KEY MESSAGES

• Engage the patient as a willing partner – encourage self-management plans.

• Use asthma therapy to gain ‘asthma control’.

• Adopt a stepwise approach to asthma therapy.

• Do not skip steps.

• At all steps ensure good education, compliance & inhaler technique.

• STEP UP to gain & maintain control.

• STEP DOWN if well controlled.

• If asthma is not controlled look for a reason! Is the diagnosis secure? Characterise asthma – ask ‘what is driving this patient’s asthma?’ Consider comorbidities & treat.

• STEP 1:
  Start with a short-acting β-agonist when needed (anticholinergics are not usually indicated in asthma).

• STEP 2:
  ✓ Add in low dose inhaled steroid. Prescribe CFC-free Beclometasone (BDP) by brand (Qvar or Clenil Modulite) to avoid confusion.
  ✓ Ultrafine particle steroids (QVAR) should be first line choice
  ✓ If using Qvar, prescribe at ½ dose of other BDP preparations.
  ✓ Clenil is dose equivalent to CFC-BDP.
  ✓ Never use long acting β-agonist (LABA) or leukotriene antagonist (LTRA) as monotherapy.

• STEP 3:
  ✓ Consider choices of add-on therapy (LABA or LTRA) to inhaled steroid.
  ✓ Tailor choice to patient.
  ✓ Montelukast is 1st line LTRA.
  ✓ Formoterol is 1st line LABA.
  ✓ In order to prevent LABA monotherapy, prescribe in combination with inhaled corticosteroid.
  ✓ Consider using Symbicort or Fostair as ‘Single Inhaler as Maintenance & Reliever’ if deemed appropriate.
  ✓ If not controlled at step 3 refer to a Specialist.

• STEPS 4 & 5:
  Patient care should be supervised by a Specialist.

• EXACERBATIONS:
  ✓ After any exacerbation ask ‘why has this patient lost asthma control?’
✓ Ensure that all patients are on inhaled steroid post exacerbation.
✓ Follow-up patients post exacerbation to ensure ‘control’ regained.

INTRODUCTION

Asthma prevalence in the United Kingdom showed a steady increase over the final decades of the 20th Century and it has only recently begun to plateau. It is estimated that there are just over 5 million asthmatics in the UK today. The direct health economic impact of this common disease through healthcare needs is considerable. There is also a considerable unappreciated societal burden created by associated disability, lost working days and impaired schooling. Recent data from Asthma UK and the British Thoracic Society shows that:

- 5.4 million people in the UK currently receive treatment for asthma which accounts for 1 in 12 adults (4.3 million) and 1 in 11 children (1.1 million)
- There were 1,143 deaths from asthma in the UK in 2010 (up from 2009).
- In 2008-09 there were 79,794 UK asthma related hospital admissions of which 30,740 were children aged 14 or under.
- It is estimated that 75% asthma admissions are potentially preventable.
- UK Asthma related health expenditure is estimated at £1 billion/year.
- 33% of asthma admissions in 2011 were in current smokers
- It is estimated that ‘difficult to treat’ disease accounts for >80% of UK asthma related health expenditure (direct and indirect costs).

This Guideline offers a structured approach for the care of adults (from the age of 17 onward) with asthma covering the spectrum of Primary and Secondary Care within our locality, placing expert opinion plus National (BTS/ NICE/SIGN) and International (Global Initiative for Asthma (GINA)) recommendations in a local context.

The aim of this Guideline is to ultimately achieve better management of asthma in our Community. To achieve this goal the notion of establishing ‘asthma control’ is strongly emphasised, as outlined by the GINA 2012 Update.

The Guideline provides a core diagnostic pathway. It goes on to explain the concept of assessing asthma control, treating to establish control and monitoring to maintain control. The importance of ‘stepping down’ therapy when stable is described.

A treatment algorithm is defined that allows a logical approach to asthma management that can be individually tailored to the patients’ disease. In particular, potential strategies at Step 3 are described in detail. Concepts such as ‘Single inhaler as Maintenance & Reliever Therapy’ (eg. Symbicort SMART & Fostair MART) and ‘One Airway-One Disease’ are explained. A ‘holistic’ approach that looks beyond ‘just asthma’ is encouraged and explained. Emphasis on self-management is made, including ‘asthma action plans’, to facilitate a successful patient-carer relationship. The Guideline goes on to provide guidance on management of acute exacerbations. Information on costs of therapy is also provided. Finally a list of useful contacts and learning resources (BTS, NICE, GINA) are included at the end of the document.
We hope that this document proves a useful tool to improve the experience of the local asthma patient. A revision will be undertaken in 2016.
ADULT ASTHMA GUIDELINE

DIAGNOSIS & INVESTIGATIONS

‘Asthma is a chronic inflammatory disorder of the airways. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning.’

