

# COMPASS Therapeutic Notes on the Management of Chronic Asthma in Adults and Older Children

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Glossary	
BDP	Beclometasone Dipropionate
Churg-Strauss syndrome	A form of vasculitis, featuring blood vessels in the lungs, skin, nerves, and abdomen
Chromones	Collective term for sodium cromoglicate and nedocromil sodium
CSM	Committee on the Safety of Medicines
DPI	Dry Powder Inhaler
Dysphonia	Difficulty and/or pain whilst speaking
FEV <sub>1</sub>	Forced Expiratory Volume in one second
HFA	Hydrofluoroalkane
HPA	Hypothalamic Pituitary Axis
ICS	Inhaled Corticosteroid
IgE	Immunoglobulin E
LABA	Long-Acting Beta -2 Agonist
LTRA	Leukotriene Receptor Antagonist
MHRA	Medicines and Healthcare products Regulatory Agency
PEF	Peak Expiratory Flow
pMDI	Pressurised Metered Dose Inhaler

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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 bronchitis, 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. Patients will typically have intermittent symptoms of cough (particularly at night or in the early morning), wheeze, breathlessness, chest tightness and sputum production. Underlying these symptoms there is a process of variable airways obstruction, airway hyperresponsiveness and chronic inflammation.

## Managing Chronic Asthma – 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).<sup>10</sup> The familiar stepwise approach to asthma management is maintained in the most recent BTS/SIGN guidance update (2009),<sup>10</sup> although there are a number of important changes and shifts in emphasis. For example:

- € The level of treatment is dictated by an assessment of control rather than by an assessment of "severity".
- € The need to check adherence, inhaler technique and trigger-factor exposure before initiating new drug therapy is stressed.
- € There is a greater focus on "stepping

down" treatment, where appropriate. € More detailed advice on when to "step up" is also provided.

### *What are the aims of asthma management?*

The aim of asthma management is control of the disease with minimal side-effects. Asthma control is defined as:<sup>10</sup>

- € No daytime symptoms
- € No night time awakening due to asthma
- € No need for rescue medication
- € No exacerbations
- € No limitations on activity including exercise
- € Normal lung function (FEV<sub>1</sub> and/or PEF > 80% predicted or best) - with minimal side-effects.

The BTS/SIGN guideline on asthma reflects a new emphasis on recognising that each patient will have different goals for their asthma management and that some individuals may wish to balance perfect control against the potential side-effects or inconvenience of taking medication. The focus on patient-set targets recognises the need for dialogue with patients to achieve a workable partnership, recognising their needs and preferences as well as the ideal of perfect control. This should result in patients who are better informed and who are able to make rational decisions<sup>11</sup> – thereby reducing poor adherence with regular preventer therapy and poor outcomes.<sup>12,13</sup>

### Some asthma statistics...

- i Asthma is a problem worldwide, with an estimated 300 million affected individuals.<sup>1,2</sup>
- i 5.2 million people in the UK are currently receiving treatment for asthma, nearly 1 million of whom are children.<sup>3,4</sup>
- i More than 150,000 people in Northern Ireland have asthma: 115,000 adults and 35,000 children.<sup>5</sup>
- i Asthma is the most common chronic disease in children, with a prevalence of between 17% and 23%.<sup>4</sup>
- i More than 4.1 million GP consultations for asthma occur each year in the UK.<sup>3</sup>
- i Each year a GP with 2000 patients will see approximately 85 people with asthma, and each of these will consult three times a year on average.<sup>6</sup>
- i There are about 1500 deaths a year from asthma in the UK.<sup>7</sup>
- i The prevalence of asthma has increased in most countries since the 1970s. Levels may have plateaued in some developed countries.<sup>8,9</sup>

## Stepwise approach for adults and children over 5 years.<sup>10</sup>

### At any step, before starting a new drug or stepping up treatment:

- € Re-check compliance, inhaler technique and eliminate trigger factors.
- € Confirm with the person his/her understanding of the role of treatment.

### At any stage:

- € If treatment is stepped-up without effect, do not forget to step it back down. This is of particular importance with inhaled corticosteroids.
- € If a trial of a new agent is shown to be ineffective, stop the drug.

### Step ONE: Inhaled reliever therapy when required

Prescribe an inhaled short-acting  $\beta_2$ -agonist, such as salbutamol or terbutaline, for use 'as required' (unless the individual has been shown to benefit from regular use). Choose an effective delivery mechanism on the basis of convenience and cost.

Good asthma control is associated with little or no need for the short-acting  $\beta_2$ -agonist. Using **two or more canisters of short-acting  $\beta_2$ -agonist per month, or taking more than 10-12 puffs per day** is a marker of poorly controlled asthma that puts the individual at risk of fatal or near fatal asthma.

Move to **Step TWO** if the person:

- € Is having symptoms three times a week or more, or
- € Is waking with symptoms one night a week or more, or
- € Has had an exacerbation requiring oral corticosteroids in the past two years, or
- € Is using their inhaled short-acting  $\beta_2$ -agonist three times a week or more.

### Step TWO: Introduction of regular preventer therapy

Add an inhaled corticosteroid (ICS).

**Starting ICS doses:**

- Adults and children over 12 years: Start with 400 micrograms BDP or equivalent daily\*.
- Children aged 5-12 years: Start with 200 micrograms BDP or equivalent daily\*.

Importantly, the dose of ICS should be titrated to the lowest dose at which effective control of asthma is maintained. A trial of low dose ICS should last for at least 3 months to assess therapeutic benefit.<sup>14</sup> With the exception of ciclesonide, the daily dose of inhaled corticosteroids should be split and given in two separate doses. Most inhaled steroids (except ciclesonide) are slightly more effective when taken twice rather than once daily, but may be used once daily in some patients with milder disease.<sup>10,15</sup>

Note: Higher doses of ICS may be needed in people who are smokers or ex-smokers.<sup>16</sup>

Inhaled corticosteroids are the first-choice preventer drug. Alternative, less effective prevention therapies in patients taking short-acting beta-agonists alone include chromones or leukotriene receptor antagonists.

### Step THREE: Initial 'add-on' therapy

Meta-analyses suggest that in asthma not controlled by moderate dose ICS, better outcomes are obtained by **adding** an LABA to a moderate dose of ICS than by increasing the ICS dose to a maximum first.<sup>17,18</sup>

No exact dose of ICS can be deemed the correct dose at which to add another therapy. An absolute threshold for introduction of add-on therapy in all patients cannot be defined. BTS/SIGN indicates that add-on therapy may be considered for:

- € Children (5-12 years) who are not adequately controlled by 400 micrograms BDP or equivalent per day\*.
- € Adults and children over the age of 12 who are not adequately controlled by 200-800 micrograms BDP or equivalent per day\*.

The duration of a trial of add-on therapy depends on the desired outcome. For example, to prevent nocturnal waking requires a relatively short trial (days or weeks), while to prevent exacerbations of asthma or to reduce use of oral corticosteroids requires a longer trial, e.g. weeks or months. If there is no response to treatment the drug should be discontinued.

If the child has a good response to the LABA but symptom control is still inadequate, continue the LABA and increase the ICS dose to:

- € Child (5-12 years) 400 micrograms per day BDP (or equivalent)\*.
- € Adult and child over 12 years: 800 micrograms per day BDP (or equivalent)\*.

If the person is receiving these higher ICS doses and control remains poor, go the **Step FOUR**.

If the person does not respond to LABA, STOP IT and increase ICS dose to:

- € (Child 5-12 years) 400 micrograms per day of BDP (or equivalent)\*.
- € Adult and child over 12 years: 800 micrograms per day BDP (or equivalent)\*. Unless the person is already on this dosage.

If symptom control remains inadequate consider an alternative add-on treatment, such as an LTRA or modified-release theophylline, before moving on to **Step FOUR**.

### Step FOUR: Persistent poor control

Either:

- € Increase the ICS to the maximum recommended dose, OR
- € Consider starting a fourth drug that is not already being used (e.g. LTRA, modified-release theophylline, or an oral modified-release  $\beta_2$ -agonist). Use caution when adding oral modified-release  $\beta_2$ -agonist in patients already on an LABA.

### Step FIVE: Continuous/frequent courses of oral corticosteroids

Before proceeding to **Step FIVE**, consider referring patients with inadequately controlled asthma, especially children, to specialist care.

For the small number of patients not controlled at Step FOUR, use daily oral corticosteroids in the lowest dose providing adequate control. Patients should be counselled about potential side-effects and all other alternative treatments must be considered.

\* For dose equivalents to BDP, see **Table ONE**.

## 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  $\beta_2$ -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.

### Inhaled short-acting $\beta_2$ -agonists

For the majority of patients in *Step ONE*, an inhaled, short-acting  $\beta_2$ -agonist is the recommended reliever treatment.<sup>1,10,19</sup> Short-acting  $\beta_2$ -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  $\beta_2$ -agonist, salbutamol. Because a regular schedule of administration four times a day does not improve outcomes, as compared with "as-needed" administration,<sup>20</sup> the short-acting  $\beta_2$ -agonists are recommended for use only as needed. Overuse of short-acting  $\beta_2$ -agonists is a marker of uncontrolled asthma and has been associated with increased deaths due to asthma.<sup>21</sup>

### What are the adverse effects of inhaled short-acting $\beta_2$ -agonists?

Inhaled short-acting  $\beta_2$ -agonists have minimal adverse effects. Overuse can

cause tremor, headache, muscle cramps, and palpitations. Hypokalaemia may result from high doses of inhaled or oral  $\beta_2$ -agonists; this may be potentiated by concomitant treatment with theophylline, corticosteroids, diuretics, and by hypoxia. The CSM advises that plasma potassium should be monitored in people with severe asthma.<sup>22</sup> There is some evidence from post-marketing data that myocardial ischaemia is associated with short-acting  $\beta_2$ -agonists. The Medicines and Healthcare products Regulatory Agency (MHRA) has issued advice that people with a history of heart disease (including angina or rhythm disturbance), should seek medical advice if symptoms such as shortness of breath or chest pain occur, as this may indicate worsening heart disease.<sup>23</sup>



### Prescribing notes: Out-dated practices

- i The practice of administering a short-acting  $\beta_2$ -agonist before using an inhaled corticosteroid to improve delivery of the steroid to the lower airways has been abandoned as unnecessary.<sup>24</sup>
- i Similarly, there is no need for patients to wait more than 10-15 seconds between puffs when a dose of two or more puffs is required.<sup>25</sup>

### 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 exacerbations and reducing asthma mortality.<sup>10,13,26-33</sup> 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.<sup>34</sup>

### Comparison of ICS efficacy

The various ICS do not differ in efficacy.<sup>6,35</sup> Adverse effects are class effects and do not differ significantly between the different ICS at either low or high doses. For the most part, differences in ICS are in dosing schedule (once or twice daily), the method of delivery (MDI, DPI etc.) and the dose and dosing flexibility.<sup>35-37</sup> Beclometasone, budesonide, or fluticasone are recommended<sup>6</sup> because they are available in a range of formulations at different doses and for a range of ages.

