

## Guidelines for the management of chronic asthma in adolescents and adults

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# Guidelines for the management of chronic asthma in adolescents and adults

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## Introduction

Asthma prevalence is increasing worldwide and surveys indicate that the majority of patients in developed and developing countries do not receive optimal care and are therefore not well controlled. The aim of these guidelines is to promote a better standard of treatment based on advances in the understanding of the pathophysiology and pharmacotherapy of asthma and to encourage uniformity in the management of asthma.

The South African Thoracic Society first published guidelines for the management of chronic persistent asthma in 1992 and the second revision in 2000. The current revision is prompted by:

- The revised classification and new evidence on the safety and optimal use of asthma medication
- An ongoing need to emphasize the use of anti-inflammatory medication as the foundation of asthma treatment
- The positioning of leukotriene modifiers in the maintenance treatment of chronic asthma
- An emphasis on defining and achieving control of asthma

### ESSENTIAL STEPS IN THE MANAGEMENT OF ASTHMA TO ACHIEVE CONTROL:

- A. Establish the diagnosis of asthma.....20
- B. Assess severity.....21
- C. Implement asthma treatment .....21
  1. Set goals for control of asthma
  2. Preventive/avoidance measures
  3. Pharmacotherapy
- D. Achieve and monitor control .....25

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### EVIDENCE

The strategies recommended in these guidelines are classified according to the **Evidence Category** in Table 1 and denoted as “**Evidence A, B, C and D.** For details about these see Table 10 in the Additional Notes section.

**Table 1:** Categories of evidence for management strategies in asthma (Reproduced with permission from Global Initiatives for Asthma 2006)

Evidence Category	Sources of Evidence
A	Randomised controlled trials. Rich body of data.
B	Randomised controlled trials. Limited body of data.
C	Nonrandomised trials. Observational studies.
D	Panel consensus judgment.

### METHOD

This 2007 asthma guideline update was developed following a meeting with a working group constituted by the SA Thoracic Society. The working group is chaired by Prof UG Lalloo. The contribution by the working group is gratefully acknowledged. Meetings were held with the working group on the 2 3 July 2005, subsequently the editorial board was convened and met on the 30 March 2007 to develop and finalize this guideline document. The meetings were sponsored by the National Asthma Education Program (NAEP) of the SA Thoracic Society. This was possible through unrestricted educational grants to NAEP from the SA Thoracic Society, GSK, Astra-Zeneca, MSD, Altana Madaus and Boeringher Ingelheim. The document is viewed as a living document that will be updated periodically.

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## A. ESTABLISH THE DIAGNOSIS OF ASTHMA

### 1. Definition of asthma

Asthma is a chronic inflammatory condition of the airways which is usually allergic in origin and is characterised by hyperresponsive airways that constrict easily in response to a wide range of stimuli.

### 2. Symptoms and signs of asthma

The characteristic symptoms of asthma are cough, wheeze, dyspnoea or shortness of breath, and tightness of the chest.

Patterns of symptoms that suggest asthma are:

- Variability: day and night, day to day, seasonal
- Precipitation by a range of factors including environmental allergens (house dust mite, grass pollens, animal dander, occupational exposures), non-specific irritants (smoke, dusts and fumes), cold weather and exercise
- Response to bronchodilators and corticosteroids

Wheeze is a cardinal sign of asthma but may be absent at the time of consultation because airway constriction does not always result in detectable signs.

### 3. Lung function in asthma

Spirometric lung function tests, including measurement of peak expiratory flow, are useful in the diagnosis, assessment of severity and management (monitoring) of asthma. It may be abnormal even when symptoms and signs are absent. It may also be normal when asthma is quiescent. The commonest abnormality is a reduction in forced expiratory volume in 1 sec ( $FEV_1$ ) and peak expiratory flow (PEF). The ratio of  $FEV_1$  to forced vital capacity (FVC) to below 70% is characteristic of obstructive airways disease. The degree of reduction is generally related to severity of the asthma. Asthma improvement is usually mirrored by an improvement in  $FEV_1$  and PEF.

Significant reversibility of the airway obstruction is the major physiological characteristic of asthma. The standardised criteria are an increase in  $FEV_1$  of >12% and 200 ml, 15-30 min following the inhalation of 200-400 µg of salbutamol, or a 20% improvement in PEF from baseline. It should be noted, however, that many asthma patients will not exhibit reversibility at each assessment, particularly those on treatment, and thus the test lacks sensitivity and repeated testing at different visits is advised.

Conversely, asthma can also be confirmed by demonstrating increased hyperresponsiveness to bronchoconstrictor stimuli, particularly in subjects with normal spirometry. This is the principle of the methacholine/histamine challenge test. Exercise-induced bronchoconstriction may also be used to diagnose inducible airway obstruction. The  $FEV_1$  or PEF is measured at baseline and the patient asked to exercise (e.g. run for about 6 min) and the measurements repeated 5-10 minutes following cessation of exercise. A fall of 20% in PEF (15% in  $FEV_1$ ) in this setting is supportive of a diagnosis of asthma. Exercise induced bronchoconstriction may be the only manifestation of asthma in some.

Another option is to demonstrate diurnal variation in PEF of more than 20%. This can also be used to identify environmental (including occupational) causes of asthma symptoms by monitoring PEF 2-4 times each day for at

least 2 weeks. To measure diurnal variation, the PEF is measured first thing in the morning before treatment is taken, when values are often lowest, and last thing at night, when values are usually higher. There are several methods of calculating the diurnal PEF variability. A common way is the difference between the maximum and the minimum value for the day, expressed as a percentage of the mean daily PEF value, and averaged over 2 weeks.