The diagnosis of asthma is a clinical one, often made problematic by the lack of a simple or clear definition of the disease. It is important to remember that no single test can diagnose asthma. A secure diagnosis is based upon the principles of a thorough history, a relevant physical examination of the chest and nose, and performing relevant tests as directed by the individual patients’ presentation.

Important steps in the initial diagnosis of asthma are outlined in the table below.

The differential diagnosis of asthma (see below) is wide and consideration should be given to a variety of conditions depending upon individual circumstances. More than one condition may co-exist within the same individual.

**In situations of diagnostic doubt early specialist review is encouraged.**

**Differential Diagnoses:**

- COPD
- Bronchiectasis
- Cystic Fibrosis
- Tumour
- Foreign body
- Interstitial lung disease
- Pulmonary emboli
- Aspiration
- Vocal cord dysfunction
- Hyperventilation syndrome
- Cardiac disease
- Psychological morbidity
- Obesity / deconditioning
- Non-adherence

**Asthma v COPD:**

The differentiation of asthma from Chronic Obstructive Pulmonary Disease (COPD) is important since there are key differences in therapeutic approaches to these common airway diseases.

COPD is rare below the age of 35 years and in the absence of a smoking history, so be wary of making that diagnosis in those circumstances. COPD is usually associated with chronic, generally progressive symptoms as opposed to the characteristically variable pattern seen most commonly in asthma. Furthermore asthma often occurs in the setting of allergic comorbidities (eg rhinitis) and asthmatic family history.

Objective tests such as Peak Expiratory Flow monitoring or spirometry with bronchodilator or corticosteroid reversibility can help by demonstrating fixed airflow
obstruction (COPD) or variability/reversibility (asthma). Finally it should be noted that COPD and asthma can coexist in the same patient.
## SYMPTOMS

Episodic/variable:
- Wheeze
- Breathlessness
- Chest tightness
- Cough
- Mucus production

## SIGNS

- None (common)
- Wheeze – diffuse, bilateral, expiratory (+/- inspiratory)
- Tachypnoea
- Nasal disease

### Other Important Information:

- Personal or family history of asthma/atopy (eczema, rhinitis, food allergy).
- Recognised triggers – pollens, dust, animals, foods or additives (salicylates / sulphites), medications, exercise, viral infections, chemicals, irritants.
- History of symptom worsening with aspirin/NSAIDs/ ß-blockers.
- Occupation.
- Smoking history.

### Objective Measurements

- > 20% diurnal variation on ≥ 3 days in a week for 2 weeks on Peak Expiratory Flow (PEF) diary.
- $\text{FEV}_1 \geq 15\%$ (and 200 ml) increase after short acting ß-agonist (eg salbutamol 400 micrograms by pMDI/spacer or 2.5 milligrams by nebuliser).
- $\text{FEV}_1 \geq 15\%$ (and 200 ml) increase after 14 DAY Prednisolone trial (30milligrams/day).
- $\text{FEV}_1 \leq$
<table>
<thead>
<tr>
<th><strong>Indications for Specialist Opinion:</strong></th>
<th><strong>Potentially helpful Specialist Tests:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diagnostic doubt</td>
<td>• Chest x-ray</td>
</tr>
<tr>
<td>• Poor treatment response</td>
<td>• Full pulmonary function tests</td>
</tr>
<tr>
<td>• STEP 4 of asthma therapy</td>
<td>• Full blood count</td>
</tr>
<tr>
<td>• Unexpected clinical findings (eg crackles, clubbing, cyanosis, heart failure)</td>
<td>• Total IgE</td>
</tr>
<tr>
<td>• Spirometry/PEF don’t match clinical picture</td>
<td>• Skin prick test to common aeroallergens</td>
</tr>
<tr>
<td>• Suspected occupational asthma</td>
<td>• Specific IgE to Aspergillus</td>
</tr>
<tr>
<td>• Persistent breathlessness (not episodic or without wheeze)</td>
<td>• Aspergillus precipitins</td>
</tr>
<tr>
<td>• Unilateral or fixed wheeze</td>
<td>• Immunoglobulins</td>
</tr>
<tr>
<td>• Stridor</td>
<td>• Alpha-1-antitrypsin levels</td>
</tr>
<tr>
<td>• Persistent chest pain</td>
<td>• ANCA</td>
</tr>
<tr>
<td>• Weight loss</td>
<td>• Induced sputum for differential cell count / fungal stain</td>
</tr>
<tr>
<td>• Persistent cough/ sputum</td>
<td>• HRCT Chest</td>
</tr>
<tr>
<td>• Non-resolving pneumonia</td>
<td>• Histamine bronchial challenge</td>
</tr>
<tr>
<td></td>
<td>• Exhaled nitric oxide</td>
</tr>
<tr>
<td></td>
<td>• Bronchoscopy plus biopsy/lavage</td>
</tr>
</tbody>
</table>
THE CONCEPT OF CONTROL

