clinical difference was seen between ICS/LABA and ICS/LTRA in terms of severe exacerbations.

Clinical harm was reported in terms of FEV_1 (% predicted) but according to NICE, the difference is small, and unlikely to be clinically significant given the normal variability of FEV_1 (% predicted).

Overall, NICE considered these differences to be too small to justify the additional cost of LABA.

What does this mean in practice?

In terms of what this means in practice, clinicians now have a *choice* to prescribe a LABA or a LTRA if low dose ICS does not control symptoms effectively.

LTRAs are substantially cheaper than LABAs and certainly cost is an consideration when prescribing within the Health Service. However, other factors such as patient preference, compliance, concomitant diseases (e.g. rhinitis) and risk of exacerbation are also important considerations when deciding on the best treatment for the individual.[121]

Please note: there is no need to switch people who are currently well controlled on current treatment.

Long-acting β_2-agonists

Addition of a long-acting β_2-agonist (LABA) is a treatment option when a low dose of inhaled corticosteroids +/- leukotriene receptor antagonist 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 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 add-on therapy to ICS in children under five years of age is a leukotriene receptor antagonist (montelukast).[7]

What are the differences between LABAs?

Features distinguishing the LABAs that are 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

► A LABA should only be started in patients who are **already on ICS**.
► A 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.

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 ICS/formoterol in a single inhaler as rescue medication instead of a short-acting β_2 agonist, in addition to its regular use as maintenance therapy has been shown to be an effective treatment regime.[4,7]

The following all have a MART license:

- DuoResp Spiromax® 160/4.5 (budesonide / formoterol)
- Fobumix Easyhaler® 160/4.5 (budesonide / formoterol)
- Symbicort Turbohaler® 100/6, 200/6 (budesonide / formoterol)
- Fostair® MDI 100/6 (beclomethasone / formoterol)

Both NICE and BTS/SIGN agree that MART may be considered for adult patients who are poorly controlled on ICS/LABA.[4,7] SIGN also recommend MART as an option for adult patients who are not controlled on medium dose ICS.[7]

NICE recommend starting a MART regimen at a low maintenance dose ICS, with the option to increase to a medium maintenance dose ICS if uncontrolled.[4] If however the moderate maintenance dose ICS in the MART regimen does not control asthma symptoms, a high maintenance dose ICS in a fixed-dose regimen is then advised.[4] This is because the evidence for high dose ICS in a MART regimen is lacking.

Prescribing Points – MART

► There is no need for another reliever inhaler.
► The total regular dose of daily ICS is not decreased.
► Patients taking rescue ICS / formoterol ≥ once a day on a regular basis should have their treatment reviewed.
► Careful education of patients on this regimen is essential, and directions should be put into their Asthma Action Plan.[4,7]
► NICE advise that a MART regimen can be used from age 5 years and above. However, MART regimens do not have a UK license for use in children and young people — refer to individual inhaler prescribing material for licensed age ranges.

Leukotriene receptor antagonists (LTRAs)

The leukotriene receptor antagonist (LTRA) montelukast has a small and variable bronchodilator effect.
Montelukast reduces symptoms (including cough), improves lung function, and reduces airway inflammation and asthma attacks.
Montelukast is less effective than ICS when used alone as controller medication, which is why NICE and BTS/SIGN continue to recommend it as add-on therapy.[4,7]
When used as add-on therapy, montelukast may reduce the dose of ICS required by patients with moderate to severe asthma and may improve asthma control in patients whose asthma is not controlled with ICS.[7,18-30]

Children

The first choice add-on therapy to ICS in children under five years of age is a leukotriene receptor antagonist.[7]
Montelukast is licensed for use in children 2–5 years of age.[2]

When should a LTRA be reviewed?