If spirometry shows obstruction, a 2 week trial of oral prednisone (40 mg daily) may help to distinguish asthma from chronic obstructive pulmonary disease (COPD). In asthma there would be a significant improvement in  $FEV_1$  from baseline (>12% and 200 ml).

#### Diagnostic lung function values

##### Reversibility:

- An increase in  $FEV_1$  of >12% and 200 ml, 15-30 min after the inhalation of 200-400µg of salbutamol, or a 20% improvement in PEF from baseline.

##### Hyperresponsiveness:

- Methacholine/histamine challenge
- Exercise: A fall of 20% in PEF (or 15% in  $FEV_1$ ) measured 5-10 minutes apart after cessation of exercise (e.g. running for 6 minutes)

##### Diurnal variation:

- Diurnal variation in PEF of more than 20%

##### Distinguishing between COPD and asthma when $FEV_1$ shows obstruction:

- Improvement of  $FEV_1$  from baseline (>12% and 200ml) after a 2 week trial of oral prednisone (40 mg daily).

### 4. Making/confirming the diagnosis of asthma

The diagnosis of asthma is made by following these steps:

#### Step 1

Suspect asthma on basis of symptoms and signs particularly if there is variability

#### Step 2

Search for associated factors such as:

- Related atopic disorders – allergic rhinitis, allergic conjunctivitis, eczema
- Family history of asthma or other allergic disorders
- Onset of, or presence of symptoms during childhood
- Identifiable triggers for symptoms, and relieving factors such as improvement with a bronchodilator, or deterioration with exercise
- Exposure to known asthma sensitizers in the workplace (Table 8 in Additional Notes).
- Conduct spirometric lung function test or measure PEF. Repeat 15-30min after administration of 200-400µg of salbutamol, preferably via a spacer to ensure drug delivery to the airways.
- Optional tests include:
  - Full blood count to check eosinophil count
  - Total serum IgE
  - Skin prick tests or RAST in blood to look for evidence of atopy
  - Methacholine or histamine or exercise challenge tests

The optional tests are generally more costly but may be required as supportive evidence for asthma when the clinical and lung function data is not confirmatory. Measurement of exhaled nitric oxide (NO) and allergen challenge tests should only be done in research centres.

**B. ASSESSMENT OF ASTHMA SEVERITY**

When asthma is **first** diagnosed, it is convenient for implementation of treatment to classify it as **mild intermittent** or **chronic persistent** asthma that is **mild, moderate or severe** (Table 2). However, the severity is variable, does not predict response to treatment and is of little value in patients already on treatment. Periodic assessment of asthma control and review of management are more relevant.

**Table 2:** Assessment of asthma severity using symptoms and PEF in patients presenting for the **first** time on no treatment

INTERMITTENT	CHRONIC PERSISTENT		
	Mild	Moderate	Severe
I	II	III	IV
DAYTIME SYMPTOMS* ≤2/week	DAYTIME SYMPTOMS 3-4/week	DAYTIME SYMPTOMS >4/week	DAYTIME SYMPTOMS Continuous
NIGHT SYMPTOMS** ≤1/month	NIGHT SYMPTOMS 2-4/month	NIGHT SYMPTOMS >4/month	NIGHT SYMPTOMS Frequent
PEF ≥80%	PEF ≥80%	PEF 60-80%	PEF <60%

\*any of cough, tight chest and wheeze;  
\*\* any of cough, tight chest, wheeze and night wakening

**C. IMPLEMENT ASTHMA TREATMENT**

**1. SET GOALS OF ASTHMA TREATMENT TO ACHIEVE CONTROL**

The emphasis of modern asthma treatment is to achieve control. A patient’s asthma is well controlled when the goals of asthma management are achieved and maintained. The Global Initiative for Asthma (GINA) goals for asthma treatment is widely acknowledged and are:

- a. Achieve and maintain control of symptoms
- b. Maintain normal activity levels, including exercise
- c. Maintain pulmonary function as close to normal as possible
- d. Prevent asthma exacerbations
- e. Avoid adverse effects from asthma medications
- f. Prevent asthma mortality.

**Table 3:** Classification of drugs used in the maintenance treatment of asthma

CONTROLLERS		RELIEVERS
Anti-inflammatory action to prevent asthma attacks	Sustained bronchodilator action but weak or unproven anti-inflammatory effect	For quick relief of symptoms and use in acute attacks as PRN dosage only
<b>Inhaled corticosteroids</b> 1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Ciclesonide	<b>Long-acting β<sub>2</sub> agonists</b> 1. Salmeterol 2. Formoterol	<b>Short-acting β<sub>2</sub> agonists</b> 1. Salbutamol 2. Fenoterol 3. Terbutaline
<b>Leukotriene modifiers</b> 1. Montelukast 2. Zafirlukast <b>Oral corticosteroids</b> 1. Prednisone 2. Prednisolone 3. Methylprednisone 4. Methylprednisolone	<b>Sustained-release theophylline preparations</b>	<b>Anti-cholinergics</b> Ipratropium bromide

Achievement of the goals will also reduce asthma-related morbidity and mortality.

**2. PREVENTATIVE/AVOIDANCE MEASURES**

Avoidance of triggers wherever possible helps to minimise asthma severity and reduces asthma exacerbations. Practical measures include:

- a. Avoid exposure to personal and second-hand tobacco smoke
- b. Avoid contact with furry animals
- c. Reduce pollen exposure
- d. Reduce exposure to house dust mite
- e. Avoid sensitisers and irritants (dust and fumes) which aggravate or cause asthma especially in the workplace
- f. Avoid food and beverages containing preservatives
- g. Avoid drugs that aggravate asthma such as beta blockers (including in eye drops), and aspirin and non-steroidal anti-inflammatory drugs

**3. PHARMACOTHERAPY**

Maintenance treatment of asthma is determined by severity on presentation, current asthma medication, patient profile and level of control.