The goal of asthma management strategy is to establish and maintain disease control using the lowest possible dose of medication. Central to this aim is a good patient-carer relationship that engages the patient as a willing and knowledgeable partner. Opportunities to enhance patients understanding of asthma should always be taken.

In most cases asthma control can be achieved using conventional therapy under the guidance of a multidisciplinary team of healthcare professionals. To realise that aim there needs to be a continual process that includes assessment of control, applies appropriate therapy to gain control and finally encourages monitoring (by patient and healthcare professional) to maintain control at lowest effective doses of therapy.

Defining Asthma Control

Asthma control can be defined as ‘Controlled’, ‘Partially Controlled’ or ‘Uncontrolled’ as outlined in the table below.

<table>
<thead>
<tr>
<th></th>
<th>CONTROLLED (All of the following)</th>
<th>PARTIALLY CONTROLLED (Any measure present in any week)</th>
<th>UNCONTROLLED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daytime Symptoms</strong></td>
<td>None (twice or less weekly)</td>
<td>More than twice weekly</td>
<td></td>
</tr>
<tr>
<td><strong>Limitation of activity</strong></td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td><strong>Nocturnal Symptoms</strong></td>
<td>None</td>
<td>Any</td>
<td>3 or more features of partly controlled asthma present in any week.</td>
</tr>
<tr>
<td><strong>Reliever medication</strong></td>
<td>None (twice or less weekly)</td>
<td>More than twice weekly</td>
<td></td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>Normal</td>
<td>&lt;80% personal best or predicted</td>
<td></td>
</tr>
<tr>
<td><strong>Exacerbation</strong></td>
<td>None</td>
<td>Any in past year</td>
<td>Any in past week</td>
</tr>
</tbody>
</table>

**ACTION**

<table>
<thead>
<tr>
<th></th>
<th>MAINTAIN CONTROL &amp; FIND LOWEST CONTROLLING STEP</th>
<th>CONSIDER STEPPING UP TO GAIN CONTROL</th>
<th>STEP UP UNTIL CONTROLLED &amp; TREAT ANY EXACERBATION</th>
</tr>
</thead>
</table>

The patient should be actively engaged in monitoring their asthma control so placing them ‘in control’ of their disease. A simple questionnaire can aid that process, ideally as part of a Written Asthma Action Plan (see later). An example of a simple asthma control questionnaire is given below, and should be used to assess asthma control.

**Asthma Control Questionnaire:**

1. Has your asthma awakened you at night?
2. Have you needed more reliever medications than usual?
3. Have you required urgent medical review?
4. Has your peak flow been below your personal best?
5. Are you participating in your usual activities?

**Loss of asthma control should prompt a search as to why that has happened.**

**Treating to Achieve Control:**

A stepwise approach to asthma management is recommended using a 5 Step Treatment Strategy (See Algorithm). The aim is to control symptoms by controlling underlying airway inflammation.

In treatment naïve cases with only intermittent symptoms, treatment should be begun with as needed reliever only (Step 1). In treatment naïve cases with persistently symptomatic asthma, therapy should commence with regular controller therapy in the form of inhaled glucocorticosteroid (ICS - Step 2). If control remains suboptimal then treatment should be ‘stepped up’ and reviewed repeatedly to assess for achievement of control (Steps 3-5). At least 2 months should be allowed to judge efficacy of any new controller therapy (longer if more severe disease).