### Do the "newer" inhaled corticosteroids offer any therapeutic advantage?

Ciclesonide and mometasone are newer, once-daily inhaled corticosteroids. Neither drug is licensed for children younger than 12 years.

**Mometasone** (Asmanex<sup>®</sup>) is formulated as a dry powder inhaler. Whether it offers any substantial advantages over other ICS formulations is not clear.<sup>38</sup> It can be given once daily, but twice daily use may be more effective.<sup>38</sup>

**Ciclesonide** (Alvesco<sup>®</sup>) is a newer once daily ICS delivered via a pressurised metered dose inhaler. It was launched in January 2005 in the UK. It is claimed to have novel release and distribution properties resulting in lung-targeted anti-inflammatory effects. Ciclesonide has low systemic bioavailability and minimal effect on endogenous cortisol production.<sup>39</sup> Evidence from clinical trials suggests that ciclesonide has less systemic activity and fewer local oropharyngeal side-effects than conventional inhaled steroids.<sup>40-44</sup> The clinical benefit of this is not clear as the exact efficacy to safety ratio compared to other ICS has not been fully established.

**Table ONE: Equivalent doses of ICS relative to BDP and current licensed age indications<sup>10</sup>**

Steroid	Equivalent dose	UK licence covers		
		> 12 years	5-12 years	< 5 years
Beclometasone dipropionate CFC	400 mcg	No longer available.		
<b>Beclometasone</b>				
Clenil modulite <sup>®</sup>	400 mcg	✓	✓	✓
Asmabec Clickhaler <sup>®</sup>		✓	Over age 6	✗
Dry powder (Becodisks <sup>®</sup> )		✓	✓	✓
Easyhaler <sup>®</sup>		✓	✗	✗
Pulvinal <sup>®</sup>		✓	Over age 6	✗
Filair <sup>®</sup>		✓	✓	✓
Qvar <sup>®</sup>	200-300 mcg	✓	✗	✗
Fostair <sup>®</sup>	200 mcg	Over age 18	✗	✗
<b>Budesonide</b>				
Turbohaler <sup>®</sup>	400 mcg	✓	✓	✗
Metered dose inhaler <sup>®</sup> CFC		✓	✓	Over age 2
Easyhaler <sup>®</sup>		✓	Over age 6	✗
Novolizer <sup>®</sup>		✓	Over age 6	✗
Symbicort <sup>®</sup>		✓	Over age 6	✗
Symbicort <sup>®</sup> (regular and as required, "SMART" regimen)		Over age 18	✗	✗
<b>Fluticasone</b>				
Metered dose inhaler (HFA)	200 mcg	✓	✓	Over age 4
Accuhaler <sup>®</sup>		✓	✓	Over age 4
Seretide <sup>®</sup> HFA		✓	✓	Over age 4
Seretide Accuhaler <sup>®</sup>		✓	✓	Over age 4
<b>Mometasone</b>	200 mcg	✓	✗	✗
<b>Ciclesonide</b>	200-300 mcg	✓	✗	✗

## Inhaled corticosteroids – the safety issues

As with all effective medicines, the benefits of inhaled corticosteroids 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.<sup>45,46</sup>

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.<sup>47</sup> For most patients, dose escalation to high doses produce little additional clinical benefit.<sup>47,48</sup>

### 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.<sup>49</sup>
- € **Hoarseness and dysphonia** - Use of a spacer device does not appear to alleviate this.
- € **Cough** - Cough can usually be overcome by changing either the ICS itself or the delivery system.<sup>35</sup>

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. Local adverse events rates may vary by ICS dose, device, and potency.<sup>50-53</sup>

### 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).<sup>54</sup> 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.<sup>55-57</sup>

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

- € **Adrenal suppression**<sup>54,58,59</sup> – Meta-analysis found that marked adrenal suppression can occur with ICS doses > 1500 micrograms per day (> 750 micrograms per day for fluticasone), although there is a considerable degree of inter-patient variability.<sup>54</sup> The CSM have issued warnings about the

use of ICS, particularly in relation to fluticasone.<sup>60-62</sup>

- € **Decreased bone mineral density (BMD)**<sup>63,64</sup> - Three large observational studies<sup>57,65,66</sup> have reported an inverse relationship between dose of ICS and BMD. Further, people who use ICS have an increased risk of fracture.<sup>67</sup>
- € **Cataracts and glaucoma.**<sup>55,56</sup>
- € **Easy bruising.**<sup>68</sup>

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

In children, high doses of ICS ( $\geq 400$  micrograms/day ( $\geq 200$  micrograms/day for fluticasone) may be associated with systemic side-effects, including **growth failure** and **adrenal suppression**.<sup>10</sup> The CSM has 'strongly advised that the paediatric licensed doses of all ICS should not be exceeded'.<sup>61</sup> 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.<sup>10</sup>

BTS/SIGN recommends that for children treated with  $\geq 800$  micrograms BDP or equivalent per day.<sup>10</sup>

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

### Childhood growth:


In children, growth retardation is a concern. Expected growth decreases by an average of approximately 1cm in the first year after initiating ICS in growing children,<sup>26,69</sup> but evidence from studies in prepubescent school-age children suggests that even when these children continue to receive long-term treatment with ICS, they ultimately reach their normal predicted height.<sup>26,70</sup> See **Table TWO**.

### Bone mineral density:

Studies in children with chronic asthma treated with ICS suggest no adverse effect of inhaled corticosteroids on bone mineral density.<sup>73-75</sup> However, *oral* or *systemic* corticosteroid use increases the risk of fracture. The risk of fracture increases with the number of courses given.<sup>75-82</sup>

### HPA Suppression/Acute adrenal crisis in children:

The dose of ICS required to put a child at risk of clinical adrenal insufficiency is




**Prescribing notes: Inhaled corticosteroids**

- i Some patients will be using other topical steroids (e.g. skin and nasal preparations) and the total steroid load should be considered and kept as low as is consistent with therapeutic effectiveness.
- i Previous advice to double the dose of ICS at the time of an exacerbation has been invalidated.<sup>10</sup> Doubling the dose of ICS has been reported to be **INEFFECTIVE** in preventing exacerbations of asthma.<sup>83,84</sup>

unknown. However, it is recognised that:

- € ICS doses of less than 200 micrograms BDP (or equivalent) daily is normally **not** associated with any significant suppression of the HPA axis in children.<sup>1</sup>
- € In a small number of children, doses of ICS at or above 400 micrograms per day of BDP (or equivalent) have been associated with adrenal suppression.<sup>6</sup>

Presenting symptoms of adrenal crisis are non-specific, and include anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, decreased level of consciousness, hypoglycaemia and seizures. Acute adrenal crisis may be precipitated by infection, trauma, surgery, or rapid reduction in corticosteroid dosage. Consider the possibility of adrenal insufficiency in any child maintained on ICS<sup>10</sup> (particularly fluticasone)<sup>85,86</sup> presenting with a decreased level of consciousness. Serum biochemistry and blood glucose levels should be checked urgently. Consider whether intramuscular hydrocortisone is required. Advise parents to immediately report non-specific symptoms, such as anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, decreased consciousness and seizures, in children using ICS.



**Prescribing note: ICS and HPA Axis suppression in children**

The exact dose and duration of ICS treatment to put a child at risk of adrenal insufficiency is unknown, but is likely to be 1000 micrograms or more of BDP (or equivalent) daily.<sup>10</sup>

**Table TWO: Summary: Corticosteroids and growth in children.**<sup>70-72</sup>

- € Uncontrolled or severe asthma adversely affects growth and final adult height.
- € No long-term controlled studies in children have reported any statistically or clinically significant adverse effects on growth using 100-200 micrograms per day of inhaled BDP (or equivalent).
- € Growth retardation may be seen with all corticosteroids when a high dose is administered. Growth retardation is dose-dependent.
- € Children aged 4-10 years appear to be more susceptible to growth retardation than adolescents.
- € Children with asthma treated with inhaled corticosteroids attain normal adult height (predicted from family members) but at a later age.



### Prescribing note: Steroid treatment cards

People using oral corticosteroids or prolonged high doses of ICS (off-label high doses, or maximum doses in conjunction with oral steroids), should be given a **steroid treatment card** which gives guidance on minimizing risk and provides details of prescriber, drug, dosage, and duration of treatment.<sup>62</sup>

### Long-acting $\beta_2$ -agonists

Addition of a long-acting  $\beta_2$ -agonist (LABA) is the preferred treatment when a medium dose of inhaled corticosteroids alone fails to achieve control of asthma (**Step THREE**). Addition of an 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  $\beta_2$ -agonists. It also reduces the number of exacerbations and achieves clinical control of asthma in more patients more rapidly, and at a lower dose of inhaled corticosteroids than inhaled corticosteroids alone.<sup>17,18,32,87-93</sup> LABAs may also be used to prevent exercise-induced bronchospasm, and for this purpose may provide longer protection than rapid-acting inhaled  $\beta_2$ -agonists.<sup>94</sup>

Even though it has been the recommendation for some time that add-on therapy should take place *before* high-dose ICS is used, an observational study highlights the over-use of high-dose ICS and inappropriate use of add-on therapy by GPs, particularly among children.<sup>95</sup> It is recommended that GPs audit high-dose ICS and add-on therapy prescribing, especially in children, to identify those people at risk of adverse outcomes.<sup>95</sup>

#### What are the differences between salmeterol and formoterol?

Features distinguishing the two available LABAs are both practical and theoretical.<sup>96</sup> The onset of action of formoterol occurs within 5 minutes,

LABA	Inhalers available		UK licence covers		
	Aerosol MDI	DPI	> 12 years	5-12 years	< 5 years
Formoterol		Generic products - various	Adults and children over <b>6 years</b> , 12-24 mcgs twice daily		£
	Atimos Modulite <sup>®</sup>		12-24 mcgs twice daily	£	£
		Foradil <sup>®</sup>	Adults and children over <b>5 years</b> , 12-24 mcgs twice daily		£
Salmeterol	Serevent <sup>®</sup> Evohaler	Oxis <sup>®</sup> Turbohaler <sup>®</sup>	<b>Over 18</b> years 6-24 mcgs twice daily	<b>6-18 years</b> , 6-12 mcgs twice daily	£
		Serevent <sup>®</sup> Accuhaler <sup>®</sup> or Diskhaler <sup>®</sup>	50-100 mcgs twice daily	50 mcgs twice daily	£

mcgs = micrograms

whereas salmeterol has a slower onset of action (15-20 minutes).<sup>97,98</sup> The more rapid onset of action of formoterol makes it suitable for symptom relief as well as symptom prevention.<sup>99</sup>

Formoterol is a full agonist in its action at the  $\beta_2$ -receptor, whereas salmeterol is a partial agonist (and partial antagonist). The implication of this pharmacologic distinction, particularly as it might apply to the risk of fatal asthmatic attacks, is uncertain.<sup>35</sup> **Table THREE** compares available devices for formoterol and salmeterol. (Note the differences in the licensed age limits for formoterol).