A classification of asthma drugs based on current knowledge of their mode of action is presented in Table 3. They may be:

- **Relievers** short-acting bronchodilators with rapid onset of action that provide acute relief of symptoms
- **Controllers** drugs with anti-inflammatory and/or a sustained bronchodilator action

Prescribers should be acquainted with the trade names, formulations, dosage and mode of administration of each preparation. The inhaled route is recommended as drugs are delivered directly into the airways with higher lung concentrations and less systemic side effects. Inhaled medications for asthma are available as pressurised metered-dose inhalers (pMDIs), breath-actuated MDIs, dry powder inhalers (DPIs), soft mist inhalers and nebulisers. It requires training and skill to coordinate activation of the pMDI with inhalation. All patients using a pMDI should use a large volume (500 ml) spacer or holding chamber to im-

prove drug delivery to the lungs and reduce local and systemic side effects. A pMDI plus spacer is as effective as a DPI (**Evidence A**). An inhaler device should be chosen and prescribed after patients have received training in its use and have shown satisfactory technique (**Evidence B**). See section C for Additional Notes on inhaler devices.

Treatment combinations are necessary in patients with more severe asthma or mild asthma not responsive to low dose inhaled corticosteroids.

**CONTROLLERS**

There are 2 groups of controllers those with anti-inflammatory action (corticosteroids and leukotriene blockers) and those with a sustained bronchodilator action (long-acting  $\beta_2$  agonists and slow-release theophyllines).

**Anti-inflammatory agents**

Anti-inflammatory treatment is recommended for all patients with chronic persistent asthma. Inhaled corticosteroids are the most widely studied and recommended drugs in this class. Leukotriene modifiers are effective but less so than inhaled corticosteroids.

**Corticosteroids**

*Inhaled corticosteroids* are the mainstay of treatment for patients with chronic persistent asthma (**Evidence A**). The inhaled route is preferred because delivery direct to the lungs permits the use of lower doses. The equivalent effective doses of currently available inhaled corticosteroid preparations for prescription in asthma are compared to 200  $\mu\text{g}$  beclomethasone dipropionate in Table 4. Through its anti-inflammatory effects, inhaled corticosteroids reduce airway inflammation, decrease bronchial hyperresponsiveness and improve asthma control. In addition, they may modify airway remodelling and prevent an accelerated decline in lung function. Their long-term use in adequate doses has been shown to decrease exacerbations and mortality.

Systemic absorption of inhaled corticosteroids arises from oropharyngeal absorption and to a lesser extent from drug deposited in the lungs. This may be reduced by the use of a spacer device combined with mouth washing after inhalation (**Evidence A**). The former increases the fraction delivered to the lung (**Evidence A**). Both measures reduce the incidence of local side effects such as dysphonia and oropharyngeal candidiasis.

Inhaled corticosteroids are generally administered twice daily and may be used once daily as well. A low starting dose is 200-500  $\mu\text{g}/\text{day}$  of BDP equivalent and a dose above 1000  $\mu\text{g}/\text{day}$  is considered a high dose. At higher

**Table 4:** Equivalent effective metered doses of inhaled corticosteroids

STERIOD PREPARATION	EQUIVALENT METERED DOSE IN ASTHMA
Beclomethasone dipropionate	250 $\mu\text{g}$
Budesonide	200 $\mu\text{g}$
Fluticasone propionate	100 $\mu\text{g}$
Ciclesonide	80 $\mu\text{g}$

doses, the dose-response curve is relatively flat but the risk of systemic side effects such as skin bruising, cataracts and osteoporosis may be increased. Patients requiring long term use of high dose inhaled corticosteroids should be referred to a specialist for review. Strategies to minimise osteoporosis such as regular exercise, calcium supplementation and hormonal replacement in post-menopausal women should be considered.

A preferred strategy to minimise the dose of corticosteroids and improve control is the combination of long-acting  $\beta_2$  agonists (salmeterol or formoterol) with lower doses of inhaled corticosteroids (**Evidence A**). An alternative is the combination of lower dose inhaled corticosteroids with leukotriene modifiers (**Evidence A**). If these are unavailable, combination with slow-release theophyllines are a weaker alternative (**Evidence B**). Long-acting  $\beta_2$  agonists, leukotriene modifiers and slow-release theophylline must always be used in combination with at least low dose corticosteroids for maintenance treatment of asthma.

*Nebulised corticosteroids* are expensive, require high pressure nebulisers for optimal delivery and are not recommended for routine use in acute and chronic asthma.

*Oral corticosteroids* may be considered in patients with poorly controlled asthma on high doses of inhaled corticosteroids and other controller medications. Long term oral corticosteroids (>7.5mg prednisone/day), whilst relatively inexpensive, are associated with serious systemic side-effects. Such patients should be referred to a specialist for review. Alternate day dosing may reduce side effects (**Evidence D**).

**Leukotriene modifiers**

Leukotriene modifiers have been shown to improve asthma control and exert their effect within days of commencing treatment. They may be used in patients with at least mild persistent asthma as add-on treatment to inhaled corticosteroids (**Evidence A**) and may be of value in patients with aspirin-sensitive asthma. If no benefit is evident after 4 weeks, the leukotriene modifiers should be withdrawn since not all patients respond. Their routine use as monotherapy in asthma in adults is not advised (**Evidence D**).