**Starting therapy straight at Step 3 is only indicated in severe uncontrolled asthma.**

If stable control is established for 3-6 months, ‘stepping down’ should always be considered with continued assessment of control.

**The nature of and reasons for, treatment changes should always be clearly explained to the patient.**

**Monitoring to Maintain Control & Stepping Down:**

When asthma is controlled, ongoing monitoring is essential to maintain control and establish the lowest ‘step’ and dose of treatment needed, maximising safety and minimising cost. However, asthma is a variable disease, and therapy will need to be periodically adjusted in response to loss of control.

Monitoring should be by both healthcare professional and patients using tools including written management plans. There is limited data on ‘stepping down’ strategies and further research is required in this area. However as outlined in GINA 2012;
• When ICS are used alone in medium-high dose, a 50% reduction in dose can be attempted at 3 monthly intervals.
• When asthma is controlled with a combination of ICS and long acting β-agonist (LABA), the preferred approach is to initially reduce the ICS dose by 50% whilst continuing the LABA. If controlled, further reduction in ICS dose until low-dose is reached can be tried, followed by withdrawal of LABA if still stable.
• Self titration using single inhaler as Maintenance And Reliever Treatment (MART) is a useful approach, and has been shown to reduce overall steroid dose but maintain control
• When asthma is controlled by ICS plus controllers other than LABAs, the ICS dose should be reduced by 50% until low-dose is achieved. If still stable then withdrawal of the controller can be attempted.
• Controller treatment can be discontinued if the asthma is controlled on low-dose ICS with no recurrence of symptoms for more than 12 months.
AT ALL STEPS and BEFORE MOVING UP A STEP

- Ensure good inhaler technique, compliance and patient education
- Actively encourage smoking cessation and physical activity
- Advise on allergen avoidance where relevant, offer annual Influenza vaccination

### STEP 1

**As needed short acting β-agonist**

As needed short acting β-agonist (e.g., Salbutamol 200 micrograms)

PLUS REGULAR CONTROLLER THERAPY

STEP UP TO GAIN & MAINTAIN CONTROL

ONCE CONTROLLED AIM TO STEP DOWN AS TOLERATED

### STEP 2

**LOW-DOSE INHALED STEROID (ICS)** 200-500

CHOOSE A 2 MONTH TRIAL OF:

SPECIALIST REVIEW SUGGESTED & USE:

UNDER SPECIALIST GUIDANCE CONSIDER ADDITION OF:
## Adul t A s t h ma G u i d e l i n e

### Options

<table>
<thead>
<tr>
<th>200-500 micrograms daily</th>
<th>Low-dose ICS + either</th>
<th>Medium-high dose ICS 500-2000 micrograms daily BDP equivalent</th>
<th>Oral corticosteroid Maintenance Therapy (lowest controlling dose, assess bone mineral density) AND/OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Beclometasone (BDP) equivalent</td>
<td>Long-acting β-agonist (LABA) OR Leukotriene Receptor Antagonist (LTRA) OR ↑ ICS to medium-dose 500-1000 micrograms daily BDP equivalent (Try Qvar if not already used)</td>
<td>SEQUENTIALLY ADD ONE OR MORE OF: LABA OR LTRA OR Sustained release theophyllines OR Long acting anticholinergic (Tiotropium)</td>
<td>Oral steroid sparing agents AND/OR Disease modifying injection therapies AND/OR Nebuliser Therapy AND/OR Other advanced therapy (eg thermoplasty, macrolides)</td>
</tr>
<tr>
<td>Prescribe by brand:</td>
<td></td>
<td>See Step 3 of choices</td>
<td>Review responses at 2 month intervals to assess efficacy &amp; control</td>
</tr>
<tr>
<td>1st ultrafine particle (HFA) preparation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qvar (ultrafine HFA) use at half CFC-BDP dose, ie 100 – 200 µg daily.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd normal particle size preparation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clenil Modulite (CFC-free BDP)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Consider & Treat if Present at Any Stage:
- Rhinitis, Gastro-Oesophageal Reflux, Bronchiectasis, Obstructive Sleep Apnoea, Dysfunctional Breathing, Psychological Dysfunction

Treatment changes should be made on a trial basis with review of efficacy
### STEP 3 – CONSIDER CHOICE OF;

<table>
<thead>
<tr>
<th>1st</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continued low-dose ICS plus a 2 month add-on trial of EITHER:</strong></td>
<td><strong>↑ ICS dose</strong></td>
</tr>
</tbody>
</table>

**1**

**Leukotriene Receptor Antagonist (LTRA)**

Eg Montelukast 10 milligrams od

Consider 1 are any of:

- Clinical evidence of rhinitis.
- Strong aeroallergen sensitisation.
- Pronounced exertional symptoms.
- Intolerance to β-agonists.

