Diagnosis and management of asthma in primary care

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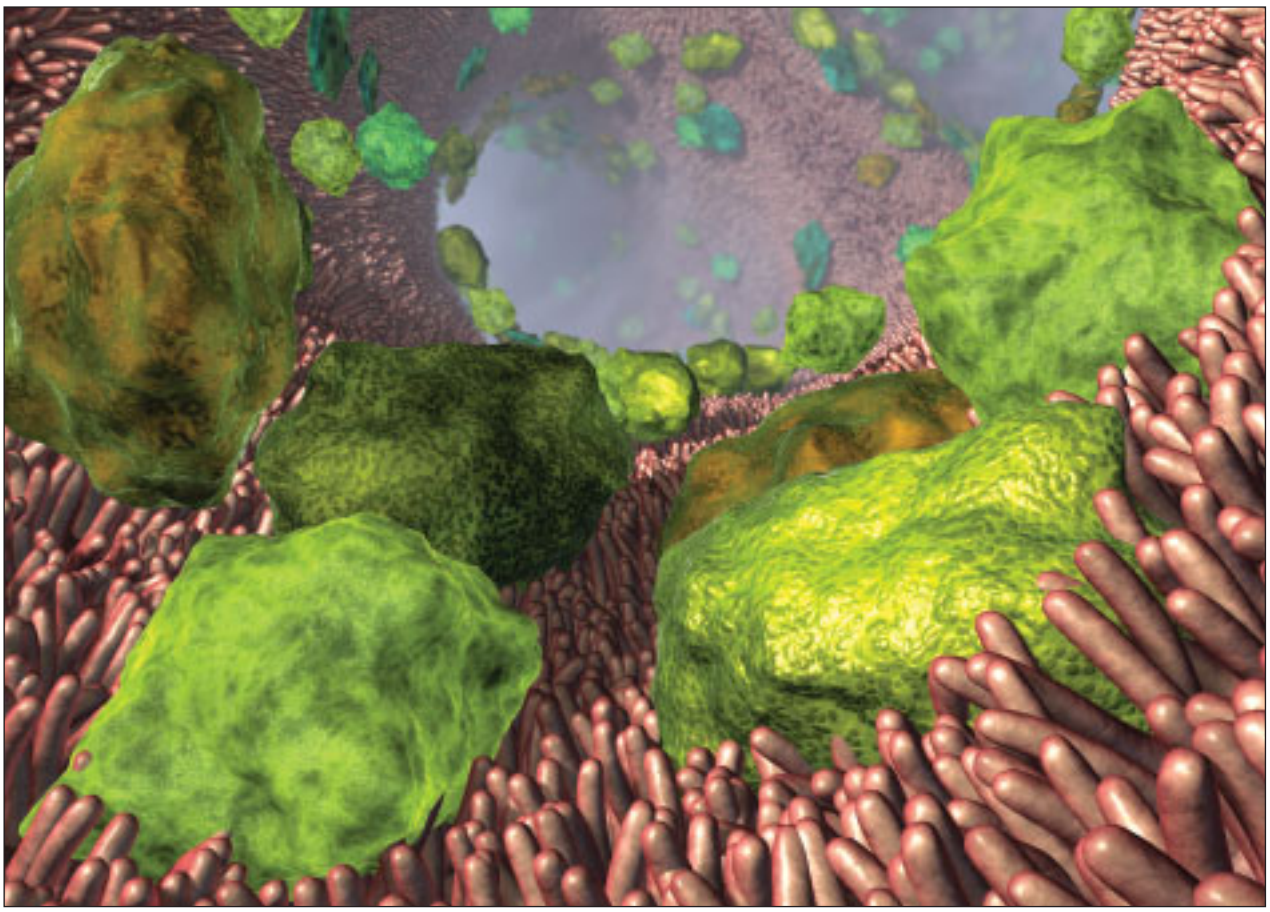

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Perfect control of asthma is now a realistic aim in patients with mild to moderate disease, although there are many factors that may limit the success of treatment. Our Drug review considers the current stepwise approach to management, followed by sources of further information, an analysis of prescription data and the Datafile.

It is still not possible to define asthma purely in terms of histopathological features. Abnormal function of the airways remains inherent in the diagnosis, and although airways inflammation is a universal feature of asthma, the precise relationship between this inflammation and the functional abnormalities is still very poorly understood. A definition of asthma therefore encompasses:

- inflammation of the airways – eosinophil influx orchestrated by cytokines released by T-cells, leading to airways damage and remodelling
- variable airways obstruction – may vary spontaneously from none to severe in the course of hours to minutes, and improves after suitable therapy
- nonspecific hyper-reactivity – refers to the tendency of asthmatic airways to constrict in response to nonspecific stimuli (including strong smells, cold air, fog, smoke, exercise, aerosol sprays, dust) that do not significantly affect nonasthmatic patients; this is again thought to be a consequence of inflammation.

In children	In adults	As part of the asthmatic predisposition
Diagnosis		
obliterative bronchiolitis vocal cord dysfunction bronchomalacia inhaled foreign bodies cystic fibrosis recent aspiration (particularly in handicapped children) developmental abnormalities of the upper airway immunoglobulin deficiencies primary ciliary dyskinesia	cystic fibrosis bronchiectasis inhaled foreign body tracheobronchomalacia recurrent aspiration chronic obstructive pulmonary disease congestive cardiac failure tumours in or impinging on central airways obstructive bronchiolitis vocal cord dysfunction bronchial amyloidosis	allergic bronchopulmonary aspergillosis pulmonary eosinophilic syndromes (for example Churg-Strauss)
Signs		
persistent productive cough excessive vomiting dysphagia abnormality of the voice/cry failure to thrive focal signs in the chest	crackles in the chest evidence of heart failure unilateral or fixed wheeze stridor persistent chest pain productive cough weight loss nonresolving pneumonia	involvement of other organs in vasculitis

Table 1. Differential diagnosis of asthma

Diagnosis of asthma

The cardinal clinical features of asthma are those of obstruction (wheeze, chest tightness, shortness of breath) and hyper-reactivity (wheeze in response to nonspecific stimuli, cough). Any one of these symptoms may present in isolation. Symptoms of asthma may show diurnal variability (worse in the early hours of the morning), so it is important to ask patients specifically about day, night and early morning symptoms.

It is fairly common to find no signs on physical examination, although if airways obstruction is severe enough there may be diffuse, expiratory wheeze on auscultation. Additional clinical signs in the chest and/or an abnormal chest X-ray suggest an alternative or additional diagnosis (see Table 1). Such patients should be referred for specialist investigation.

It is critical to document the diagnosis of asthma objectively prior to commencing any treatment. This is usually based on simple spirometric measurements made in the surgery or clinic, or on home peak expiratory flow (PEF) measurements made in a diary (see Table 2). A useful diagnostic test in children is to measure PEF before and after a vigorous, six-minute run.