#### What concerns have arisen with regard to the use of inhaled LABAs?

Concerns have been expressed about the place of LABAs, particularly after the Salmeterol Multicentre Asthma Research Trial (SMART) showed increased exacerbations and death rates in those taking salmeterol.<sup>100</sup>

Subgroup analysis of SMART showed **no significant increase in death rates in those also using ICS**,<sup>101</sup> thus LABAs should be **added** to existing ICS treatment but not replace it.

The MHRA has completed a full review of the balance of risks and benefits associated with LABAs in the management of asthma and COPD.<sup>102</sup> They have concluded that LABAs should:<sup>102</sup>

- € Be **added** if regular use of standard-dose ICS has failed to control asthma.
- € **Not be** initiated in patients with rapidly deteriorating asthma.
- € Be introduced at a low dose and the effect properly monitored before considering dose increase.
- € Be discontinued in the absence of benefit.
- € Be reviewed as clinically appropriate: stepping down when good long-term control has been achieved.

The bottom-line is that LABAs are effective in reducing asthma symptoms, but clinicians should prescribe (and patients be counselled to use), concomitant ICS.

#### Combined ICS / LABA inhalers

The greater efficacy of combinations of ICS along with LABAs has led to the

development of fixed combination inhalers that deliver both ICS and LABA simultaneously. Controlled studies have shown that delivering this therapy in a combination inhaler is as effective as giving each drug separately.<sup>104,105</sup>

It is recommended that ICS/LABA combination inhalers be reserved for use in people who are stabilised on the component drugs in the same dose ratio and who have difficulty using separate inhalers.<sup>6</sup>

Three combined ICS/LABA inhalers are available in the UK:

- € Fostair<sup>®</sup> is a combination of beclometasone and formoterol and is delivered by pMDI.
- € Seretide<sup>®</sup> is a combination of fluticasone and salmeterol and is delivered by a DPI or pMDI.
- € Symbicort<sup>®</sup> is a combination of budesonide and formoterol delivered as a DPI.



### Prescribing note: Fostair<sup>®</sup>

The ICS component of Fostair<sup>®</sup> is about twice the potency of traditional CFC-containing inhalers, which should be taken into account when switching patients.<sup>106</sup>

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

- Fixed dose ICS/LABA combination inhalers:<sup>1,10</sup>
- € Are convenient for patients.
- € Improve adherence to drug treatment, as fewer inhalations and devices are needed.<sup>107,108</sup>
- € 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.

#### What are the disadvantages of ICS/LABA combination inhalers?

One suggested limitation of inhalers containing fixed combinations of an LABA and an ICS is their lack of dosing flexibility<sup>109</sup> (the dose of the individual component drugs cannot be individually titrated without changing the inhaler). This lack of flexibility is potentially



### Prescribing notes - Long-acting $\beta_2$ -Agonists

LABA should only be started in patients who are **already on ICS**.<sup>10</sup> Advise anyone using an LABA that they must NOT stop using their ICS.

Do not start anyone with acutely deteriorating asthma on LABA therapy.<sup>6</sup> Anyone starting treatment with an LABA should be advised to report any deterioration in symptoms.

Closely monitor anyone started on an LABA, especially during the first three months of treatment.<sup>6</sup>

Only continue therapy with an LABA if it has shown benefit.<sup>6</sup>

Advise anyone who has been prescribed salmeterol that they should not use it to relieve an acute asthma attack.

important given the variable airway inflammation in asthma and the importance of “stepping down” asthma therapy.

### The Symbicort® SMART® dosing regimen

#### What is the “SMART® regimen”?

The SMART® regimen (Symbicort for Maintenance And Reliever Therapy) is a new approach to the management of moderate to severe asthma, and should not be confused with the SMART randomised controlled trial discussed earlier.

The SMART® regimen involves the use of a single Symbicort® inhaler as both maintenance and reliever treatment for adults aged 18 years and over. SMART® is designed to allow asthma patients to increase the dose of Symbicort when their asthma worsens, and avoids the need for multiple inhalers. With the SMART approach, patients take a maintenance dose both morning and night and then use the inhaler as needed to provide asthma control. A maximum of 10 extra puffs can be taken each day (i.e. 12 puffs in total). A separate reliever inhaler is NOT required and it is important that patients understand this. Using the 200/6 strength as an example, prescriptions for Symbicort SMART would be written as: “Rx Symbicort 200/6 one inhalation *bd* plus as needed”, or “budesonide/formoterol 200/6 one inhalation *bd* plus as needed”. Both the Symbicort 200/6 and 100/6 strengths may be prescribed for SMART use but Symbicort 400/12 is not licensed for use in this way.

There is evidence that the SMART® regimen may be more effective at reducing exacerbation rates in people with moderate to severe asthma symptoms compared with conventional methods.<sup>99,110,111</sup> However, the key trials of the SMART® regimen included patients who were *not* typical of most people managed in primary care:

- € All were at Step 3 or 4 of BTS/SIGN and had experienced one or more severe exacerbations in the previous 12 months.<sup>99,110-112</sup>
- € At study entry, asthma was uncontrolled in the majority of patients.<sup>99,110-112</sup>

#### Where does the SMART® regimen fit in the management of asthma?

The safety of this new approach to asthma management in a broad and diverse patient population will remain uncertain until a number of ongoing trials have fully reported.<sup>113</sup>

In the meantime, selected adult patients at step 3 who are poorly controlled or in selected adult patients at step 2 (above BDP 400micrograms per day who are poorly controlled) may benefit from the SMART regimen.<sup>99,110,111,114,115</sup>

When this management option is introduced the total regular dose of daily ICS should not be decreased. Before

Table FOUR: LTRAs – available formulations and licensed age groups		
Drug	Formulation	Licensed age groups
Montelukast	Singulair® 10mg tablets	Adults and children ≥ 15 years
	Singulair® 4mg chewable tabs	Children aged 2-5 years
	Singulair® 5mg chewable tabs	Children aged 6-14 years
	Singulair® 4mg granules	Children aged 6 months to 5 years
Zafirlukast	Accolate® 20mg tablets	Adults and children ≥ 12 years

instituting the SMART regimen, careful patient education is required.<sup>10</sup>


#### Leukotriene receptor antagonists (See Table FOUR)

Clinical studies have demonstrated that leukotriene receptor antagonists (LTRAs) have a small and variable bronchodilator effect, reduce symptoms (including cough),<sup>116</sup> improve lung function, and reduce airway inflammation and asthma exacerbations.<sup>117-119</sup> However, when used alone as controller medication, the effect of LTRAs is generally less than that of low doses of inhaled corticosteroids. LTRAs used as add-on therapy may reduce the dose of inhaled corticosteroids required by patients with moderate to severe asthma<sup>120</sup> and may improve asthma control in patients whose asthma is not controlled with inhaled corticosteroids.<sup>121-123</sup> Studies have demonstrated that LTRAs are less effective than LABAs as add-on therapy.<sup>120-128</sup>

Persons who are obese,<sup>129</sup> who smoke cigarettes,<sup>130</sup> or who have associated aspirin sensitivity<sup>131-133</sup> may particularly benefit from treatment with an LTRA.

#### What are the adverse effects of LTRAs?

LTRAs are well tolerated, and few if any class-related effects have so far been recognised.<sup>1</sup> The apparent association of LTRAs with Churg-Strauss syndrome is probably largely a result of reductions in the doses of corticosteroids unmasking the underlying disease, but a causal association in some patients cannot be entirely excluded.<sup>134-136</sup>



**Prescribing notes – LTRAs (zafirlukast, montelukast)**

Zafirlukast: if signs suggestive of liver dysfunction (anorexia, nausea, vomiting, right upper quadrant pain, fatigue, lethargy, enlarged liver, pruritus, jaundice), STOP zafirlukast and measure serum transaminases.

Do NOT start an LTRA in pregnancy. However, if a woman is already taking an LTRA and it is considered essential, treatment can be continued during pregnancy.

#### Theophylline

Theophylline is a bronchodilator and when given in a lower dose, has modest anti-inflammatory properties.<sup>137-139</sup> Evidence suggests that sustained-release theophylline has little effect as a first-line preventer.<sup>140</sup> It may provide benefit as add-on therapy in patients who do not achieve control on inhaled steroids alone.<sup>141-143</sup> As add-on therapy,

theophylline is less effective than LABAs.<sup>144,145</sup>

Theophylline has the potential for significant adverse effects due to the fact that it is highly metabolised in the liver and has a narrow therapeutic window (most people require plasma concentrations between 10-20 milligrams per litre for satisfactory bronchodilation). Great care must therefore be taken when co-administering drugs known to induce or inhibit drug metabolism. Adverse effects of theophylline include nausea, vomiting, tremor, palpitations and arrhythmias. When prescribing theophylline, the brand should be specified on the prescription. This is because of differences in bioavailability among brands; people should be maintained on the same brand of theophylline.<sup>146</sup>

#### Chromones

The precise mechanism of action of sodium cromoglicate and the related nedocromil sodium is not fully understood. They are thought to act primarily by preventing release of mediators of inflammation from sensitised mast cells through stabilisation of mast cell membranes.

Side-effects associated with these drugs are minimal and include coughing upon inhalation of the powder formulation and sore throat. Some patients find the taste of nedocromil sodium unpleasant and so it is available in mint-flavoured formulation (Tilade CFC-free Inhaler®).

Anyone prescribed a chromone should be advised:<sup>146</sup>

- € To use their sodium cromoglicate or nedocromil sodium inhaler regularly, usually four times a day.
- € Chromone inhalers should NOT be used to relieve an acute attack of asthma.
- € If inhalation of the dry powder causes bronchospasm, use their short-acting β<sub>2</sub> agonist inhaler (salbutamol or terbutaline) a few minutes prior to using the chromone inhaler.

#### Oral corticosteroids

Addition of oral corticosteroids to other controller medications may be effective<sup>147</sup> but is associated with severe side-effects and should only be considered if the person's asthma remains severely uncontrolled on Step 4 medications with daily limitation of activities and frequent exacerbations.

### How should oral corticosteroids be used?

If oral corticosteroids have to be administered on a long-term basis, attention must be paid to measures that minimise the systemic adverse effects. Daily oral corticosteroids should always be used in the lowest dose that gives adequate control. *Inhaled* corticosteroids should be maintained at the maximum recommended daily dose as given in Step FOUR.