**AVOID IN PREGNANCY**

<table>
<thead>
<tr>
<th><strong>Long-acting β-agonist (LABA)</strong></th>
<th><strong>↑ ICS to medium-dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Use in a combination device with ICS. Formulary choices; Symbicort, Fostair or Flutiform</td>
<td><strong>500-1000 micrograms</strong> <strong>BDP equivalent daily</strong></td>
</tr>
<tr>
<td>Consider 1 are any of:</td>
<td>(consider ultrafine particle inhalers if not already used eg Qvar)</td>
</tr>
<tr>
<td>• Current or recent exacerbation.</td>
<td>Consider 1</td>
</tr>
<tr>
<td>• Significant lung function variability or reversibility.</td>
<td><strong>Intolerance to β-agonist &amp; LTRA.</strong></td>
</tr>
<tr>
<td>• Intolerance to LTRA’s.</td>
<td><strong>ASSESS RESPONSE:</strong> (\text{control questionnaire})</td>
</tr>
<tr>
<td>• Pregnancy.</td>
<td><strong>IF CLINICAL IMPROVEMENT CONTINUE</strong></td>
</tr>
</tbody>
</table>

**IF NO BETTER GO TO STEP 4.**

**AVOID IN PREGNANCY**

* USE A **!
ADULT ASTHMA GUIDELINE

ASSESS RESPONSE: (control questionnaire)

IF CLINICAL IMPROVEMENT CONTINUE
STOP IF NO BETTER & SWITCH TO LABA

device in initial trial.*

ASSESS RESPONSE: (control questionnaire)

IF CLINICAL IMPROVEMENT CONTINUE
STOP IF NO BETTER & SWITCH TO LTRA

* USE A FORMOTEROL CONTAINING COMBINATION INHALER

Symbicort & Fostair can be used as Maintenance & Reliever to maintain control & aid compliance.

IF ABOVE STRATEGIES FAIL TO ESTABLISH CONTROL PROCEED TO STEP 4
Achieving control is the cornerstone of asthma management. In persistent disease this is achieved by the early use of anti-inflammatory therapy to tackle the underlying pathophysiology of this disease. **Inhaled glucocorticosteroids therefore have a crucial early role.** Non-pharmacological measures including patient education, smoking cessation, annual influenza vaccination, allergen avoidance, psychological support and physiotherapy input may also play an important role.

The Wessex Adult Asthma Algorithm offers an evidence based strategy to manage asthma. Further details of the Algorithm are given below.

**i. General Measures:**

- Check that the patient can use the inhaler device properly prior to prescription; **recheck** technique at each review.
- A pressurised Meter Dose Inhaler (pMDI) should be prescribed with a spacer device. Volumatic is first choice, however QVAR only fits the Aerochamber.
- Always assess compliance/adherence.
- Provide the patient with a written Asthma Action Plan. These are shown to improve morbidity AND MORTALITY in asthma (see resources section).
- Nebuliser therapy is no more effective than inhaled therapy and should be regarded as a ‘last resort’ option after assessment in Secondary Care.
- Physical activity should always be encouraged – consider ‘Active Options’ in selected cases.
- **Referral for assessment in Secondary Care can occur at any stage but is DEFINITELY ADVISED ONCE THE PATIENT IS INADEQUATELY CONTROLLED AT STEP 3**

**ii. Smoking Cessation:**

Smoking cessation is an important component of asthma therapy. There is clear evidence of reduced efficacy of treatment such as ICS in asthmatics who smoke. Asthmatics may also be at increased risk of developing COPD.

**iii. Allergen avoidance advice:**

Allergen avoidance measures can be helpful in individual cases where atopic sensitisation exists. Such measures are not a substitute for pharmacological therapy. **Single measures are unlikely to be useful in isolation** but some benefit may be obtained through use of multiple measures in individual cases. Allergen avoidance recommendations for house dust mite, pets and pollens are given in Appendix II.