**Sustained action bronchodilators**

**Long-acting  $\beta_2$  agonists (LABAs)**

Salmeterol and formoterol are LABAs administered twice daily because of their greater than 12 hour duration of action. They are useful for control of nocturnal symptoms and exercise-induced asthma. They are recommended as an addition to low dose inhaled corticosteroids in preference to increasing the dose of inhaled corticosteroids (**Evidence A**). Salmeterol is not suitable for acute relief of asthma symptoms because it has a delayed onset of action and is limited by the ceiling dose of 50  $\mu\text{g}$  BD. Formoterol has a rapid onset



of bronchodilation (within 10-15mins of administration) and has a wide dose range. LABAs should never be used without inhaled corticosteroids in asthma because current evidence suggests an increased risk of deaths if LABAs are used as monotherapy. Some patients may not respond to LABAs. Side effects of these drugs include palpitations and tremor.

**Slow-release (SR) theophyllines**

Most formulations of SR theophyllines have a 12 hour and some a 24 hour duration of action. They are administered orally and have a complementary mode of action to other bronchodilators. Their disadvantages include a narrow therapeutic range, drug interactions and frequent side effects (nausea, vomiting, abdominal pain, gastro-oesophageal reflux, palpitations, insomnia, irritability and seizures). They should not be used as monotherapy. There is no role for oral short-acting theophyllines in chronic asthma.

**RELIEVERS**

These include short-acting inhaled  $\beta_2$  agonists (SABAs) and the anti-cholinergic ipratropium bromide. They should be used on an as needed basis as rescue medication.

**Short-acting  $\beta_2$  agonists (SABAs)**

Short-acting  $\beta_2$  agonists (e.g. salbutamol and fenoterol) provide relief from acute symptoms of asthma and are usually used as 2 puffs as needed (**Evidence A**). With optimal maintenance therapy their use should be rare (less than once a day). The frequency of their use is a measure of asthma control. They are the most important and widely used reliever treatment for asthma.

They may only be used as the sole therapy in mild intermittent asthma where the symptoms are mild and infrequent (<2x/week) and the lung function is normal (PEF > 80% predicted), see Table 2. In chronic persistent asthma they should only be used on an as needed basis as rescue medication. Some patients with severe persistent asthma may need to use short-acting  $\beta_2$  agonists up to 6 times per day. Side effects of  $\beta_2$  agonists include tachycardia, tremor, headache and irritability.

**Anti-cholinergics (ipratropium bromide)**

This drug works by inhibiting vagally-mediated bronchoconstriction and is not the preferred reliever in asthma. It may be used in patients, particularly the elderly, who cannot tolerate  $\beta_2$  agonist side effects. It may also be of value as add-on treatment in patients who do not obtain adequate symptom relief with the short-acting  $\beta_2$  agonists alone (**Evidence B**).

**ADDITIONAL TREATMENT AND OTHER DRUGS**

- Antihistamines are not effective in adult asthma.
- Immunosuppressives including methotrexate are rarely of benefit. Patients considered for this treatment must be referred to a specialist.
- There is little scientific evidence that ionisers, oxygen therapy, acupuncture, homeopathy and exclusion diets are useful in the treatment of asthma. Their prescription is not recommended in this guideline.
- Desensitisation using immunotherapy (including sublingual) is not routinely recommended for asthma. Patients with refractory asthma sensitised to only one allergen such as house dust mite or grass pollen may be referred to a specialist for immunotherapy.
- Nebuliser use in chronic persistent asthma must be actively discouraged. With good inhaler technique assisted by spacer devices, adequate drug delivery via an inhaler is achieved with similar bronchodilatation even in patients with chronic severe asthma and inability to generate large airflow rates. Nebulisers are not a substitute for adequate controller treatment.

**TREATMENT OPTIONS**

All patients should be prescribed inhaled short-acting  $\beta_2$  agonists such as salbutamol; 200  $\mu\text{g}$  (2 puffs) as needed for use as symptom relief for acute asthma symptoms (**Evidence A**). All patients should receive inhaled corticosteroids as baseline asthma treatment except those classified as mild intermittent asthma according to the criteria in Table 2 (**Evidence A**).

**Table 5:** Levels of Asthma Control

CHARACTERISTIC	CONTROLLED (All of the following)	PARTLY CONTROLLED (Any measure present in any week)	UNCONTROLLED
Daytime symptoms	$\leq 2/\text{week}$	$> 2/\text{week}$	3 or more features of partly controlled asthma in any week
Limitation of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for reliever/ rescue treatment	$\leq 2/\text{week}$	$> 2/\text{week}$	
Lung function (PEF/FEV <sub>1</sub> )	Normal	$< 80\%$ predicted or personal best (if known)	1 in any week**
Exacerbations	None	1 or more/year*	

\* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

\*\* By definition, an exacerbation in any week makes that an uncontrolled asthma week.

The dose of corticosteroids and additional treatment is determined by:

1. The severity of asthma
2. The response to treatment

The recommended treatment plan is:

1. Add a LABA if asthma is not well controlled on low dose ICS (**Evidence A**). This option is preferred to doubling the dose of ICS; however, not all patients respond to LABAs. Never use LABAs alone.
2. An alternative is to double the dose of ICS or add leukotriene modifiers (**Evidence A**) or slow-release theophyllines (**Evidence B**)
3. Oral corticosteroids should only be used as maintenance treatment with extreme caution.
4. Referral to a specialist is recommended when asthma is difficult to control (see Section E Additional Notes).