### What are the concerns with patients taking long-term oral corticosteroids?

Patients on long term steroid tablets (e.g. longer than 3 months) or requiring frequent courses of steroid tablets (e.g. three to four times a year) will be at risk of systemic side effects such as:<sup>1,10</sup>

- € Osteoporosis
- € Arterial hypertension
- € Diabetes
- € Hypothalamic-pituitary-adrenal axis suppression
- € Obesity
- € Cataracts
- € Glaucoma
- € Skin-thinning leading to cutaneous striae and easy bruising
- € Muscle weakness

Bone mineral density should be monitored. If a significant reduction occurs, treatment with a long-acting bisphosphonate should be offered (see British Osteoporosis Society guidelines, [www.nos.org.uk](http://www.nos.org.uk)).

**Prescribing notes - Oral Steroids**

**Prednisolone tablets** are the most widely used oral steroid for maintenance therapy in chronic asthma. There is no evidence that other formulations offer any advantage.<sup>10</sup>

Reduction in **bone mineral density** commonly occurs and should be monitored. Those receiving prednisolone for over three months should be prescribed a bisphosphonate (see British Osteoporosis Society guidelines [www.nos.org.uk](http://www.nos.org.uk)).<sup>10</sup>

### Stepping down asthma treatment

Current asthma treatment guidelines<sup>1,10</sup> recommend the continuous evaluation of asthma control by healthcare professionals and patients and the stepping down of therapy to the minimum required to maintain such control.

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 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.

### How should asthma treatment be "stepped down"?

Although further research on stepping down asthma treatment is needed, some recommendations can be made based on the current evidence:

- € When medium- to high-dose ICS are being used alone, a 50% reduction in dose should be attempted at 3 monthly intervals.<sup>148-150</sup>
- € Where control is achieved at a low-dose of ICS alone, in most patients, treatment may be switched to once-daily dosing.<sup>40,151</sup>
- € When asthma is controlled with a combination of higher dose ICS and LABA, the preferred approach is to begin by reducing the dose of ICS by approximately 50% while continuing the LABA.<sup>152</sup> If control is maintained, further reduction in the ICS should be attempted until a low-dose is reached, when the LABA may be stopped. Further reduction of ICS may be possible allowing it to be eventually stopped as well.

### Omalizumab

#### 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.<sup>153,154</sup> It prevents the release of pro-inflammatory mediators and reduces allergen-induced airway reactions. Omalizumab is administered by subcutaneous injection every 2-4 weeks and the dose is based on the patient's body weight and blood IgE level.

#### What is the place of omalizumab in asthma management?

Omalizumab is as an option for the treatment of severe persistent allergic asthma as add-on therapy to optimised standard therapy, only in adults and adolescents (12 years and older) who have been identified as having severe unstable disease.<sup>155</sup> Omalizumab add-on therapy should only be initiated if the patient fulfils the following criteria of severe unstable allergic asthma:<sup>155</sup>

- € Confirmation of IgE mediated allergy

to a perennial allergen by clinical history and allergy skin testing.

- € Either two or more severe exacerbations of asthma requiring hospital admission within the previous year, or three or more severe exacerbations of asthma within the previous year, at least one of which required admission to hospital, and a further two which required treatment or monitoring in excess of the patient's usual regimen, in an accident and emergency unit.

Omalizumab add-on therapy should be initiated and monitored by a physician experienced in both allergy and respiratory medicine in a specialist centre.<sup>155</sup>

Omalizumab is on the red list of Specialist Medicines in Northern Ireland and as such the prescribing responsibility should remain with the consultant or specialist clinician and the supply should be organised via the hospital pharmacy. (See [www.ipnsm.hscni.net](http://www.ipnsm.hscni.net) for more details).

### CFC-free inhaler devices

#### Why are propellants being changed?

The change from the standard chlorofluorocarbon (CFC) propellants is being made for environmental reasons, not for any safety or clinical reasons. As a result of recognition that CFCs destroyed stratospheric ozone, an international agreement was reached to phase out their use (Montreal Protocol). The Montreal Protocol has mandated that CFC propellant should be phased out, and in the UK the transition to alternative propellants, usually hydrofluoroalkane (HFA), is well underway.

#### What are the issues around switching to the CFC-free beclometasone inhalers?

Things have gone smoothly in the transition to CFC-free bronchodilators, leading to a number of different brands that are essentially equivalent. For pMDIs containing bronchodilators, the switch from CFC to HFA inhalers does not result in a change in efficacy at the same nominal dose.<sup>156</sup> The same has not been true for inhaled beclometasone. **Qvar** and **Clenil Modulite** are HFA-pMDIs that contain beclometasone dipropionate. Although Qvar and Clenil Modulite both contain

**Table FIVE: Comparison of Qvar and Clenil Modulite**

	<b>Qvar®</b>	<b>Clenil Modulite®</b>
Devices	€ pMDI € Easi-Breathe® inhaler € Autohaler®	€ pMDI
Usual dose for mild-to-moderate asthma	100 micrograms twice daily	200 micrograms twice daily
Indications	€ Prophylactic management of mild, moderate and severe asthma € Licensed for use in patients aged 12 years and over € Where necessary, Qvar® can be used with Aerochamber® and Aerochamber Plus®	€ Prophylactic management of mild, moderate and severe asthma in adults and children € The Volumatic® spacer device must be used in patients aged 15 years and under, and for those using more than 1000 micrograms per day

the same active ingredient (BDP) there are some important differences between the products (see **Table FIVE**). **Qar** is 2-2.5 times more potent than the CFC-containing alternatives because it generates an aerosol of smaller particles, achieving greater penetration and lung deposition than CFC-MDIs. This lack of bioequivalence between new and old beclometasone MDIs means patients switching to **Qar** must start at around half their previous dose (for example **Qar** 100 micrograms rather than 200-250 micrograms beclometasone or budesonide from a CFC-MDI). The patient should then be reassessed to determine whether dose adjustment is needed. **Clenil Modulite** is the first CFC-free beclometasone MDI that is claimed to be bioequivalent with CFC-containing formulations, meaning that patients can be switched from their old device dose-for-dose.

### Smoking and asthma

#### **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<sub>1</sub> 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<sup>16,162</sup> and with short courses of oral corticosteroids.<sup>163</sup> Prescribers should be aware that higher doses of inhaled corticosteroids may be needed in patients who are smokers or ex-smokers.<sup>10</sup>

#### **Is there a link between parents who smoke and asthma in their children?**

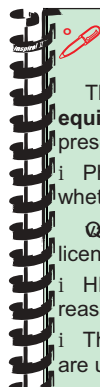
There is a direct causal relationship between parental smoking and lower respiratory tract illness in children up to 3 years of age.<sup>164</sup> Infants whose mothers smoke are four times more likely to develop wheezing illnesses in the first year of life.<sup>165</sup> Exposure to tobacco smoke in the home contributes to the severity of childhood asthma. One small study suggests that, by stopping smoking, parents can decrease the severity of asthma in their children.<sup>166</sup>

Parents who smoke should be advised about the dangers for themselves and their children, and offered appropriate support to stop smoking.

### Influenza / Pneumococcal vaccines in asthma

#### **Are patients with asthma recommended to have the annual 'flu vaccine?**

The annual flu vaccination is recommended for all people with asthma older than 6 months who have



### Prescribing notes - CFC-free beclometasone inhalers

The two CFC-free beclometasone pMDIs (**Qar**™ and **Clenil™ Modulite™**) are **not equipotent**. Thus, prescribers wishing to prescribe CFC-free beclometasone should prescribe by **brand name**.<sup>106,157</sup>

i Pharmacists receiving generic prescriptions for beclometasone must establish whether a CFC-free product is required and if so, which brand is to be dispensed.<sup>106,158</sup>

**Qar**™ is **not** licensed in children 12 years or younger.<sup>159</sup> **Clenil™ Modulite™** is licensed for use in children.<sup>160</sup>

i HFA inhalers may feel and taste different to CFC inhalers. Patients should be reassured that this should not affect the efficacy of their products.

i The changeover provides an ideal opportunity for pharmacists to ensure that patients are using the right inhalation technique.<sup>161</sup>

required hospital admission for an exacerbation of asthma, or who need continuous or frequent repeated use of inhaled or oral steroids.<sup>167</sup>

#### **Should someone with asthma receive the pneumococcal vaccine?**

Asthma is **not** an indication for the pneumococcal vaccine **unless** the asthma is so severe as to require continuous or frequently repeated use of systemic steroids (Individuals on systemic steroids for more than a month at a dose equivalent to prednisolone at 20 milligram or more per day (any age), or for children under 20 kilograms, a dose of 1 milligram or more per kg per day.)<sup>168</sup>

### Patient education, self management and action plans

Many patients with asthma would like a greater say in how their condition is managed. For example, in a cross-sectional survey of adults with asthma, 72.2% of 230 respondents considered that they had little active involvement in treatment decisions, and 55.2% were less involved than they would have liked.<sup>169</sup> With this in mind, the Northern Ireland Strategic Framework document for respiratory conditions<sup>170</sup> advocates a partnership approach between health professionals and patients to promote self-management of the condition. Self-management education should be offered, including written asthma action plans focusing on individual needs, to all people with asthma.<sup>10</sup>

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. It is recommended that patients should be offered self-management education that focuses on individual needs, and be reinforced by a **written personalised action plan**.<sup>10</sup>

#### **What areas should patient education cover?**

See **Table SIX**.

#### **What is an asthma action plan?**

An asthma action plan helps an individual make changes to their treatment in response to changes in their level of asthma control, as indicated by symptoms and/or PEF, in accordance with written predetermined guidelines.<sup>171-173</sup> Written personalised action plans as part of self-management education have been shown to improve health outcomes for people with asthma.<sup>174-185</sup> A consistent finding in many studies has been improvement in patient outcomes such as self-efficacy, knowledge and confidence.<sup>174,175,184,185</sup>

#### **What should an action plan include?**

Although several versions of action plans exist, all share certain features:

- ⊖ Patients monitor their symptoms and/or PEF, to detect deviations from the usual state of controlled asthma.
- ⊖ Warning signs and symptoms, potential precipitating factors or personal triggers are included.
- ⊖ Patient-initiated treatment options to restore control are explicitly provided in writing in the form of 2-4 clearly specific action points.
- ⊖ Expected response time, danger signs and contact information.

**Note:** Although many of the guidelines advise increasing the dosage of ICS in

### **Table SIX: Suggested content for an educational programme/discussion<sup>10</sup>**

Tailor the education and advice to each person's individual social, emotional and disease status and age. Discuss:

- The nature of the disease
- The nature of the treatment
- Areas where the individual most wants treatment to have effect
- How to use the treatment. Include instruction on inhaler technique
- Self-monitoring/self-assessment skills
- A personalised asthma action plan with identified goals
- How to recognise and manage acute exacerbations
- Appropriate allergen or trigger avoidance.