**iv. Drugs: Inhaled Corticosteroids (ICS):**

ICS should be started at low-dose (Step 2) in any partially controlled or uncontrolled steroid naïve asthmatic. **It is especially important to remember this in previously controlled steroid naïve patients recovering from an exacerbation.** In this context low-dose means 200-500 micrograms conventional Beclometasone (BDP) equivalent. Prescribe by brand to avoid confusion.

**Steroid Inhaler Equivalence:**
Chlorofluorocarbon (CFC)-free BDP (eg Clenil), and Budesonide (eg Pulmicort) are dose equivalent in clinical practice. Fluticasone (eg Flixotide) and CFC-free ultrafine BDP (eg Qvar) are effective at half the dose of Clenil and Budesonide.

Ultra-fine Particle ICS:
Lung deposition of ICS to the peripheral airways is improved if the particles of steroid are ‘ultrafine’, as delivered by HFA (hydrofluoroalkane) solution inhalers such as ‘QVAR’. In addition these medications reduce oropharyngeal side effects and allow disease control at a reduced steroid dose. Due to these benefits, we recommend these drugs as first line choice ICS. They should be prescribed by brand at half dose of other BDP forms. Qvar is available at doses of 50 and 100 micrograms strength, which are equivalent to 100, and 200 micrograms of CFC-BDP and Clenil Modulite. Use ultrafine BDP (QVAR) if uncontrolled on alternatives prior to stepping up.

v. Combination Inhalers:
The number and variety of combination inhalers continues to grow, and will expand further over the next few years. Preference should be given to formulary choices which contain a rapid onset LABA (eg Formoterol).
- Symbicort contains Formoterol & Budesonide.
- Fostair contains Formoterol & CFC-free ultrafine BDP.
- Flutiform contains Formoterol and fluticasone.

vi. Single Inhaler as Maintenance & Reliever Therapy (Symbicort SMART or Fostair MART):
The LABA Formoterol is a full β-receptor agonist with a rapid onset of action plus lack of tolerance that enables repeated dosing. This means that it can be used repeatedly to relieve acute bronchoconstriction. Added reliever use of Formoterol/ICS combinations has been shown to reduce severe exacerbation rates, improve symptom control, reduce reliever therapy use and lower overall steroid load. Use of Symbicort (Budesonide/Formoterol) and Fostair (BDP/Formoterol) as both maintenance and reliever therapy has now been licensed in the UK. Guidelines for this technique are:

- Take an extra dose of combination inhaler if symptomatic. If no relief after 10 minutes the patient can repeat up to the maximum dose for each drug. The maximum inhalations per day of Fostair is 8, for Symbicort 200/6 it is 12 inhalations a day. For most patients this will mean they can use 4 reliever puffs of Fostair or 8 of symbicort. If no relief is obtained at that point medical review is needed.

vii. Step 3 of Choices:
At step 3 there are choices of therapy which can be tailored to patient characteristics, or to treatment response. Prior to stepping up, check compliance and inhaler technique. Generally adding in either a leukotriene receptor antagonist (LTRA) or a long acting beta agonist (LABA) is preferable to increasing further the dose of inhaled corticosteroid (ICS), whilst neither LABA or LTRA should be used for monotherapy.
Reasons to try LABA first: recent exacerbations, significant variability in symptoms or peak flow, pregnancy. Use formoterol in a combination device.

Reasons to try LTRA first: co-existent rhinitis, aeroallergen sensitisation or exertional symptoms. Use montelukast 10mg nocte.

If neither LTRA or LABA are tolerated: increase the dose of ICS and consider ultrafine particle steroid if not already used.

**viii. Step 4/5:**

At this stage, specialist assessment is indicated if not already obtained. Any aggravating factors and comorbidities present should be characterised and treated if possible. Once this is done, increase ICS to medium to high dose, and definitely use an ultrafine preparation. Hereafter, sequentially add further control medication or interventions as shown in the table below, attempting to control disease whilst minimising side effects.