LTRAs do not work for everyone. Therefore a short trial (e.g. for 28 days) is advisable to identify those patients who will respond to this therapy class.[119,120] Decisions to take at the review will depend on the age of the patient:

For **children aged under 5 years:** if there is no evidence of therapeutic benefit after the month trial, then the LTRA should be stopped and the child referred to a healthcare professional with expertise in asthma for further investigation and management [4]

For **children aged 5 to 16 years**, if asthma is uncontrolled on a paediatric low dose of ICS and an LTRA as maintenance therapy, *consider* stopping the LTRA and starting a LABA in combination with the ICS.

For **adults (aged 17 years and over)** whose asthma is uncontrolled on a low dose of ICS and an LTRA as maintenance therapy, offer a LABA in combination with the ICS, and review LTRA treatment as follows:

- discuss with the person whether or not to continue LTRA treatment
- take into account the degree of response to LTRA treatment.[4]

Prescribing Point – Leukotriene receptor antagonists (montelukast)

► Prescribe montelukast 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 to ensure that they are also using inhaler therapy.

Tiotropium

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

Tiotropium in the Spiriva® Respimat® device (i.e. not the Handihaler® or Braltus Zonda®) has a license for asthma. It is licensed as an add-on maintenance bronchodilator treatment in patients aged 6 years and older with severe asthma who experienced one or more severe asthma exacerbations in the preceding year.[17]

BTS/SIGN position tiotropium as an option as add-on therapy (on a trial basis) for adult patients who do not respond to ICS plus LABA. In such a circumstance, the LABA should be stopped and tiotropium added to the ICS .[7]

NICE do not make a recommendation in their guideline on tiotropium in asthma.[4]

What is the evidence for tiotropium in asthma?

A review of RCTs in adults taking tiotropium bromide in addition to ICS plus LABA, compared with ICS plus LABA, reported fewer asthma exacerbations (although results were inconclusive), improved lung function and some benefits relating to asthma control in those taking tiotropium, but no improvement in quality of life. Evidence relating to serious adverse effects was inconclusive but fewer non-serious adverse events were reported in those taking tiotropium. In two of the three trials included in the review, patients were taking high dose ICS, although it was not possible to draw conclusions about the effect of tiotropium in those taking different doses of ICS plus LABA.[4,125] There is insufficient evidence to suggest that addition of tiotropium to ICS in patients inadequately controlled on ICS alone has any benefit over addition of LABA to ICS.[4,126]

People in the 2 RCTs supporting the licence extension for tiotropium in asthma had persistent airway obstruction, with FEV_1 and FEV_1/FVC ratios similar to those in people with moderate COPD.[17]

Expert opinion suggests that tiotropium is 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.[17,127]

Prescribing Point – Tiotropium

► In patients with moderate to severe renal impairment (creatinine clearance ≤ 50ml/min), only use tiotropium (Spiriva® Respimat®) if the benefits outweigh the risks.[127,128]

► Review treatment one to two months following treatment initiation. [127]

Oral corticosteroids

For the small number of patients who are not adequately controlled with inhaled therapies, 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. All other alternative treatments must be considered.[7]