#### D. ACHIEVE AND MONITOR CONTROL

Patients should be reviewed frequently until control is achieved and thereafter less often. A self management plan is recommended for all patients (see Section F of Additional Notes). Asthma control may be assessed using a simplified scheme for recognising controlled, partly controlled, and uncontrolled asthma in a given week as provided in Table 5 (**Evidence D**). An exacerbation is defined as an increase in asthma symptoms requiring a consultation with a health care provider. At each visit the patient should be assessed for adherence and level of asthma control. It is possible to achieve complete control of asthma in most patients and this should be achieved with minimal side effects. Validated measures for assessing clinical control of asthma are the Asthma Control Test (ACT) (<http://www.asthmacontrol.com>) or the Asthma Control Questionnaire (ACQ) (<http://www.qoltech.co.uk/Asthma1.htm>). They are suitable for self-assessments by patients, and provide a reproducible objective measure that may be charted over time.

Patients with poor asthma control should be assessed for the following:

- Reasons for poor adherence and misunderstanding the difference between relievers and controllers
- Poor inhaler technique
- Exposure to trigger factors at home and work
- Presence of gastro-oesophageal acid reflux disease
- Rhinitis and sinusitis
- Use of medications that may aggravate asthma such as aspirin, non-steroidal anti-inflammatory drugs and  $\beta$  blockers
- Other medical conditions (e.g. cardiac disease)

Step up treatment when control is not achieved after attention to the above factors. Step down is recommended when total control is achieved and maintained for at least 3 months. Within a self management plan, well-motivated patients could also be advised to vary treatment according

to PEF and symptom frequency.

Treatment with short courses of oral prednisone should be considered in known or newly diagnosed asthmatics in the following circumstances in order to prevent severe deterioration and to gain rapid control of asthma:

- Symptoms and/or lung function (PEF) progressively deteriorating acutely or over several days and associated with increased use of inhaled rescue medication
- Lack of sustained relief from rescue medication
- Repeated drops in PEF over 1 or more days to below 60% of previous best value
- Frequent night time symptoms
- Requirement for emergency treatment

Recommended procedure for the prescription of a short course of oral prednisone

- Prednisone 30-40mg / day for 7-14 days
- Once daily (morning) dosing
- Stop abruptly after course (there is no need to tail off if used for the recommended duration)
- Inhaled corticosteroids for maintenance treatment should be commenced or continued
- A step-up in maintenance controller treatment is usually indicated
- Patients requiring oral corticosteroids for more than 14 days should be referred to a specialist.

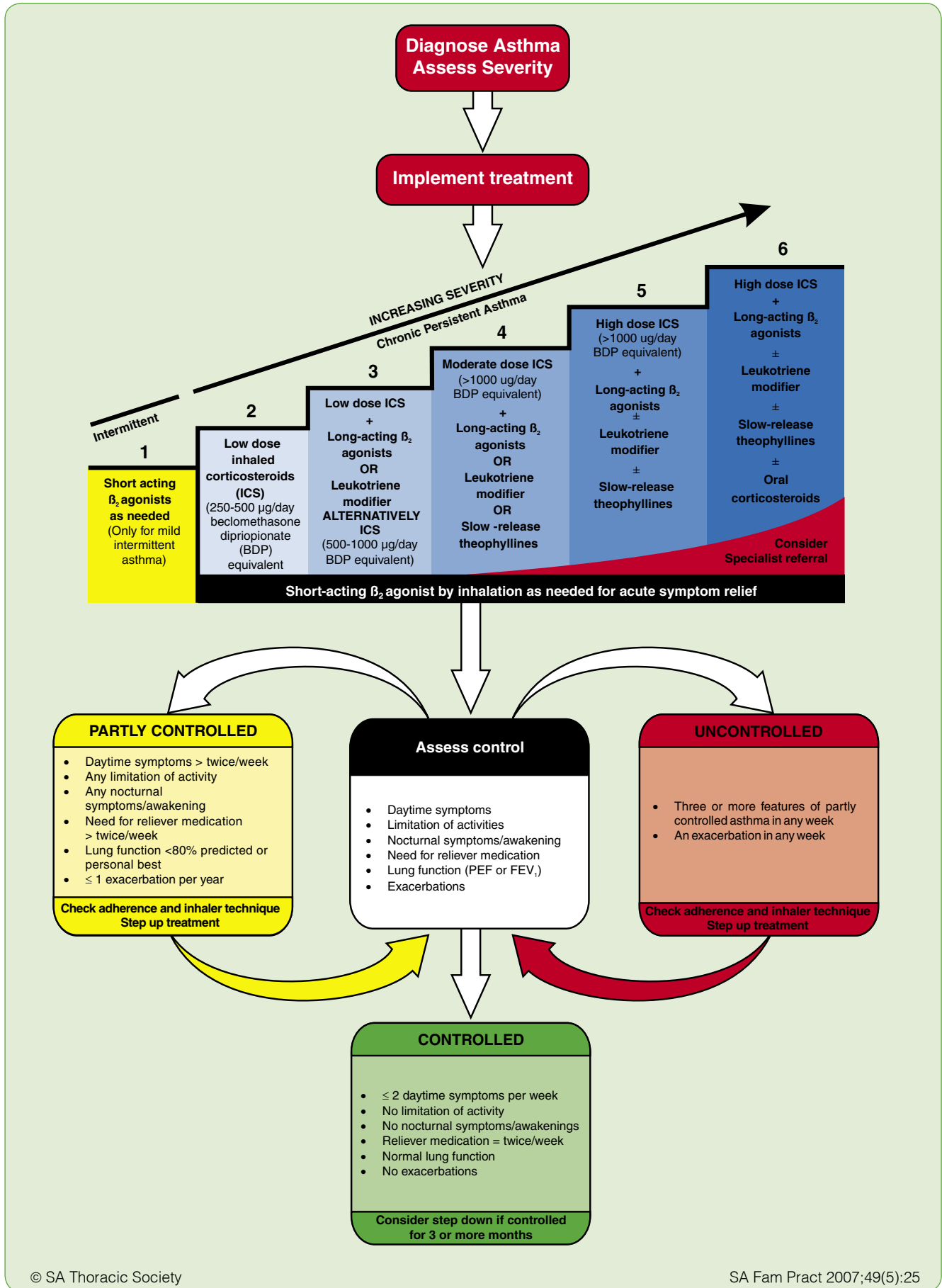
#### ASTHMA EDUCATION

Optimal management of a chronic disease like asthma requires the active participation of patients. To achieve this patients require education about asthma and a detailed written management or action plan (**Evidence A**). A systematic approach is necessary to ensure that all relevant details are included and education should be staged over several visits. Details of a self management plan are presented in Section F of Additional Notes. The use of nurse educators and other specially trained healthcare professionals is cost-effective. Goals of asthma education include:

- An explanation of the nature of asthma and its allergic basis
- A description of the different classes of drugs and their purpose in treatment (i.e. as-needed "relievers" and regular "controllers")
- Advice on prevention strategies (allergen and tobacco smoke avoidance)
- The correct choice and use of inhalers and the opportunity to practice under supervision
- How to recognise worsening asthma
- In some patients, particularly those requiring stabilisation or patients who have had a recent exacerbation or deterioration, the use of a PEF meter and chart
- Introduction to the National Asthma Education Programme (NAEP) the official asthma education programme of the South African Thoracic Society. This provides educational material for the self management of asthma. Contact details are provided in Section G of Additional Notes.

Figure 1 is a summary of the treatment plan.

Figure 1: Algorithm for diagnosis and management of chronic asthma





**ADDITIONAL NOTES**

**A. DIFFERENTIAL DIAGNOSIS OF ASTHMA, WHEEZE AND AIRWAY OBSTRUCTION**

There are many causes of airway obstruction that cause symptoms and signs that may mimic asthma. These are listed in Table 6. Asthma must be distinguished from COPD particularly when a patient develops airway obstruction for the first time in the 5th decade or later. The features that help to differentiate between asthma and COPD are summarised in the Table 7. The SA Thoracic Society has issued guidelines for the diagnosis and management of COPD in a separate guideline statement.

**Table 6:** Causes of airway obstruction

<p><b>WIDESPREAD AIRWAY OBSTRUCTION</b> <i>May present with wheeze.</i></p>	<ul style="list-style-type: none"> <li>• Asthma</li> <li>• COPD</li> <li>• Bronchiolitis</li> <li>• Pulmonary congestion /oedema (left ventricular failure, mitral valve stenosis)</li> </ul>
<p><b>TRACHEAL OBSTRUCTION</b> <i>May present with stridor</i></p>	<ul style="list-style-type: none"> <li>• Extrinsic compression (thyroid, lymph nodes)</li> <li>• Lesions in the lumen or wall (stenosis, stricture, tumour)</li> <li>• Cartilage (tracheomalacia, relapsing polychondritis)</li> </ul>
<p><b>BRONCHIAL OBSTRUCTION</b> <i>May present with localised wheeze</i></p>	<ul style="list-style-type: none"> <li>• Extrinsic compression (lymph nodes)</li> <li>• Lesions arising from the wall (tumour, stenosis, endobronchial TB, sarcoidosis) Luminal lesion (foreign body)</li> </ul>
<p><b>LARYNX</b> <i>May present with wheeze and/or stridor</i></p>	<ul style="list-style-type: none"> <li>• Vocal cord dysfunction</li> <li>• Tumours</li> </ul>

**B. DIFFERENTIATING ASTHMA FROM COPD**

**Table 7:** Differentiating features between asthma and COPD

Features suggesting asthma	Features suggesting COPD
Young age of onset	Long history of smoking
Presence of atopy and/or allergic rhinitis	Usually non-atopic
Diurnal and/or day to day and seasonal variation in symptoms and lung function	Insidious onset of symptoms and persistent dyspnoea Slow progression of symptoms
Often normal examination and normal/near normal spirometry while in a stable state	Hyperinflation and abnormal spirometry while in a stable state. Progressive deterioration in lung function over time
Marked improvement after bronchodilator and/or 2 week trial of systemic corticosteroids*.	Poor response to bronchodilator and/or 2 week trial of systemic corticosteroids

\*>12% and 200ml improvement in FEV1 or 20% in PEF

**C. ROUTES OF ADMINISTRATION OF ASTHMA DRUGS INHALED, ORAL or PARENTERAL**

Asthma treatment for adults can be administered in different ways: inhaled, orally or parenterally (by subcutaneous, intramuscular, or intravenous injection). The major advantage of inhaled therapy is that drugs are delivered directly into the airways, producing higher local concentrations with significantly less risk of systemic side effects. Inhaled medications for asthma are available as pressurised metered-dose inhalers (pMDIs), breath-actuated MDIs, dry powder inhalers (DPIs), soft mist inhalers, and nebulisers (rarely indicated for the treatment of chronic asthma in adults).

Inhaler devices differ in their efficiency of drug delivery to the lower respiratory tract, depending on the form of the device, formulation of medication, particle size, velocity of the aerosol cloud or plume (where applicable), and ease with which the device can be used by the majority of patients. It requires training and skill to coordinate activation of the pMDI with inhalation, and a breath-actuated MDI may be helpful for patients who have difficulty with this. Most patients make mistakes with a pMDI alone. They are less likely to do so if they also use a large volume (500 ml) spacer or holding chamber to improve drug delivery, increase lung deposition, and reduce local and systemic side effects. The drug should be given by repeated single activations of the MDI into the spacer, each followed by inhalation (normal/tidal breathing is as effective as single deep breaths). There should be minimal delay between pMDI activation and inhalation. The spacer should be compatible with the pMDI being used. Spacers should be cleaned monthly (washed in detergent and allowed to air dry) and ideally should be replaced at least every year.