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pro-drug inhaled corticosteroids</td>
<td>Ciclesonide</td>
<td>Excellent lung penetration and lack of oral side effects make this ICS preparation useful as additional therapy at step 4/5</td>
</tr>
<tr>
<td></td>
<td>(Alvesco)</td>
<td></td>
</tr>
<tr>
<td>Theophyllines</td>
<td>Eg Phyllocontin</td>
<td>Narrow therapeutic range, multiple interactions and side effects. Check levels at 1 week, if no improvement after 1 month, stop</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Long acting</td>
<td>Tiotropium improves lung function and reduces exacerbation frequency in asthmatics not controlled on ICS/LABA</td>
</tr>
<tr>
<td></td>
<td>(tiotropium)</td>
<td></td>
</tr>
<tr>
<td>Regular antibiotics</td>
<td>Azithromycin</td>
<td>Azithromycin may be useful in neutrophilic asthma not controlled by other treatment. Doxycycline may help in salicylate sensitive asthma where staphylococcus colonisation and toxin production are more common</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td></td>
</tr>
<tr>
<td>Biological therapies</td>
<td>Omalizumab</td>
<td>Now indicated in allergen driven, IgE mediated asthma who need oral steroids more than 4 times per year</td>
</tr>
<tr>
<td></td>
<td>(Xolair)</td>
<td></td>
</tr>
<tr>
<td>Continuous intravenous therapy</td>
<td>terbutaline</td>
<td>Only indicated in ‘brittle’ asthmatics who have had full specialist MDT review</td>
</tr>
<tr>
<td></td>
<td>infusions</td>
<td></td>
</tr>
</tbody>
</table>
Often, however, these therapies can be avoided by optimisation of standard therapy and treatment of comorbidities, as such they should only be offered after specialist multidisciplinary assessment. Specialist management is mandatory for this ‘difficult to treat’ end of the asthma spectrum; we often prefer to consider these patients as having a multifactorial ‘difficult breathing syndrome’ as below.

<table>
<thead>
<tr>
<th>Alternative immunosuppressives</th>
<th>Mycophenolate mofetil</th>
<th>Only indicated in difficult to treat asthmatics who have had full specialist MDT review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway muscle ablation</td>
<td>Bronchial thermoplasty</td>
<td>Only indicated in ‘brittle’ asthmatics who have had full specialist MDT review</td>
</tr>
</tbody>
</table>
THE DIFFICULT BREATHING SYNDROME AND SPECIFIC CONSIDERATIONS IN DIFFICULT ASTHMA

In most asthmatics, steps 1 to 4 of the above management strategy will deliver optimal disease control. However in some patients asthma may prove ‘difficult’ to control. We have developed the concept of the ‘Difficult Breathing Syndrome’ to emphasise the multifactorial nature of difficult to treat asthma.

Often many of the comorbidities detailed below coalesce with ‘difficult’ asthma to generate a multifactorial ‘Difficult Breathing Syndrome’. In order to address the ‘difficult asthma’ each element contributing to the patients difficult breathing syndrome should be addressed. In such cases it is first worth considering:

- **Is it asthma?**
  Consider the wide differential diagnoses above, is it asthma + another disease?
- **If it is asthma, is compliance/adherence good?**
- **If it is asthma, is inhaler technique good?**
- **If it is asthma, are there complicating factors?**
  The following are asthma complicating factors that often contribute to the ‘difficult breathing syndrome’.

The nasal airway: One Airway-One Disease:
Always inspect the nose in a patient with asthma. Co-existent rhinitis is a frequent finding in asthma (‘one airway-one disease’) and treatment may help improve asthma control. LTRAs treat both upper and lower airway inflammation, and can be used with regular antihistamines, nasal steroids, and allergen avoidance measures.

Atopy:
Allergen exposure is a potent trigger in atopic asthma and rhinitis. Skin prick testing should be performed to common aeroallergens in all severe asthmatics.

Salicylate Sensitivity:
Up to 20% of patients with difficult asthma may have salicylate sensitivity. Patients typically have non-atopic ‘difficult’ asthma, rhinitis and nasal polyps and may also have urticaria and angioedema. Dietary salicylates are sufficient to cause problems. Management includes aspirin/NSAID avoidance, LTRAs and salicylate free diets.

Gastro-Oesophageal Reflux Disease (GORD):
GORD is common, and is 3 times more common in severe asthma. Medical therapy and lifestyle measures aimed at acid suppression/ reducing reflux can be helpful.

Drugs:
Certain drugs such as beta-blockers (including topical ocular preparations), NSAIDs and aspirin may worsen asthma control and should be screened for.
Dysfunctional Breathing:
This may be found in up to 40% of asthmatics and management through ‘breathing control training’ can lead to improved symptom control in individual cases. Treatment by a chest physiotherapist is essential to educate and train the patient in this regard.

Vocal Cord Dysfunction:
Vocal cord dysfunction may be present in 20-40% of patients with difficult asthma. A multidisciplinary approach addressing causes and involving a team including speech therapists and physiotherapists carries the best hope of successful treatment.