The 'gold standard' of asthma diagnosis is the histamine or methacholine challenge test (performed in hospital laboratories). Although sensitive and discriminative, it is rarely needed to diagnose asthma. It is reserved for cases where the diagnosis is in doubt, for example in patients with chronic cough whose peak flow variability is not clearly diagnostic of asthma.

In children, the diagnosis of asthma may be more difficult, particularly in those not old enough to perform spirometry reliably. In such cases, diagnosis rests on a suggestive history of typical symptoms, daily variability of these symptoms and the presence of characteristic exacerbating factors. A personal or family history of atopy is suggestive. Objective confirmation of wheezing by a healthcare professional is important.

Ultimately, the diagnosis may depend on a good response to a trial of anti-asthma therapy. A clear response to bronchodilators is helpful, but for more chronic symptoms a trial of inhaled corticosteroids is

more appropriate. A poor response should prompt careful review of the diagnosis. However the diagnosis is made, this should always be documented clearly in the patient's records.

Pharmacological therapy

Guidelines have been published by the British Thoracic Society in collaboration with the Scottish Intercollegiate Guidelines Network (BTS/SIGN), and the latest update to these guidelines (July 2007) is available online.[1] The advantage of such guidelines is that they attempt to rationalise therapy, hopefully based on properly designed clinical trials. A disadvantage is that they tend to discourage consideration of the hopes, fears, aspirations, disease patterns and exacerbating factors in each individual patient. This is also necessary for effective management.

Asthma therapy is designed to address the two main pathophysiological features of airways inflammation and inappropriate airways constriction. To reduce inflammation, the cornerstone of therapy is treatment with a topical corticosteroid. This is referred to as 'preventer' therapy to help the patient understand that it must be taken regularly, even in the absence of symptoms, to control inflammation. To control inappropriate bronchospasm, both short-acting and long-acting beta-agonists are used. These are referred to as 'relievers'.

The management of asthma in adults and children is summarised in Figure 1. Although this 'stepwise' approach implies tailoring treatment to suit symptoms, in practice it is often considered advantageous to treat patients with somewhat more than they are anticipated to need in the first instance, especially if they have severe symptoms. This promotes confidence in the treatment because the patient can usually sense a rapid improvement.

After this it is important to consider 'stepping down' if the patient has remained stable for a considerable period: the BTS/SIGN guidelines suggest reduction of inhaled steroids by 25-50 per cent every three months if disease remains well controlled. It is also legitimate to move down to the previous step of therapy if asthma control is satisfactory.

In patients at steps 1-3 of the treatment guidelines, perfect control of asthma is a realistic aim. This is defined as absence of symptoms, day and night, no or minimal need for reliever medication, no disease exacerbations, no limitations on physical activity and normal lung function, defined as forced expiratory volume in one second (FEV_1) or PEF >80 per cent of the predicted value, with <20 per cent diurnal variability.

- >20% diurnal variability for more than 3 days per week for 2 weeks in a PEF diary
- increase in PEF of 20% (or 15% with a 200ml improvement in FEV_1) after short-acting $beta_2$-agonist or course of inhaled (6 weeks) or oral steroids (30mg prednisolone daily for 2 weeks)
- fall in FEV_1 or PEF of 20% after a 6-minute run (children)
- positive histamine or methacholine challenge test (occasionally needed in difficult cases)

Table 2. BTS/SIGN criteria for objective diagnosis of asthma (any one of these features is diagnostic)

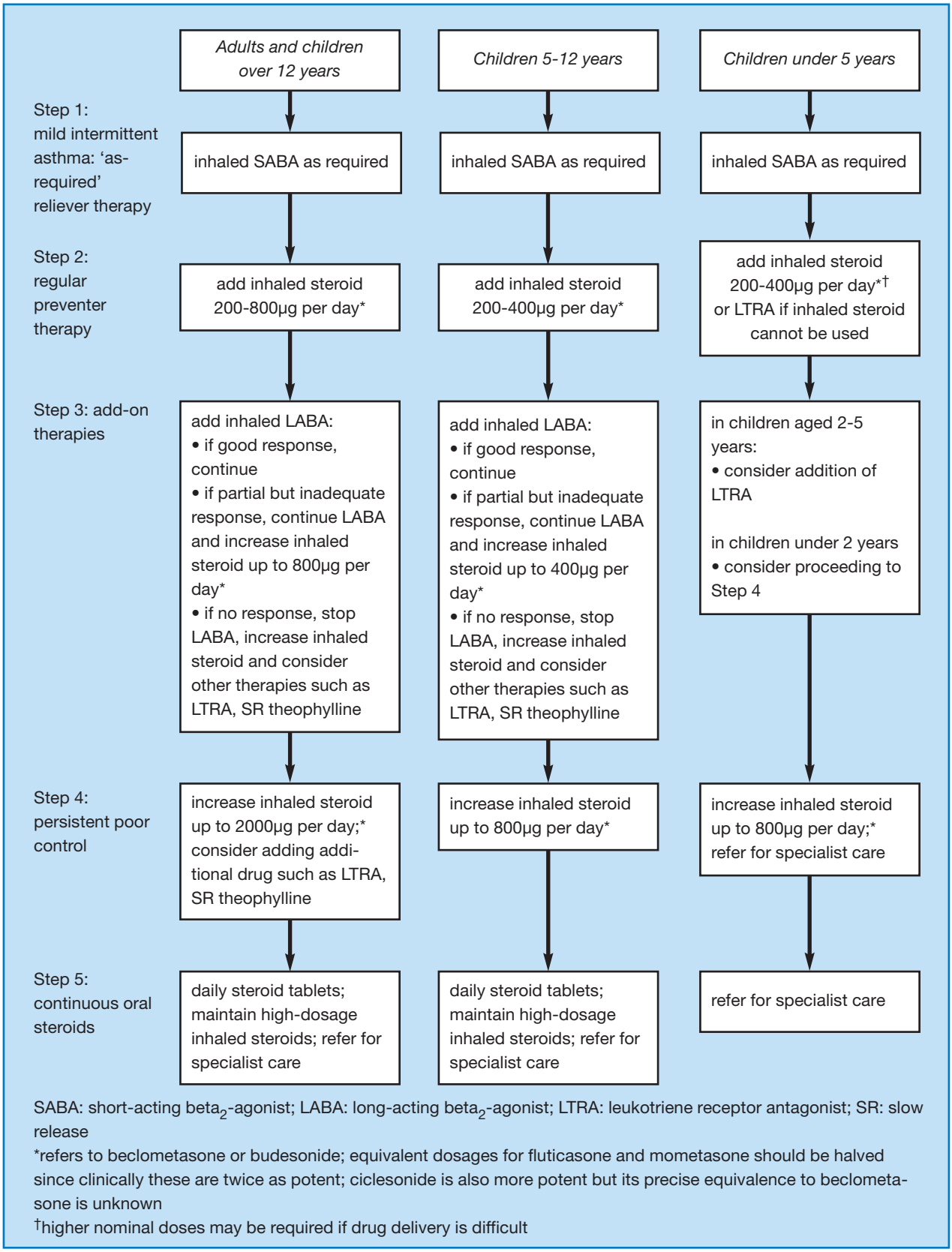
In those patients who continue to have severe, troublesome symptoms despite maximal step 3 therapy, perfect asthma control is not a realistic aim, and management becomes a question of balancing the requirements of a reasonable quality of life against the risks of high-dose steroid and other medication. The patient's view should be taken into account when making such choices.