Prevention of oral steroid side effects

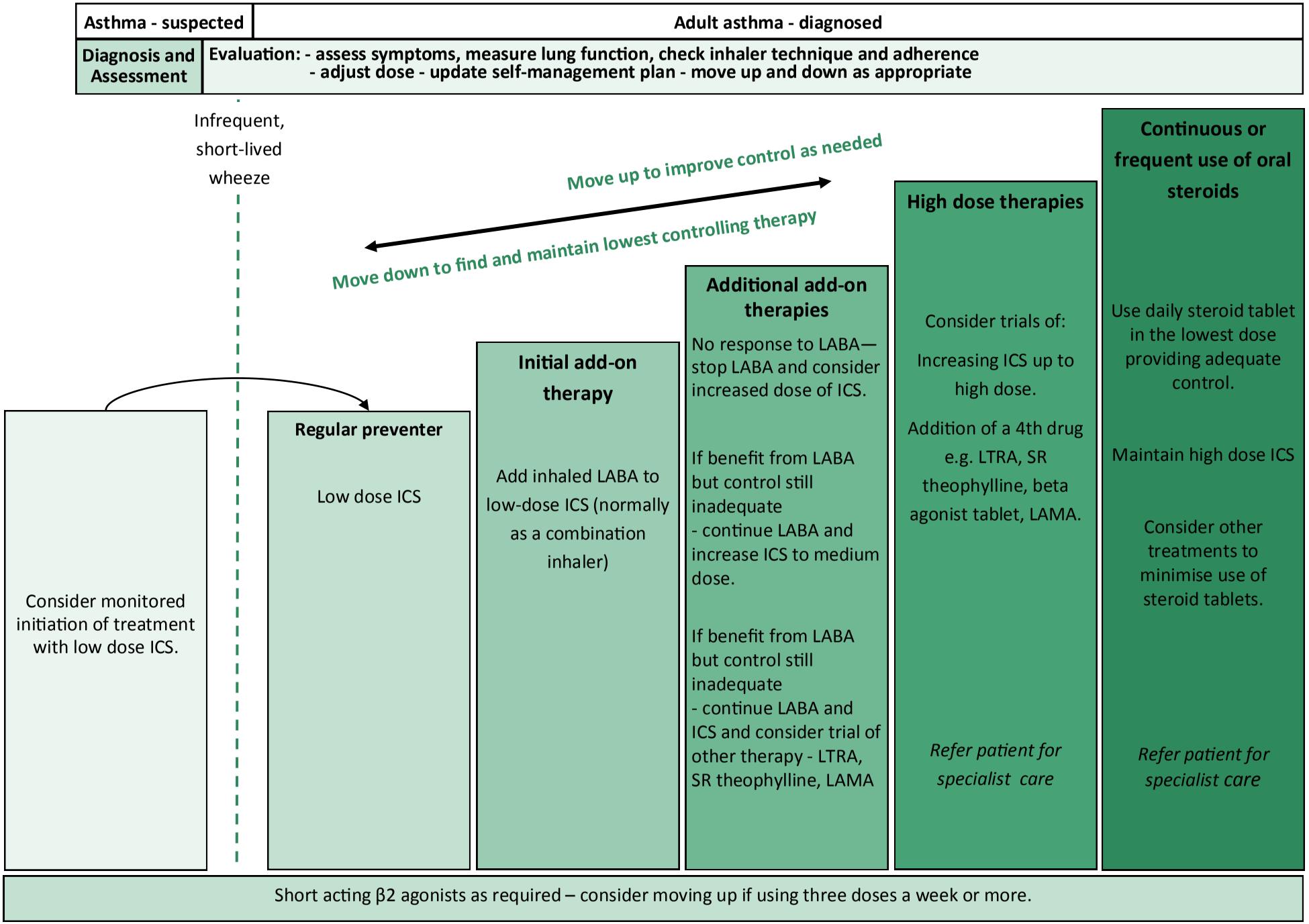
Patients who have been taking oral steroids for longer than three months or who require three or more courses a year will be at increased risk of systemic steroid side effects.[7]

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.

Adapted from BTS/SIGN Asthma management algorithm (Adults) 2016



NICE 2017 Asthma Guidance (adults)

Move up or down to control symptoms

1	Offer a SABA to newly diagnosed
2	Offer a low dose of an ICS
3	Offer a LTRA in addition to low dose ICS
4	Offer a LABA in combination with low dose ICS and review LTRA
5	Offer to change ICS +LABA maintenance therapy to a MART regimen with low dose ICS, +/- LTRA
6	Consider increasing ICS to moderate dose; continue on MART or change to fixed dose ICS/LABA with SABA reliever
7	Increase ICS to high dose (only as fixed dose with LABA – not MART), +/- LTRA with SABA as reliever

BTS/SIGN 2016 Asthma Guidance (adults)