Patient Information Leaflets and proforma asthma action plans are available from Clinical Knowledge Summaries (CKS) ( [www.cks.nhs.uk](http://www.cks.nhs.uk) ) and the National Asthma Campaign ( [www.asthma.org.uk](http://www.asthma.org.uk) )

response to worsening symptoms or PEF, doubling the dose of ICS at the time of an exacerbation is of unproven value,<sup>10</sup> and is not recommended.

Examples of self-management plans can be found on the Asthma UK website ([www.asthma.org.uk](http://www.asthma.org.uk)).

### Reviewing and monitoring someone with asthma

Regular review of people with asthma is associated with a reduced exacerbation rate and improved symptom control<sup>179</sup> and is a recommendation of national guidelines.<sup>10</sup> The context of the review will vary according to the needs of the individual patient, but in primary care, asthma is best monitored by routine clinical review on at least an annual basis.<sup>10</sup> This is reinforced by the inclusion of asthma review in the General Medical Services (GMS) Quality and Outcomes Framework (QoF) (See **Table SEVEN**).

#### How should someone with asthma be reviewed?

The factors that should be monitored and recorded include:<sup>10</sup>

- € Symptomatic asthma control: best assessed using questions such as the Royal College of Physicians' 'three questions' (see **Table EIGHT**).
- € Lung function, assessed by spirometry or PEF.
- € Exacerbations, oral corticosteroid use and time off work/school since last assessment.
- € Inhaler technique.
- € Compliance (can be assessed by reviewing prescription refill frequency).
- € Bronchodilator reliance (can be assessed by reviewing prescription refill frequency).
- € Possession of and use of a written personal action plan

The General Practice Airways Group (GPIAG) together with Asthma UK has developed an asthma status measure and patient self-assessment checklist to provide support for GPs carrying out asthma reviews. It can be downloaded at: ([www.gpiag.org/news/gp\\_diagnostic\\_tool.pdf](http://www.gpiag.org/news/gp_diagnostic_tool.pdf))

#### Web sites:

- € **British Thoracic Society:** [www.brit-thoracic.org.uk](http://www.brit-thoracic.org.uk)
- € **Asthma UK:** [www.asthma.org.uk](http://www.asthma.org.uk)
- € **Lung and Asthma Information Agency:** [www.laia.ac.uk](http://www.laia.ac.uk)
- € **General Practice Airways Group:** [www.gpiag.org](http://www.gpiag.org)
- € **Global Initiative for Chronic Obstructive Lung Disease:** [www.goldcopd.com](http://www.goldcopd.com)
- € **National Institute for Healthcare and Clinical Excellence (NICE):** [www.nice.org](http://www.nice.org)
- € **Global Initiative for Asthma:** [www.ginasthma.com](http://www.ginasthma.com)

**Table SEVEN: Asthma QoF Indicators for GMS contract 2009/10**

	Indicator	Points	Payment Stages
<b>ASTHMA 1</b> Records	The practice can produce a register of patients with asthma, excluding patients with asthma who have been prescribed no asthma-related drugs in the previous twelve months.	4	
<b>ASTHMA 8</b> Initial management	The percentage of patients aged eight and over diagnosed as having asthma from 1 April 2006 with measures of variability or reversibility.	15	40-80%
<b>ASTHMA 3</b> Ongoing management	The percentage of patients with asthma between the ages of 14 and 19 in whom there is a record of smoking status in the previous 15 months.	6	40-80%
<b>ASTHMA 6</b> Ongoing management	The percentage of patients with asthma who have had an asthma review in the previous 15 months.	20	40-70%

3. Asthma UK. Where do we stand? Asthma in the UK today. [www.asthma.org.uk](http://www.asthma.org.uk) 2004;
4. NICE. Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years. NICE Technology Appraisal Guidance 131 2007;
5. Asthma UK Northern Ireland. 16-5-2006. Ref Type: Internet Communication
6. Asthma. Clinical Knowledge Summaries ([www.cks.library.nhs.uk](http://www.cks.library.nhs.uk)) 2008;
7. Pinnock, H. and Shah, R. Asthma. *BMJ* 2007; 334: 847-850.
8. Anderson, H. R. Prevalence of asthma. *BMJ* 2005; 330: 1037-1038.
9. Rees, J. Asthma control in adults. *BMJ* 2006; 332: 767-771.
10. British Thoracic Society and Scottish Intercollegiate Guidelines Network. British Guideline on the Management of Asthma. A national clinical guideline. Revised June 2009. Ref Type: Generic
11. Haughney, J., Barnes, G., Partridge, M., et al. The Living & Breathing Study: a study of patients' views of asthma and its treatment. *Prim.Care Respir.J* 2004; 13: 28-35.
12. Ernst, P., Spitzer, W. O., Suissa, S., et al. Risk of fatal and near-fatal asthma in relation to inhaled corticosteroid use. *JAMA* 1992; 268: 3462-3464.
13. Suissa, S., Ernst, P., Benayoun, S., et al. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N.Engl.J Med.* 2000; 343: 332-336.
14. Zeiger, R. S., Bird, S. R., Kaplan, M. S., et al.
16. Tomlinson, J. E., McMahon, A. D., Chaudhuri, R., et al. Efficacy of low and high dose inhaled corticosteroid in smokers versus non-smokers with mild asthma. *Thorax* 2005; 60: 282-287.
17. Masoli, M., Weatherall, M., Holt, S., et al. Moderate dose inhaled corticosteroids plus salmeterol versus higher doses of inhaled corticosteroids in symptomatic asthma. *Thorax* 2005; 60: 730-734.
18. Shrewsbury, S., Pyke, S. and Britton, M. Meta-analysis of increased dose of inhaled steroid or addition of salmeterol in symptomatic asthma (MIASMA). *BMJ* 2000; 320: 1368-1373.
19. Using beta 2-stimulants in asthma. *Drug Ther.Bull.* 1997; 35: 1-4.
20. Drazen, J. M., Israel, E., Boushey, H. A., et al. Comparison of regularly scheduled with as-needed use of albuterol in mild asthma. *Asthma Clinical Research Network. N.Engl.J Med.* 1996; 335: 841-847.
21. Spitzer, W. O., Suissa, S., Ernst, P., et al. The use of beta-agonists and the risk of death and near death from asthma. *N.Engl.J Med.* 1992; 326: 501-506.
22. CSM. Beta-agonists, xanthines and hypokalaemia. *Current Problems in Pharmacovigilance* 1990; 28: 3.
23. MHRA. Short-acting beta agonists: myocardial ischaemia. *Drug Safety Update* 2007; 1: 10.
24. Mackay, A. D. and Dyson, A. J. How important is the sequence of administration of inhaled beclomethasone dipropionate and salbutamol in asthma. *Br.J Dis.Chest* 1981; 75: 273-276.
25. Lawford, P. and McKenzie, D. Pressurized aerosol inhaler technique: how important are inhalation from residual volume, inspiratory flow rate and the time interval between puffs? *Br.J Dis.Chest* 1983; 77: 276-281.
26. Long-term effects of budesonide or nedocromil in children with asthma. The Childhood Asthma Management Program Research Group. *N.Engl.J Med.* 2000; 343: 1054-1063.
27. Adams, N., Bestall, J. M., Lasserson, T. J., et al. Inhaled fluticasone versus inhaled beclomethasone or inhaled budesonide for chronic asthma in adults and children. *Cochrane.Database.Syst.Rev.* 2005; CD002310.
28. Barnes, P. J. and Adcock, I. M. How do corticosteroids work in asthma? *Ann.Intern.Med.* 2003; 139: 359-370.
29. Calpin, C., Macarthur, C., Stephens, D., et al. Effectiveness of prophylactic inhaled steroids in childhood asthma: a systemic

**Table EIGHT: Royal College of Physicians' - 'three questions' for assessing asthma control.**<sup>186</sup>

In the last week/month:	Yes	No
Have you had difficulty sleeping because of your asthma symptoms (including cough)?	1	0
Have you had your usual asthma symptoms during the day (e.g. cough, wheeze, chest tightness, or breathlessness)?	1	0
Has your asthma interfered with your usual activities (e.g. housework, work, school, etc)?	1	0
Three questions score (0-3). Answering "no" to all questions is consistent with controlled asthma.		
The RCP three questions score should be used only: - For people who are at least 16 years old - After the diagnosis of asthma has been established		

#### Reference List

1. Global Strategy for Asthma Management and Prevention 2008. [www.ginasthma.org](http://www.ginasthma.org) 2008;
2. Masoli, M., Fabian, D., Holt, S., et al. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59: 469-478.

- Short-term and long-term asthma control in patients with mild persistent asthma receiving montelukast or fluticasone: a randomized controlled trial. *Am.J.Med.* 2005; 118: 649-657.
15. Hodges, I. G. and Netherway, T. A. Once-Daily Fluticasone Propionate is as Effective as Twice-Daily Treatment in Stable, Mild-to-Moderate Childhood Asthma. *Clin.Drug Investig.* 2005; 25: 13-22.