In the UK, approximately 85 per cent of patients have mild disease controllable at steps 1, 2 or 3 of medication. These patients are managed largely in primary care and rarely need to visit hospital. The remaining 15 per cent of patients have more severe, persistent symptoms (steps 4 or 5), and often require regular review by a hospital specialist. These patients are also more likely to require hospital admission.

Steps 1-3

Patients with very mild symptoms may take a short-acting beta-agonist when required. There is no merit in regular dosing. The exact threshold for the introduction of inhaled steroids has never been firmly established, but should certainly be considered in patients using beta-agonist three times per week or more, waking with symptoms one night a week or having had an exacerbation of asthma in the past two years. Abnormal spirometry is also an indication, but not an absolute requirement, since some patients meeting the aforementioned criteria may have near-normal lung function.

There are five inhaled steroids currently available for asthma therapy in the UK: beclometasone, budesonide, fluticasone (Flixotide), mometasone (Asmanex) and ciclesonide (Alvesco). Both fluticasone and mometasone are, as a rule of thumb, clinically twice as potent as beclometasone and budesonide. The exact dose equivalent of ciclesonide is unknown, but 160µg once daily (the standard licensed dose) is probably at least as effective as beclometasone 400µg daily in



SABA: short-acting beta$_2$-agonist; LABA: long-acting beta$_2$-agonist; LTRA: leukotriene receptor antagonist; SR: slow release

*refers to beclometasone or budesonide; equivalent dosages for fluticasone and mometasone should be halved since clinically these are twice as potent; ciclesonide is also more potent but its precise equivalence to beclometasone is unknown

†higher nominal doses may be required if drug delivery is difficult

Figure 1. Current recommended stepwise management of asthma in adults and children

divided dosages. Inhaled steroids, if used at dosages up to 800µg per day in adults and 400µg per day in children (these thresholds refer to beclometasone and budesonide) are extremely safe. The only commonly encountered problems are oral thrush and hoarseness of the voice. At such dosages, from the point of view of efficacy (but not necessarily patient preference or suitability) there is little to choose between the available steroid preparations.

Ciclesonide is activated by de-esterification only in the respiratory tract, and not in the mouth, and may be particularly helpful for patients with oropharyngeal side-effects.

Where higher dosages of inhaled steroids are necessary at Step 3 and above, the decreased bioavailability of fluticasone, mometasone and ciclesonide coupled with their increased local potency may offer a more favourable benefit/risk ratio.

One clear product of asthma research in the last few years has been the demonstration that early addition of a regular long-acting beta-agonist – salmeterol (Serevent) and formoterol are currently available in the UK – exerts a steroid-sparing effect in asthmatic patients inadequately controlled at Step 2 and also results in fewer symptoms and disease exacerbations.[2,3] Consequently for such patients, the best course is to add in a long-acting beta-agonist first before raising inhaled steroid dosages above the thresholds stated above. For this reason, inhalers are now available that combine a fixed dosage of long-acting beta-agonist with variable dosages of inhaled steroid (*eg* Seretide, Symbicort).

These preparations are convenient for the patient and may encourage compliance. A potential disadvantage is that inhaled steroid dosages cannot be increased without a new prescription. To obviate this, the patient may be prescribed an extra, steroid-only inhaler to take regularly but temporarily (for example, in the event of sudden deterioration). Alternatively, it should be noted that budesonide/formoterol (Symbicort) combinations are licensed for additional 'as-required' use for disease exacerbation. Before adding on any therapy at step 3 or subsequently, compliance, inhaler technique and exposure to trigger factors should be reviewed.

- incorrect or additional diagnosis
- inadequate dosages
- poor patient compliance or understanding
- allergen exposure
- exercise-induced asthma
- allergic bronchopulmonary aspergillosis
- drugs: beta-blockers, aspirin/NSAIDs
- smoking (active or passive)
- occupational disease
- hormonal: premenstrual asthma, thyroid dysfunction
- underlying vasculitis (Churg-Strauss syndrome)
- true steroid resistance

Table 3. Factors that may compromise patient response to asthma therapy

Leukotrienes are produced by a wide variety of inflammatory cells. They are the most potent natural bronchoconstrictors known, and also increase mucus secretion and promote vascular leakage. The leukotriene receptor antagonists montelukast (Singulair) and zafirlukast (Accolate) have been shown to improve lung function and symptoms, reduce disease exacerbation and spare inhaled therapy.[4,5] The response to these drugs is less predictable compared with that to long-acting beta-agonists, and they are not recommended as first-line therapy at Step 3, but may be useful adjuncts to therapy (this should preferably be documented objectively, for example by PEF monitoring).

They also ameliorate symptoms of allergic rhinitis and can be useful for treating patients with seasonal, pollen-induced asthma with rhinitis. They are also a substitute for preventer therapy in children under five in whom it is found impossible for whatever reason to use inhaled steroids (which should always otherwise be used as first-line therapy).

Theophyllines are weak relaxers of bronchial smooth muscle and also inhibit inflammatory cells. Theophylline dosages must be individualised and monitored (this is often neglected in clinical practice, but essential to prevent overdosage). Addition of inhaled anticholinergics, cromoglicate (Intal) and nedocromil (Tilade) at this stage rarely confers more than marginal additional benefit.

Step 4

There are few clear studies informing the best course of treatment for Step 4 patients. Options include increasing inhaled steroids up to 2000µg per day in adults or 800µg per day in children (dosages refer to beclometasone/budesonide), while maintaining therapy with a long-acting beta-agonist, and/or adding a leukotriene receptor antagonist, oral theophylline or oral slow-release beta-agonist.

Inhaled steroid dosages should not be increased over these limits: this has led to adrenal crisis on rapid withdrawal in children. Consider the possibility of adrenal insufficiency in any child maintained on more than 400µg per day of beclometasone/budesonide (or equivalent) presenting with shock or impaired consciousness. If there is doubt such patients should be

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Figure 2. Inhaler technique training is recommended: up to half of patients do not use their inhaler correctly

given intramuscular hydrocortisone. Always titrate inhaled steroids to the lowest effective dosage in children (but be wary of inadequate treatment).

Other steroid systemic effects (see Step 5) are possible at these high dosages. Drugs should be altered one at a time, while monitoring efficacy, and discontinued if not objectively effective.

Step 5

If patients are deemed to require oral steroids long term, maximal dosages of inhaled steroids and other add-on therapy if shown to be effective should be continued. Inhaled steroids are still the most effective drug for minimising the requirement for oral steroids.[6,7] Patients on regular oral steroids should be monitored (and treated if practicable) for the development of:

- hypertension
- diabetes mellitus
- osteoporosis (see guidelines from the British Osteoporosis Society, www.nos.org.uk)
- poor growth and cataract in children.