Dry powder inhalers are generally easier to use, but they require a minimal inspiratory flow rate which may be difficult for some patients. A pMDI + spacer is as effective as a DPI (**Evidence A**). Some patients may prefer a DPI or prefer not to carry a large volume spacer. Choice of delivery device should be based on correct technique and patient preference. The patient should have their inhaler technique assessed, ideally by a specifically trained health care worker. An inhaler device should be prescribed after patients have received training in its use and have demonstrated satisfactory technique (**Evidence B**). Their inhaler technique should be continually reassessed as part of a structured clinical review (see Section F Asthma Education). In mild and moderate exacerbations of asthma, a pMDI + spacer is at least as good as a nebuliser in adults and children from the age of two (**Evidence A**). DPIs are not currently recommended for acute asthma (**Evidence D**).

CFC inhaler devices are being phased out due to the impact of CFCs upon the atmospheric ozone layer, and are being replaced by HFA devices. For pMDIs containing bronchodilators, the switch from CFC to HFA inhalers does not result in a change in efficacy at the same nominal

dose. However, for some glucocorticosteroids, the HFA formulations provide an aerosol of smaller particle size that results in less oral deposition (with associated reduction in oral side effects), and correspondingly greater lung deposition. A spacer is thus only necessary with HFA inhalers if coordination is poor. This may result in greater efficacy at equivalent ex-actuator doses, but also greater systemic exposure and risk of side effects. Information on various inhaler devices available can be found on the GINA Website (<http://www.ginasthma.org>).

#### D. SPECIAL CLINICAL CIRCUMSTANCES

There are several clinical circumstances where special precautions and adjustments to asthma management and treatment may be required. These are summarised as follows:

##### Pregnancy

Ideally pregnancy should be planned and optimal control achieved prior to conception. The effect of pregnancy is unpredictable: asthma control may remain the same, deteriorate or improve and may vary in different trimesters in successive pregnancies. Current evidence suggests that corticosteroids,  $\beta_2$  agonists and theophyllines are safe in pregnancy. New drugs for which safety data in pregnancy are not available should be avoided. It is essential that asthma should be optimally controlled during pregnancy through the use of appropriate doses of inhaled corticosteroids, which have been shown to decrease exacerbations. Acute exacerbations should be managed very actively to prevent foetal damage. Poor control of asthma is much more dangerous to both the mother and foetus than any asthma drug.

##### Menstruation

Pre-menstrual exacerbations of asthma are common. The mechanism is not well understood. When severe they may require an increase in the dose of inhaled corticosteroids or a low dose of oral prednisone for 2-3 days commencing 1-2 days before menstruation.

##### Exercise

Exercise-induced asthma (EIA) may occur as an isolated symptom but is usually an indication of sub-optimal asthma control. The preferred treatment is the use of short-acting inhaled  $\beta_2$  agonists 15-20 mins before exercise. Long-acting  $\beta_2$  agonists, leukotriene modifiers and SR theophyllines may protect against EIA for several hours after dosing.

##### Elderly patients

Asthma occurs in the elderly and is frequently overlooked or misdiagnosed. The elderly are more susceptible to adverse effects of drugs. SR theophyllines should be used with care because of their narrow therapeutic range and side effects. The elderly are also especially prone to the

side effects of corticosteroids such as osteoporosis, cataracts, glucose intolerance, hypertension and fluid retention.

##### Nocturnal asthma

Occasionally nocturnal symptoms are the sole manifestation of asthma and may be associated with marked falls in the PEF (50% or more). However, nocturnal symptoms are usually an important indicator of poor control and may signal the onset of impending severe deterioration. Long-acting  $\beta_2$  agonists and SR theophylline provide an additional benefit to that of anti-inflammatory therapy in controlling nocturnal symptoms. Sometimes a short course of oral corticosteroids is indicated.

##### Cardiac disease and hypertension

Fluid retention and hypokalaemia induced by corticosteroids and high doses of  $\beta_2$  agonists may occasionally be a problem in asthma with associated cardiac disease. Pulmonary congestion may manifest with wheezing and may be misdiagnosed as asthma particularly in patients with mitral stenosis and in the elderly.  $\beta$  blockers are contraindicated in asthma.

##### Diabetes mellitus

Particular caution is required when prescribing oral corticosteroids. Inhaled corticosteroids are safe and have no significant effect on glycaemic control.

##### Pulmonary tuberculosis

In patients who have had tuberculosis or evidence of healed tuberculosis on chest radiographs, chemoprophylaxis with isoniazid is not recommended whilst on inhaled or short course of oral corticosteroids as the risk of reactivation has not been shown to be increased.

##### Gastro-oesophageal acid reflux

Acid reflux may aggravate asthma and should be considered in patients with difficult asthma and in those with symptoms of acid reflux. The acid reflux may be asymptomatic.

##### Rhinitis and sinusitis

These may aggravate asthma and should be considered in patients with difficult asthma even in the absence of specific symptoms.

#### E. OCCUPATIONAL ASTHMA

This should be considered in every patient who develops asthma in adulthood. It requires systematic enquiry into all work exposures.