- review of the literature. *J.Allergy Clin.Immunol.* 1997; 100: 452-457.
30. Jeffery, P. K., Godfrey, R. W., Adelroth, E., et al. Effects of treatment on airway inflammation and thickening of basement membrane reticular collagen in asthma. A quantitative light and electron microscopic study. *Am.Rev.Respir.Dis.* 1992; 145: 890-899.
  31. Juniper, E. F., Kline, P. A., Vanzielegem, M. A., et al. Effect of long-term treatment with an inhaled corticosteroid (budesonide) on airway hyperresponsiveness and clinical asthma in nonsteroid-dependent asthmatics. *Am.Rev.Respir.Dis.* 1990; 142: 832-836.
  32. Pauwels, R. A., Lofdahl, C. G., Postma, D. S., et al. Effect of inhaled formoterol and budesonide on exacerbations of asthma. *Formoterol and Corticosteroids Establishing Therapy (FACET) International Study Group.* *N.Engl.J.Med.* 1997; 337: 1405-1411.
  33. Sin, D. D., Man, J., Sharpe, H., et al. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis. *JAMA* 2004; 292: 367-376.
  34. Waalkens, H. J., van Essen-Zandvliet, E. E., Hughes, M. D., et al. Cessation of long-term treatment with inhaled corticosteroid (budesonide) in children with asthma results in deterioration. The Dutch CNSLD Study Group. *Am.Rev.Respir.Dis.* 1993; 148: 1252-1257.
  35. Fanta, C. H. Asthma. *N.Engl.J Med.* 2009; 360: 1002-1014.
  36. Barnes, N. C. The properties of inhaled corticosteroids: similarities and differences. *Prim.Care Respir.J* 2007; 16: 149-154.
  37. Derendorf, H., Nave, R., Drollmann, A., et al. Relevance of pharmacokinetics and pharmacodynamics of inhaled corticosteroids to asthma. *Eur.Respir.J* 2006; 28: 1042-1050.
  38. Anon. Mometasone (Asmanex Twisthaler) for asthma. *Med.Lett.Drugs Ther.* 2005; 47: 98-99.
  39. Lee, D. K., Fardon, T. C., Bates, C. E., et al. Airway and systemic effects of hydrofluoroalkane formulations of high-dose ciclesonide and fluticasone in moderate persistent asthma. *Chest* 2005; 127: 851-860.
  40. Boulet, L. P., Drollmann, A., Magyar, P., et al. Comparative efficacy of once-daily ciclesonide and budesonide in the treatment of persistent asthma. *Respir.Med.* 2006; 100: 785-794.
  41. Buhl, R., Vinkler, I., Magyar, P., et al. Comparable efficacy of ciclesonide once daily versus fluticasone propionate twice daily in asthma. *Pulm.Pharmacol.Ther.* 2006; 19: 404-412.
  42. Niphadkar, P., Jagannath, K., Joshi, J. M., et al. Comparison of the efficacy of ciclesonide 160 microg QD and budesonide 200 microg BID in adults with persistent asthma: a phase III, randomized, double-dummy, open-label study. *Clin.Ther.* 2005; 27: 1752-1763.
  43. Pearlman, D. S., Berger, W. E., Kerwin, E., et al. Once-daily ciclesonide improves lung function and is well tolerated by patients with mild-to-moderate persistent asthma. *J.Allergy Clin.Immunol.* 2005; 116: 1206-1212.
  44. Szeffler, S., Rohatagi, S., Williams, J., et al. Ciclesonide, a novel inhaled steroid, does not affect hypothalamic-pituitary-adrenal axis function in patients with moderate-to-severe persistent asthma. *Chest* 2005; 128: 1104-1114.
  45. NICE. Inhaled corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over. *NICE Technology Appraisal Guidance* 138 2008;
  46. Manning, P., Gibson, P. G. and Lasserson, T. J. Ciclesonide versus other inhaled steroids for chronic asthma in children and adults. *Cochrane Database Syst.Rev.* 2008; CD007031.
  47. Powell, H. and Gibson, P. G. Inhaled corticosteroid doses in asthma: an evidence-based approach. *Med.J Aust.* 2003; 178: 223-225.
  48. MeReC. Chronic asthma. *MeReC Briefing* 2002; 18: 1-5.
  49. Yokoyama, H., Yamamura, Y., Ozeki, T., et al. Influence of mouth washing procedures on the removal of drug residues following inhalation of corticosteroids. *Biol.Pharm.Bull.* 2006; 29: 1923-1925.
  50. Buhl, R. Local oropharyngeal side effects of inhaled corticosteroids in patients with asthma. *Allergy* 2006; 61: 518-526.
  51. Rachelefsky, G. S., Liao, Y. and Faruqi, R. Impact of inhaled corticosteroid-induced oropharyngeal adverse events: results from a meta-analysis. *Ann.Allergy Asthma Immunol.* 2007; 98: 225-238.
  52. Randell, T. L., Donaghue, K. C., Ambler, G. R., et al. Safety of the newer inhaled corticosteroids in childhood asthma. *Paediatr.Drugs* 2003; 5: 481-504.
  53. Roland, N. J., Bhalla, R. K. and Earis, J. The local side effects of inhaled corticosteroids: current understanding and review of the literature. *Chest* 2004; 126: 213-219.
  54. Lipworth, B. J. Systemic adverse effects of inhaled corticosteroid therapy: A systematic review and meta-analysis. *Arch Intern.Med.* 1999; 159: 941-955.
  55. Cumming, R. G., Mitchell, P. and Leeder, S. R. Use of inhaled corticosteroids and the risk of cataracts. *N.Engl.J.Med.* 1997; 337: 8-14.
  56. Garbe, E., LeLorier, J., Boivin, J. F., et al. Inhaled and nasal glucocorticoids and the risks of ocular hypertension or open-angle glaucoma. *JAMA* 1997; 277: 722-727.
  57. Israel, E., Banerjee, T. R., Fitzmaurice, G. M., et al. Effects of inhaled glucocorticoids on bone density in premenopausal women. *N.Engl.J.Med.* 2001; 345: 941-947.
  58. Brown, P. H., Greening, A. P. and Crompton, G. K. Large volume spacer devices and the influence of high dose beclomethasone dipropionate on hypothalamo-pituitary-adrenal axis function. *Thorax* 1993; 48: 233-238.
  59. Mortimer, K. J., Tata, L. J., Smith, C. J., et al. Oral and inhaled corticosteroids and adrenal insufficiency: a case-control study. *Thorax* 2006; 61: 405-408.
  60. CSM. Reminder: Fluticasone propionate (Flixotide): use of high doses (more than 500 micrograms/twice daily). *Current Problems in Pharmacovigilance* 2001; 27: 10.
  61. CSM. Inhaled corticosteroids and adrenal suppression in children. *Current Problems in Pharmacovigilance* 2002; 28: 7.
  62. CHM/MHRA. High dose of inhaled steroids:new advice on supply of steroid treatment cards. *Current Problems in Pharmacovigilance* 2006; 31: 5.
  63. The Lung Health Study Research Group. Effect of inhaled triamcinolone on the decline in pulmonary function in chronic obstructive pulmonary disease. *N.Engl.J.Med.* 2000; 343: 1902-1909.
  64. Pauwels, R. A., Yernault, J. C., Demedts, M. G., et al. Safety and efficacy of fluticasone and beclomethasone in moderate to severe asthma. *Belgian Multicenter Study Group.* *Am.J Respir.Crit Care Med.* 1998; 157: 827-832.
  65. Wong, C. A., Walsh, L. J., Smith, C. J., et al. Inhaled corticosteroid use and bone-mineral density in patients with asthma. *Lancet* 2000; 355: 1399-1403.
  66. Tattersfield, A. E., Town, G. I., Johnell, O., et al. Bone mineral density in subjects with mild asthma randomised to treatment with inhaled corticosteroids or non-corticosteroid treatment for two years. *Thorax* 2001; 56: 272-278.
  67. Hubbard, R., Tattersfield, A., Smith, C., et al. Use of inhaled corticosteroids and the risk of fracture. *Chest* 2006; 130: 1082-1088.
  68. Mak, V. H., Melchor, R. and Spiro, S. G. Easy bruising as a side-effect of inhaled corticosteroids. *Eur.Respir.J* 1992; 5: 1068-1074.
  69. Sharek, P. J. and Bergman, D. A. The effect of inhaled steroids on the linear growth of children with asthma: a meta-analysis. *Pediatrics* 2000; 106: E8.
  70. Agertoft, L. and Pedersen, S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N.Engl.J.Med.* 2000; 343: 1064-1069.
  71. Sharek, P. J. and Bergman, D. A. Beclomethasone for asthma in children: effects on linear growth. *Cochrane Database Syst.Rev.* 2000; CD001282.
  72. Pedersen, S. Do inhaled corticosteroids inhibit growth in children? *Am.J Respir.Crit Care Med.* 2001; 164: 521-535.
  73. Griffiths, A. L., Sim, D., Strauss, B., et al. Effect of high-dose fluticasone propionate on bone density and metabolism in children with asthma. *Pediatr.Pulmonol.* 2004; 37: 116-121.
  74. Bahceciler, N. N., Sezgin, G., Nursoy, M. A., et al. Inhaled corticosteroids and bone density of children with asthma. *J.Asthma* 2002; 39: 151-157.
  75. Agertoft, L. and Pedersen, S. Bone mineral density in children with asthma receiving long-term treatment with inhaled budesonide. *Am.J.Respir.Crit Care Med.* 1998; 157: 178-183.
  76. Pauwels, R. A., Pedersen, S., Busse, W. W., et al. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet* 2003; 361: 1071-1076.
  77. Hopp, R. J., Degan, J. A., Biven, R. E., et al. Longitudinal assessment of bone mineral density in children with chronic asthma. *Ann.Allergy Asthma Immunol.* 1995; 75: 143-148.
  78. Schlienger, R. G., Jick, S. S. and Meier, C. R. Inhaled corticosteroids and the risk of fractures in children and adolescents. *Pediatrics* 2004; 114: 469-473.
  79. van Staa, T. P., Bishop, N., Leufkens, H. G., et al. Are inhaled corticosteroids associated with an increased risk of fracture in children? *Osteoporos.Int.* 2004; 15: 785-791.
  80. van Staa, T. P., Cooper, C., Leufkens, H. G., et al. Children and the risk of fractures caused by oral corticosteroids. *J Bone Miner.Res.* 2003; 18: 913-918.
  81. Kemp, J. P., Osur, S., Shrewsbury, S. B., et al. Potential effects of fluticasone propionate on bone mineral density in patients with asthma: a 2-year randomized, double-blind, placebo-controlled trial. *Mayo Clin.Proc.* 2004; 79: 458-466.
  82. Roux, C., Kolta, S., Desfougeres, J. L., et al. Long-term safety of fluticasone propionate and nedocromil sodium on bone in children with asthma. *Pediatrics* 2003; 111: e706-e713.
  83. Fitzgerald, J. M., Becker, A., Sears, M. R., et al. Doubling the dose of budesonide versus maintenance treatment in asthma exacerbations. *Thorax* 2004; 59: 550-556.
  84. Harrison, T. W., Osborne, J., Newton, S., et al. Doubling the dose of inhaled corticosteroid to prevent asthma exacerbations: randomised controlled trial. *Lancet* 2004; 363: 271-275.
  85. Paton, J., Jardine, E., McNeill, E., et al. Adrenal responses to low dose synthetic ACTH (Synacthen) in children receiving high dose inhaled fluticasone. *Arch Dis.Child* 2006; 91: 808-813.
  86. Russell, G. Very high dose inhaled corticosteroids: panacea or poison? *Arch Dis.Child* 2006; 91: 802-804.
  87. Woolcock, A., Lundback, B., Ringdal, N., et al. Comparison of addition of salmeterol to inhaled steroids with doubling of the dose of inhaled steroids. *Am.J Respir.Crit Care Med.* 1996; 153: 1481-1488.
  88. Greening, A. P., Ind, P. W., Northfield, M., et al. Added salmeterol versus higher-dose corticosteroid in asthma patients with symptoms on existing inhaled corticosteroid. *Allen & Hanburys Limited UK Study Group.* *Lancet* 1994; 344: 219-224.
  89. Pearlman, D. S., Chervinsky, P., Laforce, C., et al. A comparison of salmeterol with albuterol in the treatment of mild-to-moderate asthma. *N.Engl.J Med.* 1992; 327: 1420-1425.