Adults and children at Steps 4 and 5 should be considered for specialist referral.

The BTS/SIGN guidelines emphasise the possible role of psychosocial morbidity in chronic severe asthma. Self-management of asthma may be neglected in the psychiatrically ill or those living in poor social circumstances. Symptoms may be exacerbated by stress and anxiety, and occasionally used as a means of manipulating peers and relatives. Some patients become psychologically as well as physiologically dependent on medications, particularly oral steroids. Management in such cases is difficult, and unfortunately not well covered in guidelines.

Omalizumab

Omalizumab (Xolair) is a humanised monoclonal antibody that prevents IgE binding to its receptors on mast cells and other immune cells. It is presumed to act by inhibiting IgE-mediated reactions to allergens in atopic asthmatic patients, although this is by no means certain. Its principal benefit is to reduce asthma exacerbations requiring unscheduled care (A&E visits and hospital admissions) in severe patients at step 5 of therapy in whom compliance is assured and all asthma exacerbating factors eliminated as far as possible. Because of the presumed 'antiallergic' action of omalizumab, it is licensed for patients from the age of 12 years in whom allergy is considered to play a 'significant role' in their disease (these will generally be patients with clinical reactivity to allergens and positive skin prick tests).

It is given by subcutaneous injection every two or four weeks depending on the weight and total serum IgE concentration of the patient. Not all patients can be treated. It may cause soreness at the injection site but is otherwise well tolerated; a small but tangible incidence of anaphylactic reaction means that it is best given in a hospital outpatient setting. Patients must be monitored closely with peak flow and symptom diaries in order to identify those patients (some 30 per cent) who show no response, in which case the treatment is discontinued after a 16- to 20-week trial period.

The treatment is expensive and, in responding patients, potentially life long. It has recently been approved by NICE but local funding and logistical issues may delay its general availability.

Choice of inhaled device

There are few data to suggest that the potential delivery of inhaled steroids varies markedly between devices, but efficient delivery can be severely compromised with any device by inadequate inhaler technique. It should therefore be a priority to prescribe a device that the patient likes and can use efficiently.

In children under five it is usual to prescribe a metered dose inhaler (MDI) with a spacer and a facemask. Older children and adults should be given a

choice of inhalers. Some prefer an MDI, others a dry powder device. Breath-activated devices are loved by some and abhorred by others. For patients who require auditory and visual reassurance that the drug has been safely delivered, a device like the Novohaler might be considered.

Chlorofluorocarbon (CFC) containing propellants will be phased out very soon. In general, CFC and nonCFC devices are interchangeable in terms of dosage with the exception of Qvar, which should be substituted for CFC-containing beclometasone inhalers at 50 per cent of the existing dosage.

Newer inhaled steroids such as mometasone and ciclesonide have their own dosage regimens. As a rule of thumb mometasone is roughly equivalent to twice the dosage of CFC beclometasone. With ciclesonide, an 80µg daily dose is approximately equivalent to a 200µg daily dose of CFC beclometasone.

The particle size of hydrofluoroalkane (HFA) propellants, which now replace CFC propellants, is much smaller, enabling much better penetration of the drugs into the airways and somewhat obviating the need for spacer devices (although these should remain mandatory in children and those with anything less than perfect inhaler technique).

Factors compromising response to therapy

Important factors that may compromise the response of patients to therapy are summarised in Table 3. Of these, poor compliance and poor inhaler technique are by far the most important. There will be no response if the diagnosis is incorrect; consequently it is important to make, and document, the correct diagnosis. While it is important to 'step down' therapy if patients remain stable and asymptomatic, there is conversely considerable evidence that many patients remain symptomatic because they are undertreated, therefore therapy should be reviewed and increased if necessary. Patients should also be encouraged to self-manage their therapy, within reasonable limits, if they so wish.

Technique and understanding

Incorrect inhaler technique is common: one overview[8] suggested that 50 per cent of patients do not know how to use their inhalers correctly, and that this is improved by training. Training should be given by a heath professional proficient in the use of the particular inhaler device. There are few clear indications that the many inhaler devices now available differ in their effectiveness. Steroid MDIs should always be used with a spacer (and a face mask in infants) and there is no evidence that nebulised steroids are more effective than an MDI and spacer when treating chronic asthma. Inhaler technique should be reassessed periodically as part of a structured clinical review.

The Royal College of Physicians' 3 questions:[9]
- Have you had difficulty sleeping because of asthma?
- Have you had your usual asthma symptoms during the day?
- Has your asthma interfered with your usual activities?

Table 4. Assessment of morbidity during clinical review

Patient compliance is also an important issue compromising the response of patients to prescribed therapy.[9] Monitoring of patients' dosing habits with electronic recorders suggests that overall, patients take their recommended dosages of medication on only 20-73 per cent of days; this is probably a conservative estimate. Overusage is far less common.

There are many factors which are thought to influence compliance, including a tendency of patients to distrust medication (partially for fear of side-effects, reinforced by inaccurate propaganda from non-professionals and the media), a tendency to stop medication if symptoms have been stable or absent, mistrust of the use of inhalers, as opposed for example to tablets in general, and psychosocial factors as mentioned above. These factors must be exposed and addressed as far as possible. Education has been shown to increase compliance with dosing regimens.[10]

There is an assumption that compliance decreases as the number of inhalations prescribed per day increases. While some studies support this,[11] others do not.[12] It seems sensible to maximise the convenience of dosing regimens for patients, and wherever possible to use the same delivery device – one which suits the patient best – for all inhaled drugs.

In primary care, a trained nurse should review asthmatic patients identified from a refined register designed to indicate 'at-risk' patients.[13] Clinical review should be proactive and empower individuals or their parents/carers to undertake self-management effectively. Such review should include:
- measurement of lung function (PEF)
- inhaler technique
- morbidity (see Table 4)
- current treatment
- an asthma action plan (all patients in Step 3 and above, and all those who have had a severe exacerbation in the past year, should have an asthma action plan).

Asthma action plans should be focussed on individual needs and may be based on symptoms and/or PEF measurements, depending on patient ability.

They have been shown in many studies to improve health outcomes,[14-17] since most asthmatic patients deteriorate slowly and there is time for intervention. Instructions on how to deal with asthma exacerbation is an essential part of action plans: in those taking moderate dosages of inhaled steroids, briefly increasing the dosage up to five-fold is effective. More severe patients will require courses of oral steroids. A number of model plans are available from Asthma UK (www.asthma.org.uk/control).

Primary care practitioners should also consider keeping a register of high-risk patients (those admitted to hospital in the past year, those with 'brittle' asthma and those who have ever been admitted to an intensive care unit because of their asthma).

Allergen exposure

Exposure to aeroallergens clearly exacerbates asthma[18-20] and increases the risk of acute exacerbations[21] in allergic individuals. Clinical suspicion of sensitivity to particular allergens should be confirmed (when not obvious) by skin prick testing or RAST (radioallergosorbent test), performed and interpreted preferably by an allergist.