It is important to familiarise oneself with the common agents and jobs/industries that are known to cause occupational asthma and some of these are listed in Table 8

**Table 8:** Causative agents and jobs/industries associated with occupational asthma

Industry/Job type	Causative Agent/s
Animal handlers (labs./vets.)	Animals, formaldehyde
Bakeries, grain mills, farms	Flour, storage mites, fungi, insects, animal matter, amylase
Detergent manufacture	Proteolytic enzymes
Food processing	Sulphites, prawns, coffee beans, soya bean
Foundries	Resins, isocyanates
Furniture, cabinet makers, sawmills	Wood dust, formaldehyde, resins
Hospital and medical laboratories	Formaldehyde, ethylene oxide, enzymes, latex
Metal refining, plating, welding, turning, grinding, sharpening	Platinum, chrome, nickel, mineral oils, cobalt (hard metal)
Pharmaceutical manufacture, mixing	Penicillins, proteolytic enzymes
Photography	Ethylene diamine
Plastics or foam manufacture	Isocyanates, anhydrides, epoxy resins
Printing	Vegetable gums, acrylates, isocyanates
Shoe industry	Glues (acrylates), resins
Soldering	Colophony flux
Spray painting or varnishing	Isocyanates

**F. WHEN TO REFER TO A SPECIALIST**

**Table 9:** When to refer patients to a specialist/pulmonologist

<p><b>A. DIFFICULTY WITH DIAGNOSIS</b></p> <ul style="list-style-type: none"> <li>• Patients receiving multiple courses of antibiotics</li> <li>• Possibility of COPD</li> <li>• Asthma for the first time after the age of 60 years</li> <li>• Suspected vocal cord dysfunction</li> </ul>
<p><b>B. SUSPECTED OCCUPATIONAL ASTHMA</b></p>
<p><b>C. MANAGEMENT PROBLEMS</b></p> <ul style="list-style-type: none"> <li>• Brittle asthma</li> <li>• Recurrent exacerbations &gt;2 per month</li> <li>• Recent discharge following admission for severe exacerbation</li> <li>• Oral corticosteroid dependence</li> <li>• Poor control despite intensive treatment</li> <li>• Pregnancy</li> <li>• Co-existing significant medical illnesses like thyroid disease, collagen vascular disease, peptic ulcer, cardiac failure</li> <li>• Frequent school or work absenteeism</li> <li>• Significant corticosteroid side effects</li> <li>• Consideration for immunosuppressive treatment or desensitisation</li> <li>• Consideration for disability grant or medical boarding for asthma</li> </ul>

**G. ASTHMA EDUCATION AND SELF MANAGEMENT (ACTION) PLANS**

The effective management of asthma requires the development of a partnership between the person with asthma and his or her health care professional. The aim of this partnership is to enable patients with asthma to gain the knowledge, confidence, and skills to assume a major role

in the management of their asthma. The partnership is formed and strengthened as patients and their health care professionals discuss and agree on the goals of treatment, develop a personalised, written self management action plan including self-monitoring, and periodically review the patient's treatment and level of asthma control. The ability or willingness of patients to take responsibility varies and thus the information and skills training required by each patient will differ. All require certain core information and skills, but most education must be personalised. Action plans are one of the most effective interventions available in asthma for both adults and children and can be issued by any health care worker and used in all health care environments (especially in secondary care with moderate to severe disease, and those who have had recent exacerbations **(Evidence A)**. They may be based on symptoms and/or peak flows (depending on age and ability). The use of a personalised written asthma action plan does not improve lung function but does result in fewer days lost from work and school, fewer emergency department visits and hospital admissions, fewer nocturnal symptoms, less use of rescue medication and better quality of life.

A systematic approach is necessary to ensure that all relevant details are included and education should be staged over several visits. The use of nurse educators and other specially trained healthcare professionals is cost-effective.

**Goals of asthma education include:**

- An explanation of the nature of asthma and its allergic basis
- A description of the different classes of drugs and their purpose in treatment ( i.e. as-needed “relievers” and regular “controllers”)
- Advice on preventative strategies (allergen and tobacco smoke avoidance)
- The correct choice and use of inhalers and the opportunity to practice under supervision
- Emphasis on the importance of regular follow-up and when to request earlier review
- How to recognise worsening asthma
- How to recognise potential side-effects of drugs

**Key components of a self-management plan:**

- The use of a *PEF meter and chart*, particularly in those requiring stabilisation or patients who have had a recent exacerbation or deterioration,
- Realistic goals of treatment in terms of symptom relief and/or PEF
- Advice on *how to recognise changes in the asthma* (via symptoms and/or peak flow rates) and when to make adjustments to treatment according to a predetermined schedule
- *Written instructions on treatment* which include the class, name, strength, dose and frequency of each of the asthma medications prescribed
- Instruction on when and *how to initiate short courses of oral prednisone*
- Details on *when and how to obtain access to medical care in emergencies*
- Arrangements for a Medic-Alert for patients on high dose inhaled or oral corticosteroids, known drug hypersensitivities (like aspirin and penicillin) and brittle asthma

Patients should be introduced to the National Asthma Education Programme (NAEP), the official asthma education programme of the South African Thoracic Society, which provides free educational material and action plans for the self-management of asthma. Their contact details are: National Asthma Education Programme (South Africa) - <http://www.asthma.co.za>, PO Box 72128 Parkview 2122, Fax: 011 678 3069, Tel: 011 643 2755, email: [naepr@netactive.co.za](mailto:naepr@netactive.co.za).

Other sites offering educational material include:

- Allergy Society of South Africa (ALLSA) <http://www.allergysa.org>
- The Global Initiative for Asthma <http://www.ginasthma.com>
- National Asthma Campaign (UK) [www.asthma.org.uk](http://www.asthma.org.uk)
- National Heart, Lung and Blood Institute (US) [www.nhlbi.nih.gov/](http://www.nhlbi.nih.gov/)
- Medic Alert: (021) 425 7328

## H. LEVELS OF EVIDENCE FOR ASTHMA MANAGEMENT

**Table 10:** Description of Levels of Evidence

Evidence Category	Sources of Evidence	Definition
A	Randomised controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomised controlled trials (RCTs). Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Non-randomised trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

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