90. Kesten, S., Chapman, K. R., Broder, I., et al. A three-month comparison of twice daily inhaled formoterol versus four times daily inhaled albuterol in the management of stable asthma. *Am.Rev.Respir.Dis.* 1991; 144: 622-625.
91. Wenzel, S. E., Lumry, W., Manning, M., et al. Efficacy, safety, and effects on quality of life of salmeterol versus albuterol in patients with mild to moderate persistent asthma. *Ann.Allergy Asthma Immunol.* 1998; 80: 463-470.
92. Bateman, E. D., Boushey, H. A., Bousquet, J., et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study. *Am.J.Respir.Crit Care Med.* 2004; 170: 836-844.
93. Drugs for asthma. *Treat.Guidel.Med.Lett.* 2008; 6: 83-90.
94. Nelson, J. A., Strauss, L., Skowronski, M., et al. Effect of long-term salmeterol treatment on exercise-induced asthma. *N.Engl.J Med.* 1998; 339: 141-146.
95. Thomas, M., Turner, S., Leather, D., et al. High-dose inhaled corticosteroid use in childhood asthma: an observational study of GP prescribing. *Br.J Gen Pract.* 2006; 56: 788-790.
96. Lotvall, J. Pharmacological similarities and differences between beta2-agonists. *Respir.Med.* 2001; 95 Suppl B: S7-11.
97. Palmqvist, M., Persson, G., Lazer, L., et al. Inhaled dry-powder formoterol and salmeterol in asthmatic patients: onset of action, duration of effect and potency. *Eur.Respir.J.* 1997; 10: 2484-2489.
98. van Noord, J. A., Smeets, J. J., Raaijmakers, J. A., et al. Salmeterol versus formoterol in patients with moderately severe asthma: onset and duration of action. *Eur.Respir.J.* 1996; 9: 1684-1688.
99. O'Byrne, P. M., Bisgaard, H., Godard, P. P., et al. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *Am.J.Respir.Crit Care Med.* 2005; 171: 129-136.
100. Bisgaard, H. and Szeffler, S. Long-acting beta2 agonists and paediatric asthma. *Lancet* 2006; 367: 286-288.
101. Nelson, H. S., Weiss, S. T., Bleecker, E. R., et al. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. *Chest* 2006; 129: 15-26.
102. MHRA. Asthma: Long-acting beta-2 agonists. [www.mhra.gov.uk](http://www.mhra.gov.uk) (accessed 17/01/2008) 2008;
103. BMA / RPSGB. British National Formulary. BNF 57. 2009.
104. Laloo, U. G., Malolepszy, J., Kozma, D., et al. Budesonide and formoterol in a single inhaler improves asthma control compared with increasing the dose of corticosteroid in adults with mild-to-moderate asthma. *Chest* 2003; 123: 1480-1487.
105. Kips, J. C., O'Connor, B. J., Inman, M. D., et al. A long-term study of the antiinflammatory effect of low-dose budesonide plus formoterol versus high-dose budesonide in asthma. *Am.J Respir.Crit Care Med.* 2000; 161: 996-1001.
106. CHM/MHRA. Inhaled products that contain corticosteroids. *Drug Safety Update* 2008; 1: 6-7.
107. Stoloff, S. W., Stempel, D. A., Meyer, J., et al. Improved refill persistence with fluticasone propionate and salmeterol in a single inhaler compared with other controller therapies. *J.Allergy Clin.Immunol.* 2004; 113: 245-251.
108. Currie, G. P., Devereux, G. S., Lee, D. K., et al. Recent developments in asthma management. *BMJ* 2005; 330: 585-589.
109. Barnes, P. J. Scientific rationale for inhaled combination therapy with long-acting beta2-agonists and corticosteroids. *Eur.Respir.J.* 2002; 19: 182-191.
110. Kuna, P., Peters, M. J., Manjra, A. I., et al. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. *Int.J Clin.Pract.* 2007; 61: 725-736.
111. Rabe, K. F., Atienza, T., Magyar, P., et al. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study. *Lancet* 2006; 368: 744-753.
112. Bousquet, J., Boulet, L. P., Peters, M. J., et al. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. *Respir.Med.* 2007; 101: 2437-2446.
113. Cates, C. J. and Lasserson, T. J. Combination formoterol and budesonide as maintenance and reliever therapy versus inhaled steroid maintenance for chronic asthma in adults and children. *Cochrane Database Syst.Rev.* 2009; CD007313.
114. Scicchitano, R., Aalbers, R., Ukena, D., et al. Efficacy and safety of budesonide/formoterol single inhaler therapy versus a higher dose of budesonide in moderate to severe asthma. *Curr.Med.Res.Opin.* 2004; 20: 1403-1418.
115. Vogelmeier, C., D'Urzo, A., Pauwels, R., et al. Budesonide/formoterol maintenance and reliever therapy: an effective asthma treatment option? *Eur.Respir.J* 2005; 26: 819-828.
116. Dicipingaitis, P. V., Dobkin, J. B. and Reichel, J. Antitussive effect of the leukotriene receptor antagonist zafirlukast in subjects with cough-variant asthma. *J Asthma* 2002; 39: 291-297.
117. Lipworth, B. J. Leukotriene-receptor antagonists. *Lancet* 1999; 353: 57-62.
118. Drazen, J. M., Israel, E. and O'Byrne, P. M. Treatment of asthma with drugs modifying the leukotriene pathway. *N.Engl.J Med.* 1999; 340: 197-206.
119. Barnes, N. C. and Miller, C. J. Effect of leukotriene receptor antagonist therapy on the risk of asthma exacerbations in patients with mild to moderate asthma: an integrated analysis of zafirlukast trials. *Thorax* 2000; 55: 478-483.
120. Lofdahl, C. G., Reiss, T. F., Leff, J. A., et al. Randomised, placebo controlled trial of effect of a leukotriene receptor antagonist, montelukast, on tapering inhaled corticosteroids in asthmatic patients. *BMJ* 1999; 319: 87-90.
121. Price, D. B., Hernandez, D., Magyar, P., et al. Randomised controlled trial of montelukast plus inhaled budesonide versus double dose inhaled budesonide in adult patients with asthma. *Thorax* 2003; 58: 211-216.
122. Vaquerol, M. J., Casan, P., Castillo, J., et al. Effect of montelukast added to inhaled budesonide on control of mild to moderate asthma. *Thorax* 2003; 58: 204-210.
123. Virchow, J. C., Jr., Prasse, A., Naya, I., et al. Zafirlukast improves asthma control in patients receiving high-dose inhaled corticosteroids. *Am.J Respir.Crit Care Med.* 2000; 162: 578-585.
124. Nelson, H. S., Busse, W. W., Kerwin, E., et al. Fluticasone propionate/salmeterol combination provides more effective asthma control than low-dose inhaled corticosteroid plus montelukast. *J Allergy Clin.Immunol.* 2000; 106: 1088-1095.
125. Fish, J. E., Israel, E., Murray, J. J., et al. Salmeterol powder provides significantly better benefit than montelukast in asthmatic patients receiving concomitant inhaled corticosteroid therapy. *Chest* 2001; 120: 423-430.
126. Ringdal, N., Eliraz, A., Pruzinec, R., et al. The salmeterol/fluticasone combination is more effective than fluticasone plus oral montelukast in asthma. *Respir.Med.* 2003; 97: 234-241.
127. Deykin, A., Wechsler, M. E., Boushey, H. A., et al. Combination therapy with a long-acting beta-agonist and a leukotriene antagonist in moderate asthma. *Am.J Respir.Crit Care Med.* 2007; 175: 228-234.
128. Laviolette, M., Malmstrom, K., Lu, S., et al. Montelukast added to inhaled beclomethasone in treatment of asthma. Montelukast/Beclomethasone Additivity Group. *Am.J.Respir.Crit Care Med.* 1999; 160: 1862-1868.
129. Peters-Golden, M., Swern, A., Bird, S. S., et al. Influence of body mass index on the response to asthma controller agents. *Eur.Respir.J* 2006; 27: 495-503.
130. Lazarus, S. C., Chinchilli, V. M., Rollings, N. J., et al. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma. *Am.J Respir.Crit Care Med.* 2007; 175: 783-790.
131. Dahlen, B., Nizankowska, E., Szczeklik, A., et al. Benefits from adding the 5-lipoxygenase inhibitor zileuton to conventional therapy in aspirin-intolerant asthmatics. *Am.J Respir.Crit Care Med.* 1998; 157: 1187-1194.
132. Kim, S. H., Ye, Y. M., Hur, G. Y., et al. CysLTR1 promoter polymorphism and requirement for leukotriene receptor antagonist in aspirin-intolerant asthma patients. *Pharmacogenomics.* 2007; 8: 1143-1150.
133. Dahlen, S. E., Malmstrom, K., Nizankowska, E., et al. Improvement of aspirin-intolerant asthma by montelukast, a leukotriene antagonist: a randomized, double-blind, placebo-controlled trial. *Am.J Respir.Crit Care Med.* 2002; 165: 9-14.
134. Wechsler, M. E., Finn, D., Gunawardena, D., et al. Churg-Strauss syndrome in patients receiving montelukast as treatment for asthma. *Chest* 2000; 117: 708-713.
135. Wechsler, M. E., Pauwels, R. and Drazen, J. M. Leukotriene modifiers and Churg-Strauss syndrome: adverse effect or response to corticosteroid withdrawal? *Drug Saf* 1999; 21: 241-251.
136. Harrold, L. R., Andrade, S. E., Go, A. S., et al. Incidence of Churg-Strauss syndrome in asthma drug users: a population-based perspective. *J Rheumatol.* 2005; 32: 1076-1080.
137. Sullivan, P., Bekir, S., Jaffar, Z., et al. Anti-inflammatory effects of low-dose oral theophylline in atopic asthma. *Lancet* 1994; 343: 1006-1008.
138. Kidney, J., Dominguez, M., Taylor, P. M., et al. Immunomodulation by theophylline in asthma. Demonstration by withdrawal of therapy. *Am.J.Respir.Crit Care Med.* 1995; 151: 1907-1914.
139. Barnes, P. J. Theophylline: new perspectives for an old drug. *Am.J.Respir.Crit Care Med.* 2003; 167: 813-818.
140. Dahl, R., Larsen, B. B. and Venge, P. Effect of long-term treatment with inhaled budesonide or theophylline on lung function, airway reactivity and asthma symptoms. *Respir.Med.* 2002; 96: 432-438.
141. Rivington, R. N., Boulet, L. P., Cote, J., et al. Efficacy of Uniphyll, salbutamol, and their combination in asthmatic patients on high-dose inhaled steroids. *Am.J.Respir.Crit Care Med.* 1995; 151: 325-332.
142. Evans, D. J., Taylor, D. A., Zetterstrom, O., et al. A comparison of low-dose inhaled budesonide plus theophylline and high-dose inhaled budesonide for moderate asthma. *N.Engl.J.Med.* 1997; 337: 1412-1418.
143. Ukena, D., Harnest, U., Sakalauskas, R., et al. Comparison of addition of theophylline to inhaled steroid with doubling of the dose of inhaled steroid in asthma. *Eur.Respir.J.* 1997; 10: 2754-2760.
144. Davies, B., Brooks, G. and Devoy, M. The efficacy and safety of salmeterol compared to theophylline: meta-analysis of nine controlled studies. *Respir.Med.* 1998; 92: 256-263.
145. Wilson, A. J., Gibson, P. G. and Coughlan, J. Long acting beta-agonists versus theophylline for maintenance treatment of asthma. *Cochrane Database Syst.Rev.* 2000; CD001281.
146. BMA / RPSGB. BNF 55. 55. 2008.
147. Mash, B., Bheekie, A. and Jones, P. W. Inhaled vs oral steroids for adults with chronic asthma. *Cochrane Database Syst.Rev.* 2000; CD002160.
148. Powell, H. and Gibson, P. G. Initial starting dose of inhaled corticosteroids in adults with asthma: a systematic review. *Thorax* 2004; 59: 1041-1045.