Asthmatic symptoms related to animal dander are easily identified, and allergy to seasonal allergens (tree or grass pollens in spring/summer, moulds in late summer/autumn) may cause quite severe seasonal exacerbation of disease. In children, particularly infants aged three or under, food allergies (milk, eggs, nuts and grains are the commonest culprits) may be important triggers for asthma (as well as allergic rhinitis and eczema). House dust mite allergy may exacerbate asthma and rhinitis in clinically sensitised individuals. Specific inquiry should be made about allergens to which the patients may be sensitised in their own homes.

It has been difficult to show therapeutic benefits of avoidance of some allergens (particularly perennial allergens such as the house dust mite) on a population scale.[22,23] This may be because clinically effective avoidance of some allergens is in practice impossible. For this reason the BTS/SIGN guidelines are unable to recommend any specific measures for house dust mite avoidance, but suggest that in committed families with evidence of clinical house dust mite allergy and who wish to try avoidance, the following should be recommended: use of barrier bed covering systems (likely the most useful since most exposure to house dust mite occurs while in bed), removal from the bedroom of carpets, soft toys and soft furnishings (plastic or leather seats are best), high temperature washing of bed linen, and keeping both the temperature and humidity as low as possible.

On the other hand, many potentially avoidable allergens (family pets, food allergens) may be the most important factors compromising the response to asthma therapy in specific individuals, and these must not be missed. Avoidance of some allergens, particularly food allergens, can be difficult, and requires the expert advice of an allergist or allergy dietitian.

Atopic asthmatic patients often have concomitant allergic rhinitis, which should always be treated, usually with topical nasal steroids. Symptoms may be seasonal or perennial. A recent UK study[24] found that 76 per cent of over 7000 asthmatic patients reported symptoms of rhinitis, and over half said it made their asthma worse. Allergen avoidance advice should embrace asthma and rhinitis. Seasonal exacerbation of asthma may be severe and should usually be treated with regular preventer therapy. If leukotriene receptor antagonists are used as a treatment for asthma, they have the additional benefit of being at least as efficacious as antihistamines for the treatment of seasonal rhinitis, although a regular topical nasal steroid should also be used for anything more than very mild, intermittent symptoms.

IgE-mediated sensitisation to *Aspergillus* suggests the possibility of allergic bronchopulmonary aspergillosis, which should be managed by a specialist.

Indicator	Points	Payment stages
Records		
Asthma 1. The practice can produce a register of patients with asthma excluding patients with asthma who have been prescribed no asthma-related drugs in the last 12 months	4	
Initial management		
Asthma 8. The percentage of patients aged 8 and over diagnosed as having asthma from 1 April 2006 with measures of variability or reversibility	15	40-80%
Ongoing management		
Asthma 3. 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%
Asthma 6. The percentage of patients with asthma who have had an asthma review in the last 15 months	20	40-70%

Table 5. Quality indicator points for asthma

Allergen immunotherapy is not currently recommended for the treatment of atopic asthma. Although immunotherapy certainly reduces allergen-induced bronchospasm in atopic asthmatic patients,[25-27] there are no data showing that immunotherapy is additive with, or sparing of conventional therapy. Furthermore, life-threatening anaphylactic reactions to immunotherapy injections, while very rare, are much more common in asthmatic patients. Recent studies suggesting that immunotherapy may alter the natural history of asthma by reducing new allergic sensitisations,[28] if confirmed, might result in its more widespread use in the future for patients with mild or moderate, carefully stabilised asthma.

Drugs

Beta-blockers, including eye drops, are contraindicated in asthmatic patients since they may cause acute, severe bronchospasm.

Aspirin-sensitive patients may develop one or more of a constellation of symptoms (bronchospasm, rhinitis, GI upset and urticaria) acutely following aspirin ingestion. Aspirin sensitivity is seen in about 10 per cent of adult asthmatic patients, and is usually diagnosed by a careful clinical history of suggestive symptoms developing within minutes or hours of aspirin ingestion. This effect reflects the ability of aspirin and related NSAIDs to inhibit the cyclo-oxygenase isoenzyme COX-1. Aspirin-sensitive asthmatic patients should avoid aspirin and other COX-1 inhibitors, but it is not logical to automatically ban all asthmatic patients from using these drugs, particularly if indicated for valid therapeutic purposes. In cases of doubt the patient should be referred to an allergist for formal aspirin challenge, since sensitivity cannot be diagnosed by skin or blood tests.

Increasing evidence suggests that newer anti-inflammatory drugs such as etoricoxib (Arcoxia), which inhibit the distinct cyclo-oxygenase isoenzyme COX-2, are safe in aspirin-sensitive patients. While these are useful analgesics, it is important to remember that they do not substitute for the antiplatelet effects of aspirin.

Smoking

Maternal smoking in pregnancy impedes lung development[29] and increases the risk of allergic sensitisation of the offspring.[30] Exposure to environmental tobacco smoke (passive smoking) increases the risk of asthma exacerbation in children.[31] Smoking as a teenager increases the risk of persisting asthma.[32] It is unclear whether smoking increases symptoms or exacerbations in adult asthmatic patients; nevertheless, for all these reasons smoking should be discouraged.

Key points

- the majority of asthmatic patients have mild to moderate disease and are managed almost exclusively in primary care
- for these patients, total disease control is a realistic aim
- in more chronic, severe patients, the need for a suitable quality of life must be weighed against the possible unwanted effects of drugs
- the major medications for asthma include short- and long-acting beta$_2$-agonists, inhaled corticosteroids, leukotriene receptor antagonists and theophylline
- mild, intermittent asthma may be managed with 'as-required' inhaled short-acting beta$_2$-agonists
- mild-to-moderate asthma requires regular inhaled corticosteroid therapy; initially dosage should be restricted to 800µg per day of beclometasone or equivalent in adults and 400µg per day in children
- in more severe asthma it is optimal to add in a regular long-acting beta$_2$-agonist before increasing inhaled corticosteroid dosage still further; if disease is still not controlled, dosage may be increased up to 2000µg per day of beclometasone or equivalent in adults and 800µg per day in children
- leukotriene receptor antagonists and theophylline may be useful adjuncts to therapy in some patients, but a favourable objective response should be documented
- in very severe patients, additional oral corticosteroids may be necessary regularly or intermittently; maximal inhaled corticosteroid therapy and other therapy if shown to be beneficial should not be stopped
- disease control is facilitated by removing disease-exacerbating factors and ensuring adequate patient understanding, compliance and inhaler technique

Occupational asthma

Occupational asthma may now account for up to 10 per cent of cases of adult-onset asthma. It is now the commonest industrial lung disease in the developed world with over 400 reported causes. The diagnosis should be suspected and sought in all adult asthmatic patients, particularly those in high-risk occupations (paint sprayers, bakers, nurses, chemical workers, animal handlers, welders, food processing workers and timber workers). Patients should be asked if their symptoms are better when away from work or on holiday. Serial PEF measurements every two hours while at home and at work from waking to sleeping may suggest the diagnosis; analysis is best done with the aid of a criterion-based expert system (see www.occupationalasthma.com).