Move up or down to control symptoms

Regular preventer	Start low dose ICS	SABA as required at any stage. Consider moving up a step if using ≥ 3 doses of SABA per week
Initial add-on therapy	Add inhaled LABA to low-dose ICS (normally as a combination inhaler)	
Additional add-on therapies	No response to LABA — stop LABA and consider increased dose of ICS. If benefit from LABA, but control still inadequate: • continue LABA and increase ICS to medium dose. If benefit from LABA but control still inadequate: • continue LABA and ICS and consider trial of other therapy, e.g. LTRA, SR theophylline, LAMA	
High dose therapies	Consider trials of: • Increasing ICS up to high dose. • Addition of a 4th drug, e.g. LTRA, SR theophylline, beta-agonist tablet, LAMA. *Refer patient for specialist care*	
Continuous or frequent use of steroids	Use daily steroid tablet in the lowest dose providing adequate control. Maintain high dose ICS Consider other treatments to minimise use of steroid tablets. *Refer patient for specialist care*	

Choice of inhaler device

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 FOUR** 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 FOUR: 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]

Patient resources for inhaler technique

s on how to use your inhaler

PrescQIPP have produced a series of videos on how to use 17 different inhaler devices.

Inhaler technique assessment tools

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 17 types of inhaler device on the market.

Both of these resources have been uploaded to the Patient Zone section of the NI Formulary: http://niformulary.hscni.net/PatientZone/A_COPD/Pages/default.aspx.

Should inhalers be prescribed generically?

With the exception of salbutamol MDI, generic prescribing of inhalers should be avoided as this might lead to people with asthma being given an unfamiliar inhaler device which they are not able to use properly.[7]

Dry powder inhalers (DPIs)

There are a variety of different types of DPIs on the market. As DPIs differ in their method of administration, it is important that the patient is maintained on the device that they have been trained to use. It is therefore essential to specify inhaler device (e.g. Spiromax®, NEXThaler®), strength and dose when prescribing a DPI — do not prescribe generically.

Metered dose inhalers (MDIs)

In theory, when considering only the device, patients who are trained and competent in using a MDI should be able to use any MDI. However, differences in potency and cost between the different combination ICS/LABA MDIs require consideration.

Several branded generic versions of ICS / LABA MDIs are now available on the market. However they must be written by brand in order to achieve savings against comparator products.

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 a beclometasone dipropionate 250 micrograms CFC-free inhaler.[31]

Key message:

- **All inhalers should be prescribed BY BRAND with the exception of salbutamol MDI.**

NI Formulary choices

The Northern Ireland Formulary provides guidance on choices of inhalers.

Choice of device should be considered on basis of ability to use the inhaler, patient-acceptability and cost.

http://niformulary.hscni.net

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. Devices such as In-Check DIAL® and Flo Tone CR® may be used to help with technique training.

► 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.

► Prescribe inhalers by brand, with the exception of salbutamol MDI.

Community pharmacists

If a prescription is presented that is written generically for an inhaler (other than salbutamol MDI), the brand should be confirmed with the prescriber.

Self-management plans

All patients with asthma should receive an individualised self-management plan, supported by patient education.[4,7]

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]

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 report).[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]

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 PAAPs, 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 PAAPs may reduce readmission rates.[84]

Examples of self-management plans can be found:

- Asthma UK website (www.asthma.org.uk) or
- HSCB Public Health website (http://www.publichealth.hscni.net/publications/asthma-action-plan).

Self Management Good Practice Points (BTS/SIGN) [7]

► 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.

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 annual asthma review in the General Medical Services (GMS) and the NICE Quality Statements for asthma.

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 (see Northern Ireland Formulary website: http://niformulary.hscni.net/PatientZone/A_COPD/Pages/default.aspx)
- Mini asthma quality of life questionnaire or paediatric asthma quality of life questionnaire.

2) Tests of airway function

These tools are usefully supplemented by tests of airway function such as:

- Spirometry
- Peak flow variability testing.[4]

Do not routinely use FeNO to monitor asthma control, but consider FeNO measurement as an option to support asthma management in people who are symptomatic despite using ICS.[4]

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.

What you should do when a patient exhibits poor asthma control?

Before considering alteration of drug therapy, consider:

- Is there patient compliance with the existing therapy?
- Is the patient able to use their inhaler properly?
- Are there any correctable trigger factors?
- Does the patient have allergic rhinitis?
- Is the diagnosis correct? (Is there objective evidence of asthma?).