149. Hawkins, G., McMahon, A. D., Twaddle, S., et al. Stepping down inhaled corticosteroids in asthma: randomised controlled trial. *BMJ* 2003; 326: 1115.
150. Powell, H. and Gibson, P. G. High dose versus low dose inhaled corticosteroid as initial starting dose for asthma in adults and children. *Cochrane Database Syst.Rev.* 2004; CD004109.
151. Masoli, M., Weatherall, M., Holt, S., et al. Budesonide once versus twice-daily administration: meta-analysis. *Respirology.* 2004; 9: 528-534.
152. Bateman, E. D., Fairall, L., Lombardi, D. M., et al. Budesonide/formoterol and formoterol provide similar rapid relief in patients with acute asthma showing refractoriness to salbutamol. *Respir.Res.* 2006; 7: 13.
153. Presta, L. G., Lahr, S. J., Shields, R. L., et al. Humanization of an antibody directed against IgE. *J Immunol.* 1993; 151: 2623-2632.
154. MacGlashan, D. W., Jr., Bochner, B. S., Adelman, D. C., et al. Down-regulation of Fc(epsilon)RI expression on human basophils during in vivo treatment of atopic patients with anti-IgE antibody. *J Immunol.* 1997; 158: 1438-1445.
155. NICE. Omalizumab for severe persistent allergic asthma. NICE Technology Appraisal Guidance 133 2007;
156. Dolovich, M. New delivery systems and propellants. *Can.Respir.J.* 1999; 6: 290-295.
157. MHRA. Beclometasone dipropionate pressurised metered dose inhaler. Medicines and Healthcare Regulatory Agency 2006;
158. Murphy, A. Update on asthma management. *Pharmaceutical Journal* 2008; 280: 283-286.
159. Ivax Pharmaceuticals. Qvar. Summary of Product Characteristics 2003;
160. Trinity Chiesi Pharmaceuticals Ltd. Clenil Modulite. Summary of Product Characteristics 2006;
161. Anon. CFC-free inhalers. *PJ Practice Checklist.* *Pharmaceutical Journal* 2001;
162. Chalmers, G. W., Macleod, K. J., Little, S. A., et al. Influence of cigarette smoking on inhaled corticosteroid treatment in mild asthma. *Thorax* 2002; 57: 226-230.
163. Chaudhuri, R., Livingston, E., McMahon, A. D., et al. Cigarette smoking impairs the therapeutic response to oral corticosteroids in chronic asthma. *Am.J.Respir.Crit Care Med.* 2003; 168: 1308-1311.
164. Strachan, D. P. and Cook, D. G. Health effects of passive smoking. 1. Parental smoking and lower respiratory illness in infancy and early childhood. *Thorax* 1997; 52: 905-914.
165. Dezateux, C., Stocks, J., Dundas, I., et al. Impaired airway function and wheezing in infancy: the influence of maternal smoking and a genetic predisposition to asthma. *Am.J.Respir.Crit Care Med.* 1999; 159: 403-410.
166. Murray, A. B. and Morrison, B. J. The decrease in severity of asthma in children of parents who smoke since the parents have been exposing them to less cigarette smoke. *J.Allergy Clin.Immunol.* 1993; 91: 102-110.
167. Department of Health. Chapter 19 - Influenza. Immunisation against infectious disease (The Green Book) 2006; [www.dh.gov.uk](http://www.dh.gov.uk). Accessed 08/04/09;
168. Department of Health. Chapter 25 - Pneumococcal. Immunisation against infectious disease (The Green Book) 2006; [www.dh.gov.uk](http://www.dh.gov.uk). Accessed 08/04/09;
169. Caress, A. L., Beaver, K., Luker, K., et al. Involvement in treatment decisions: what do adults with asthma want and what do they get? Results of a cross sectional survey. *Thorax* 2005; 60: 199-205.
170. Department of Health, Social Services and Public Safety Northern Ireland. A Healthier Future - a strategic framework for respiratory conditions. 2006.
171. Gibson, P. G. and Powell, H. Written action plans for asthma: an evidence-based review of the key components. *Thorax* 2004; 59: 94-99.
172. Partridge, M. R. and Hill, S. R. Enhancing care for people with asthma: the role of communication, education, training and self-management. 1998 World Asthma Meeting Education and Delivery of Care Working Group. *Eur.Respir.J* 2000; 16: 333-348.
173. Fishwick, D., D'Souza, W. and Beasley, R. The asthma self-management plan system of care: what does it mean, how is it done, does it work, what models are available, what do patients want and who needs it? *Patient.Educ.Couns.* 1997; 32: S21-S33.
174. Cote, J., Cartier, A., Robichaud, P., et al. Influence of asthma education on asthma severity, quality of life and environmental control. *Can.Respir.J.* 2000; 7: 395-400.
175. Cote, J., Bowie, D. M., Robichaud, P., et al. Evaluation of two different educational interventions for adult patients consulting with an acute asthma exacerbation. *Am.J.Respir.Crit Care Med.* 2001; 163: 1415-1419.
176. Gallefoss, F., Bakke, P. S. and Rsgaard, P. K. Quality of life assessment after patient education in a randomized controlled study on asthma and chronic obstructive pulmonary disease. *Am.J.Respir.Crit Care Med.* 1999; 159: 812-817.
177. Gallefoss, F. and Bakke, P. S. Impact of patient education and self-management on morbidity in asthmatics and patients with chronic obstructive pulmonary disease. *Respir.Med.* 2000; 94: 279-287.
178. Ghosh, C. S., Ravindran, P., Joshi, M., et al. Reductions in hospital use from self management training for chronic asthmatics. *Soc.Sci.Med.* 1998; 46: 1087-1093.
179. Gibson, P. G., Powell, H., Coughlan, J., et al. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst.Rev.* 2003; CD001117.
180. Ignacio-Garcia, J. M. and Gonzalez-Santos, P. Asthma self-management education program by home monitoring of peak expiratory flow. *Am.J.Respir.Crit Care Med.* 1995; 151: 353-359.
181. Lahdensuo, A., Haahtela, T., Herrala, J., et al. Randomised comparison of guided self management and traditional treatment of asthma over one year. *BMJ* 1996; 312: 748-752.
182. Madge, P., McColl, J. and Paton, J. Impact of a nurse-led home management training programme in children admitted to hospital with acute asthma: a randomised controlled study. *Thorax* 1997; 52: 223-228.
183. Moudgil, H., Marshall, T. and Honeybourne, D. Asthma education and quality of life in the community: a randomised controlled study to evaluate the impact on white European and Indian subcontinent ethnic groups from socioeconomically deprived areas in Birmingham, UK. *Thorax* 2000; 55: 177-183.
184. Thoonen, B. P., Schermer, T. R., Van Den Boom G., et al. Self-management of asthma in general practice, asthma control and quality of life: a randomised controlled trial. *Thorax* 2003; 58: 30-36.
185. Wolf, F. M., Guevara, J. P., Grum, C. M., et al. Educational interventions for asthma in children. *Cochrane.Database.Syst.Rev.* 2003; CD000326.
186. Pearson, M. G. and Bucknall, C. E. Measuring clinical outcome in asthma: a patient focused approach. *Royal College of Physicians* 1999;

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## COMPASS THERAPEUTIC NOTES ASSESSMENT Management of Chronic Asthma in Adults and Older Children

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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## COMPASS THERAPEUTIC NOTES ASSESSMENT

### Management of Chronic Asthma in Adults and Older Children

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<b>1</b>	<b>In the management of chronic asthma:</b>		
a	If using both an inhaled salbutamol and an inhaled corticosteroid, the salbutamol should be used first to allow better penetration of the steroid into the lungs.	T	F
b	When more than one puff of an inhaler is required, patients should wait 60 seconds between puffs.	T	F
c	Inhaled, short-acting $\beta_2$ agonists should be used regularly, four times daily.	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
<b>2</b>	<b>Inhaled corticosteroids are effective anti-inflammatory agents and, in patients of all ages, appear to be the most effective agents for:</b>		
a	Controlling asthma symptoms	T	F
b	Improving lung function	T	F
c	Improving quality of life	T	F
d	Preventing acute exacerbations	T	F
<b>3</b>	<b>Based on the balance of risks and benefits of using inhaled long-acting <math>\beta_2</math> agonists:</b>		
a	The long-acting $\beta_2$ agonist should be added if regular use of standard-dose ICS has failed to control asthma.	T	F
b	Can be initiated in a patient whose asthma is deteriorating rapidly.	T	F
c	The long-acting $\beta_2$ agonist should be initiated at full therapeutic dose.	T	F
d	Once effective asthma control has been achieved with a long-acting $\beta_2$ agonist, the dose should be maintained.	T	F
<b>4</b>	<b>Leukotriene receptor antagonists (LTRAs):</b>		
a	When used alone as controller medication, the effect of LTRAs is generally less than that of low doses of inhaled corticosteroids.	T	F
b	In patients whose asthma is not controlled with inhaled corticosteroids, adding an LTRA may improve asthma control and reduce the dose of inhaled corticosteroids required.	T	F
c	LTRAs have no bronchodilator activity.	T	F
d	As "add-on" therapy, LTRAs are equally as effective as long-acting $\beta_2$ agonists.	T	F
<b>5</b>	<b>When stepping down asthma treatment:</b>		
a	Patients should be maintained on the minimum dose of asthma drugs which controls their condition.	T	F
b	When a person's asthma is being controlled by medium- to high-dose ICS alone, a 50% reduction in steroid dose should be attempted at 3 month intervals.	T	F
c	Where control is achieved at a low-dose of ICS alone, in most patients treatment may be switched to once-daily dosing.	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