Patients are best managed by an occupational physician. The prognosis is worse for workers who develop occupational asthma and remain exposed to the offending agent for more than one year after symptoms develop.[33]

Alternative and complementary medicine

At present there is no clear, evidence-based confirmation that herbal medicine, acupuncture, air ionisers, homoeopathy, chiropractic or breathing exercises including yoga and Buteyko improve asthma objectively, although some may discourage inappropriate overbreathing associated with anxiety. This is discussed in more detail in the BTS/SIGN guidelines.[1]

Conclusion

Of the six million or so asthmatic patients in the UK, 85 per cent have mild to moderate disease requiring steps 1, 2 or 3 of asthma treatment, and will be managed almost entirely by primary care health professionals. For these patients, total disease control is a realistic aim.

Successful therapy requires a correct, objective diagnosis (not always possible in very young children), matching of therapy to disease severity as assessed by symptoms and lung function, and recognition and elimination, wherever possible, of factors that confound therapy. Such factors include poor inhaler technique and poor understanding of the principles of disease management, exacerbation of disease by airborne and food allergens, concomitant use of drugs that may exacerbate asthma, smoking and occupational asthma triggers.

Patients with more severe disease are best managed in collaboration with a hospital specialist. Total disease control in all of these patients is not a realistic aim, and quality of life must be balanced against risks of therapy. Attention to psychosocial factors may assume a prominent role in the management of chronic, severe disease.

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Forum

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Resources

Further reading

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British guidelines on the management of asthma. BTS, SIGN. www.brit-thoracic.org.uk/c2/uploads/asthma_fullguideline2007.pdf.

Groups and organisations

Asthma UK, Summit House, 70 Wilson Street, London EC2A 2DB. Tel: 020 7786 4900; website: www.asthma.org.uk. Produces patient booklets and magazines and information for healthcare professionals. There is also a helpline: 08457 01 02 03, open from 9am until 5pm, Monday to Friday.

British Thoracic Society, 17 Doughty Street, London WC1N 2PL. Tel: 020 7831 8778; fax: 020 7831 8766; website: www.brit-thoracic.org.uk. The British Thoracic Society provides patient information about all chest diseases, and the website has links to patient support groups and lists of guidelines.

Breathe Easy Group or the British Lung Foundation, 73-75 Goswell Road, London EC1V 7ER. Tel: 08458 50 50 20; website: www.lunguk.org. This is a patient support network providing information and advice for people with lung diseases.

General Practice Airways Group, Smithy House, Waterbeck, Lockerbie, DG11 3EY. Tel: 01461 600 639 Fax: 0121 351 4455; website: www.gpiag.org. The group holds an annual scientific meeting and produces the *Primary Care Respiratory Journal*. Guidelines and information about therapy can be found on the website.

Prescription review

Recent years have seen a large shift in asthma medications to the use of combined long-acting bronchodilator/steroid inhalers. Prescribing of single formulations of short-acting beta-agonists has remained stable for the past five years, with salbutamol accounting for about 95 per cent of the 17 million scrips dispensed annually in England.

By contrast, prescribing of long-acting bronchodilators has decreased by more than one-quarter since 2002/03 and, despite the introduction of mometasone and ciclesonide, prescribing of inhaled steroids fell by almost one-third to 8.3 million scripts in 2006/07.

These changes are due to a threefold increase over the past five years in prescribing of salmeterol/fluticasone and, from a lower baseline, a fivefold increase in that of formoterol/budesonide to a total of 6.4 million scrips (see Figure 3).

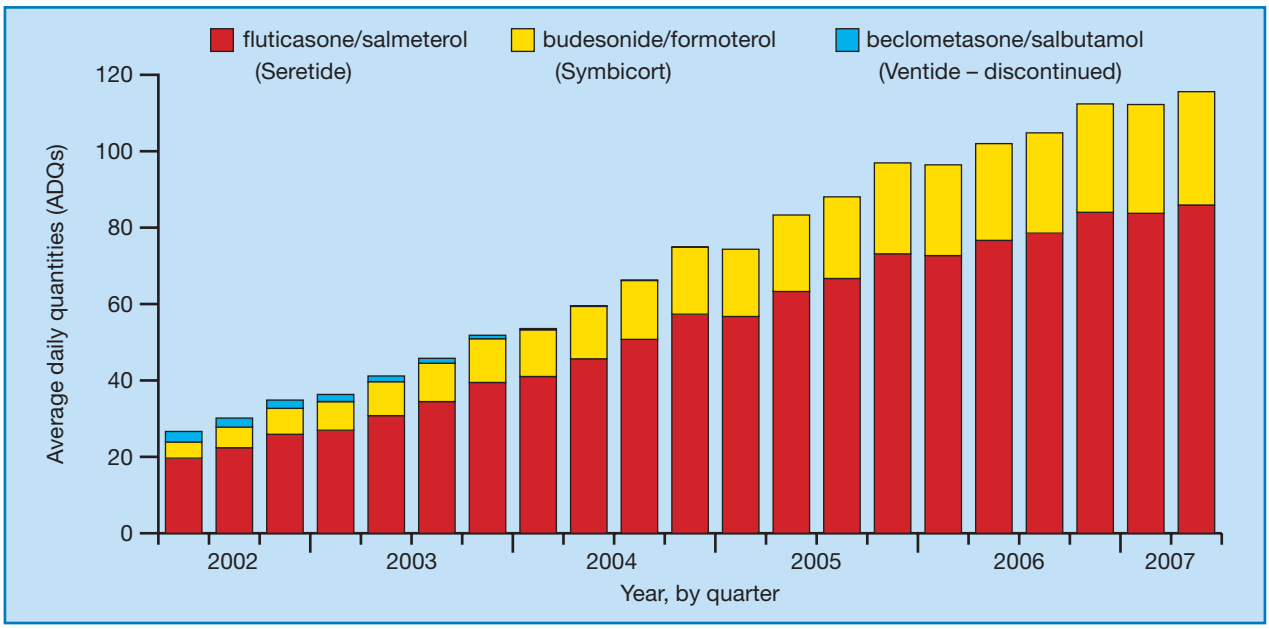

Figure 3. Usage of inhaled corticosteroid compound preparations in general practice in England by quarter, 2002-7