If asthma is controlled — consider stepping down.

Stepping down

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]

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]

Prescribing Notes: How to step down treatment

- Discuss with the person the potential risks and benefits of decreasing maintenance therapy.[4]
- The PAAP should be updated.
- 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]

Resources to help step-down are available on the Primary Care intranet http://primarycare.hscni.net/pharmacy-and-medicines-management/resources/respiratory/.

Guidance to Support the Review of Combination Inhaled Corticosteroids for Adults in Asthma.

- The BTS/SIGN guidance on the stepwise management of asthma should be used to treat patients at the step most appropriate to the initial severity of asthma.
- The dose of inhaled corticosteroids (ICS)should be titrated to the lowest dose for effective control
- Use the three Ts when reviewing asthma - (Adherence with Treatment, Inhaler Technique and Trigger Factors.)
- Complete asthma control needs to be achieved for at least 12 weeks before attempting to step patients down.
- If asthma is controlled with the combination ICS/long-acting beta 2 agonist (LABA) inhaler the preferred approach is to reduce **the ICS by approximately 25-50%** whilst continuing LABA at the same dose.
- If control is maintained after stepping down then further reduction in ICS should be attempted until lowest possible dose achieved, when the LABA may be stopped.

Figure 1. Levels of Asthma Control

	Level of Asthma Control		
	Completely Controlled	Partly Controlled	Uncontrolled
Daytime Symptoms	Twice or less per week	> Twice per week	Three or more features of partly controlled asthma
Limitation on Activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for reliever / rescue treatment	Twice or less per week	> Twice per week	
Lung Function (PEF or FEV_1)	None	None	

Table 1. Equivalence to Beclometasone dipropionate (BDP)

Inhaled Corticosteroid	Equivalent Beclometasone dipropionate (BDP) dose
400mcg **Budesonide**	400mcg BDP
400mcg **Clenil®** (Beclometasone)	400mcg BDP
200mcg **Fostair®** (Beclometasone– extra fine)	500mcg BDP
250mcg **Fluticasone propionate**	500mcg BDP
92mcg **Fluticasone furoate***	500mcg BDP*
200mcg **Qvar®** (Beclometasone – extra fine)	400mcg BDP

*The exact equivalence of fluticasone furoate to other ICS is not known. The British National Formulary (Sept 2016) notes that fluticasone furoate 92 micrograms once daily is approximately equivalent to fluticasone propionate 250 micrograms twice daily.

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1	**In the management of chronic asthma**			
	a	Reducing house dust mite levels in the home has been found to improve symptoms of asthma	T	F
	b	Inhaled corticosteroids are the most effective controller medications currently available.	T	F
	c	Higher doses of inhaled corticosteroids may be needed in patients who are smokers or ex-smokers.	T	F
	d	Complete control of asthma is defined as only 1 or 2 asthma attacks per year.	T	F
2	**In relation to inhaled corticosteroids (ICSs):**			
	a	Fluticasone furoate provides equal clinical activity to beclometasone dipropionate (BDP) and budesonide at half the dosages.	T	F
	b	Patients should be advised to double their dose of ICS during an asthma attack.	T	F
	c	Hoarseness and dysphonia due to ICS can usually be minimised by use of a spacer.	T	F
	d	Clinically important, long-term adverse systemic effects are usually not observed in adults until ICS is at a high dose (usually > 1000 micrograms BDP per day or equivalent.	T	F
3	**In relation to maintenance and reliever therapy (MART) regimens:**			
	a	There is no need for another reliever inhaler in addition to MART.	T	F
	b	The total regular dose of daily ICS should not be decreased.	T	F
	c	DuoResp Spiromax® 160/4.5, Fobumix Easyhaler® 160/4.5, Symbicort Turbohaler® 100/6, 200/6 and Fostair® MDI 100/6 are licensed for MART.	T	F
	d	There is strong evidence for high dose ICS in a MART regimen.	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	**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	T	F