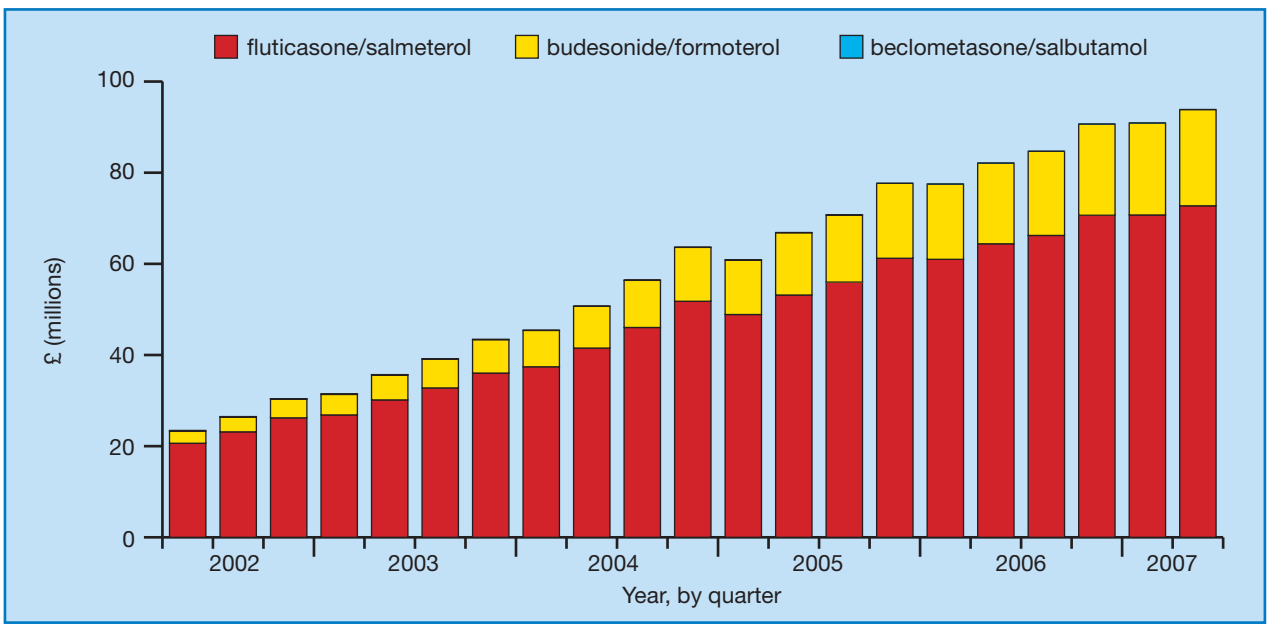

Figure 4. Cost of prescriptions for inhaled corticosteroid compound preparations in general practice in England by quarter, 2002-7

Preparations used in the treatment of asthma

Table 1. Aerosol inhaled bronchodilators

Drug	Available as	Form/strength	Cost[1]
Short-acting beta$_2$-agonists			
salbutamol	Airomir*	aerosol 100µg per puff	99p
	Airomir Autohaler*	breath-actuated aerosol 100µg per puff	£3.01
	Ventolin Evohaler*	aerosol 100µg per puff	75p (Volumatic £2.75)
	Salamol*	aerosol 100µg per puff	74p
	Salamol Easi-Breathe*		£3.15
	salbutamol aerosol inhalation*	aerosol 100µg per puff	£1.44
Long-acting beta$_2$-agonists			
formoterol	Atimos Modulite*	aerosol 12µg per puff	£31.28
salmeterol	Serevent Evohaler*	aerosol 25µg per puff	£24.38
Anticholinergic			
ipratropium bromide	Atrovent*	aerosol 20µg per puff	£2.11
Short-acting beta$_2$-agonist/short-acting anticholinergic			
salbutamol/ipratropium bromide	Combivent	aerosol 100µg/20µg per puff	£3.38

[1]NHS cost of 100 doses. Prices from *MIMS/Drug Tariff* July 2007
*CFC-free propellant

Table 2. Dry-powder bronchodilators

Drug	Available as	Form/strength	Recommended dose	Cost[1]
Short-acting beta$_2$-agonists				
salbutamol	Asmasal Clickhaler	95µg per puff	acute attack: 1-2 puffs	£2.94
	Easyhaler Salbutamol	100µg, 200µg per puff	100-200µg as required	£1.73-£3.46
	Ventolin Accuhaler	200µg per puff	1 puff as required	£8.53
	Pulvinal Salbutamol	200µg per puff		£5.05
terbutaline sulphate	Bricanyl Turbohaler	500µg per puff	1 puff as required	£6.92
Long-acting beta$_2$-agonists				
formoterol	Foradil	12µg per cap	1 cap twice daily	£48.71
	Oxis Turbohaler	6µg, 12µg per puff	1-2 puffs daily	£41.33
	Formoterol Easyhaler	12µg per puff	1 puff twice daily	£20.67
salmeterol	Serevent Diskhaler	50µg per blister	1-2 blisters twice daily	£59.22-£118.45
	Serevent Accuhaler	50µg per blister		£48.76-£97.53
Short-acting anticholinergic				
ipratropium bromide	Atrovent Aerocaps	40µg per cap	1-2 caps 3 or 4 times daily	£10.53-£21.06 (Aerohaler £14.53)

[1]NHS cost of 100 doses. Prices from *MIMS/Drug Tariff* July 2007

Table 3. Oral drugs for the treatment of asthma

Drug	Available as	Form/strength	Adult daily dosage range[1]	Cost[2]
Leukotriene receptor antagonists				
montelukast	Singulair	10mg tabs	10mg daily	£26.97
	Singulair Paediatric	4mg, 5mg chewable tabs	4-5mg daily	£25.69
		4mg sachet granules	4mg daily	£25.69
zafirlukast	Accolate	20mg tabs	20mg twice daily	£28.26
Long-acting beta$_2$-agonist				
bambuterol	Bambec	10mg, 20mg tabs	10-20mg once daily	£12.05-£13.14
Short-acting beta$_2$-agonists				
orciprenaline	Alupent Syrup	10mg per 5ml	20mg 4 times daily	£8.44
terbutaline	Bricanyl Tablets	5mg tabs	2.5-5mg 3 times daily	£1.72-£3.44
	Bricanyl Syrup	1.5mg per 5ml sugar-free susp	10-15ml 3 times daily	£7.28-£10.92
salbutamol	Ventmax SR	4mg, 8mg sust-rel caps	8mg twice daily	£10.28
	Ventolin Syrup	2mg per 5ml syrup	2-8mg 3-4 times daily	£1.68-£8.96
	Volmax	4mg, 8mg cont-rel tabs	8mg twice daily	£11.77
	salbutamol	2mg, 4mg tabs	4mg 3-4 times daily	£4.56-£6.08
		2mg per 5ml sugar-free oral soln		£10.58-£14.11
Sympathomimetics				
ephedrine	CAM	4mg per 5ml sugar-free elixir	20ml 3-4 times daily; max 5 days	£16.65-£22.20[3]
	ephedrine	15mg, 30mg tabs	15-60mg 3 times daily	£10.26-£26.64
Sympathomimetic/xanthine				
ephedrine/ theophylline	Franol Plus	15mg/120mg tabs	1 tab 3-4 times daily	£6.74-£8.98
Xanthines				
theophylline	Nuelin SA	175mg sust-rel tabs	175-350mg twice daily after food	£2.98-£5.95
	Nuelin SA-250	250mg sust-rel tabs	250-500mg twice daily after food	£4.16-£8.33
	Slo-Phyllin	60mg, 125mg, 250mg sust-rel caps	250-500mg twice daily	£4.34-£8.68
	Uniphyllin Continus	200mg, 300mg, 400mg sust-rel tabs	200-400mg twice daily	£3.13-£5.65
aminophylline	Phyllocontin Continus	225mg sust-rel tabs	225-450mg twice daily	£2.54-£5.08
	Phyllocontin Forte	350mg sust-rel tabs	350-700mg twice daily	£4.22-£8.44

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007 [3]5 days' treatment as specified in SPC

Table 4. Inhaled aerosol preventers

Drug	Available as	Form/strength	Adult daily maintenance dosage[1]	Cost[2]
Corticosteroids				
beclometasone	Aerobec Autohaler	breath-actuated aerosol 50µg, 100µg per puff	300-800µg daily in divided doses	£3.22-£8.58
	Aerobec Forte Autohaler	breath-actuated aerosol 250µg per puff	1000-2000µg daily in divided doses	£9.39-£18.77
	Beclazone	aerosol 50µg, 100µg, 200µg per puff	300-800µg daily in divided doses	£2.39-£8.29
	Beclazone 250 inhaler	aerosol 250µg per puff	1000µg daily in divided doses	£8.26
	Beclazone Easi-Breathe	breath-actuated aerosol 50µg, 100µg per puff	300-800µg daily in divided doses	£4.33-£11.53
	Beclazone 250 Easi-Breathe	breath-actuated aerosol 250µg per puff	1000µg daily in divided doses	£11.34
	Becloforte	aerosol 250µg per puff for use with Volumatic (£2.75)	1000-2000µg daily in divided doses	£3.91-£7.83
	Becotide	aerosol 100µg, 200µg per puff for use with Volumatic (£2.75)	400-800µg daily in divided doses	£2.28-£4.56
	Clenil Modulite*	aerosol 50µg, 100µg, 200µg, 250µg	200-2000µg daily in divided doses	£2.16-£18.98
	Filair	aerosol 50µg, 100µg per puff	300-800µg daily in divided doses	£2.05-£8.20
	Filair Forte	aerosol 250µg per puff	1000-2000µg daily in divided doses	£8.97-£17.93
	Qvar*	aerosol 50µg, 100µg per puff	100-800µg daily in divided doses	£2.20-£17.63
	Qvar Autohaler*	breath-actuated aerosol 50µg, 100µg per puff	100-800µg daily in divided doses	£2.20-£17.63
	Qvar Easi-Breathe*	breath-actuated inhaler 50µg, 100µg per puff		£2.17-£17.34
	beclometasone	aerosol 50µg, 100µg, 250µg per puff	200-1000µg daily in divided doses	£1.64-£8.19
budesonide	Pulmicort Inhaler	aerosol 200µg per puff	400-1600µg daily in divided doses	£5.85-£23.40
	Pulmicort LS	aerosol 50µg per puff for use with Nebuhaler (£4.28)	50-400µg daily	£1.02-£8.21
ciclesonide	Alvesco*	aerosol 80µg, 160µg, per puff	80-160µg once daily	£6.66-£7.84
fluticasone	Flixotide Evohaler*	aerosol 50µg, 125µg, 250µg per puff for use with Volumatic (£2.75)	100-1000µg twice daily	£5.08-£50.78

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007 *CFC-free propellant

Table 4. Inhaled aerosol preventers (cont.)

Drug	Available as	Form/strength	Adult daily maintenance dosage[1]	Cost[2]
Anti-inflammatories				
sodium cromoglicate	Intal Fisonair	aerosol 5mg per puff with 2-piece 700ml spacer device	5-10mg 4 times daily	£20.52-£41.04
nedocromil sodium	Tilade*	aerosol 2mg per puff	4mg 2-4 times daily	£39.94-£79.88

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007 *CFC-free propellant

Table 5. Inhaled combination preventers/relievers

Drug	Available as	Form/strength	Adult daily maintenance dosage[1]	Cost[2]
Beta$_2$-agonist/corticosteroids				
formoterol/ budesonide	Symbicort Turbohaler	6µg/100µg	1-4 puffs twice daily	£7.70-£30.80
		6µg/200µg		£8.87-£35.47
		12µg/400µg	1-2 puffs twice daily	£17.73-£35.47
salmeterol/ fluticasone	Seretide Accuhaler	50µg/100µg aerosol	1 puff twice daily	£29.11
		50µg/250µg		£34.20
		50µg/500µg		£38.19
	Seretide Evohaler*	25µg/50µg MDI	2 puffs twice daily	£16.93
		25µg/125µg		£34.21
		25µg/250µg		£58.14

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007 *CFC-free propellant

Table 6. Inhaled dry-powder preventers

Drug	Available as	Form/strength	Adult daily maintenance dosage[1]	Cost[2]
Corticosteroids				
beclometasone	Asmabec Clickhaler	dry-powder inhaler 50µg, 100µg, 250µg per puff	200-800µg daily in divided doses	£2.74-£10.99
	Becodisks	dry-powder inhaler 100µg, 200µg, 400µg per puff	400µg twice daily or 200µg 3-4 times daily	£21.07-£21.35
	Easyhaler Beclometasone	breath-actuated dry-powder inhaler 200µg per puff	200-800µg daily in divided doses	£2.18-£8.74
	Pulvinal Beclometasone	100µg, 200µg, 400µg per puff	200-2000µg daily in divided doses	£2.88-£28.57

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007

Table 6. Inhaled dry-powder preventers (cont.)

Drug	Available as	Form/strength	Adult daily maintenance dosage[1]	Cost[2]
budesonide	Easyhaler Budesonide	breath-actuated dry-powder inhaler 100µg, 200µg, 400µg per puff	200-1600µg daily in 2 divided doses or up to 800µg once daily if taking twice-daily steroids	£2.59-£20.72
	Novolizer	breath-actuated dry-powder inhaler 200µg per puff	200-1600µg daily in 2 divided doses or up to 800µg once daily if taking twice-daily steroids	£4.16-£33.29
	Pulmicort	dry-powder inhaler 100µg, 200µg, 400µg per puff		£5.18-£41.44
fluticasone	Flixotide Diskhaler	dry-powder inhaler 50µg, 100µg, 250µg, 500µg per puff	100-1000µg twice daily	£11.86-£74.76
	Flixotide Accuhaler	dry-powder inhaler 50µg, 100µg, 250µg, 500µg per puff		£8.33-£67.46
mometasone	Asmanex Twisthaler	dry-powder inhaler 200µg, 400µg per puff	200-400µg daily	£11.20-£17.15
Anti-inflammatory				
sodium cromoglicate	Intal Spincap	20mg caps for use with Spinhaler (£1.93)	80mg daily in divided doses	£15.44

[1]Typical dosage based on *BNF/MIMS* [2]NHS cost of 28 days' treatment at dosage stated. Prices from *MIMS/Drug Tariff* July 2007