Psychological Stress:
This is a common finding in severe asthma and also a poor prognostic marker, which may significantly impair disease control. Where present the causes of this should be explored and addressed, through local Increasing Access to Psychological Therapies (IAPT) if appropriate or in conjunction with a clinical psychologist.

Bronchiectasis:
This may be a complicating feature in difficult asthma, either de-novo, in association with fungal disease and atopy (e.g. severe asthma with fungal sensitisation), or point to other diagnoses such as ciliary dyskinesia syndromes (e.g. Primary Ciliary Dyskinesia) or Cystic Fibrosis. Always consider Cystic Fibrosis if a young patients ‘asthma’ is complicated by bronchiectasis, recurrent infections and nasal polyposis.

Obesity:
Obesity is associated with poorly controlled asthma. Measures focussed on weight loss and prevention of deconditioning are central and often improve asthma control.

Obstructive Sleep Apnoea Hypopnoea Syndrome (OSAHS):
OSAHS has been identified as a contributor to frequent exacerbations in patients with difficult asthma. Consider if the patients has difficult asthma and a high BMI, a thick neck, heavy snoring/ witnessed apnoeas or excessive daytime sleepiness. Weight loss is indicated in all cases. OSAHS merits investigation with a sleep study and possible CPAP therapy. In individual cases such treatment has improved asthma control.

Occupational-related disease:
Up to 20% of adult onset asthma may be due to occupational exposure; early diagnosis improves long-term outcomes. Occupational asthma worsens during periods of work and improves when away, particularly for prolonged periods such as holidays. There is often a period of working in the environment without problems before symptoms start (lag period), this may be many years. Asthma and rhinitis often co-exist and the rhinitis may precede the asthma. Specialist review is essential.

MARKERS OF POOR OUTCOME IN ASTHMA
Certain key characteristics hallmark asthmatic patients at risk of fatal or near-fatal asthma and should always be looked for:
ACUTE EXACERBATIONS

Any exacerbation should prompt an assessment of severity, initiation of appropriate acute therapy and consideration of any need to change long-term therapy. An exacerbation should also always prompt the questions, ‘why has this patient lost asthma control’? ‘Can we prevent this next time’?

MANAGEMENT OF ACUTE SEVERE ASTHMA – COMMUNITY

Severity? The presence of ANY parameter defines severity

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathless on</td>
<td>Walking</td>
<td>Talking</td>
<td>Rest</td>
</tr>
<tr>
<td>Talks in</td>
<td>Sentences</td>
<td>Phrases</td>
<td>Words</td>
</tr>
<tr>
<td>Pulse</td>
<td>&lt;100</td>
<td>100-120</td>
<td>&gt;120 or &lt;60</td>
</tr>
<tr>
<td>Resp Rate</td>
<td>&lt;30</td>
<td>&lt;30</td>
<td>&gt;30</td>
</tr>
<tr>
<td>PEF</td>
<td>&gt;80% predicted</td>
<td>60-80%</td>
<td>&lt;60%</td>
</tr>
<tr>
<td>SaO2</td>
<td>&gt;95%</td>
<td>91-95%</td>
<td>&lt;90%</td>
</tr>
</tbody>
</table>

Treatment strategy

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat at home/surgery &amp; assess response to treatment</td>
<td>Consider admission</td>
<td>Admit immediately</td>
<td></td>
</tr>
</tbody>
</table>
Patients who have EVER been intubated / ventilated for asthma, have been hospitalised in last year, who have a history of psychiatric illness or are currently using or recently been given corticosteroids are at high risk of death and should have a low threshold for admission.

<table>
<thead>
<tr>
<th>Salbutamol 2.5 milligrams via oxygen driven nebuliser or as high dose inhaler via spacer.</th>
<th>Oxygen 40-60%. Salbutamol 2.5 - 5 milligrams via oxygen driven nebuliser. Prednisolone 40 mg. Low threshold for admission if ‘high risk’.</th>
<th>Oxygen 40-60%. Salbutamol 2.5 - 5 milligrams &amp; Ipratropium 500 micrograms via oxygen driven nebuliser. Prednisolone 40 mg.</th>
</tr>
</thead>
</table>

• Reassess in 1hr: Admit if no response to initial treatment. Continue nebuliser in ambulance. If improving, continue & step up treatment as per action plan. Complete minimum 7 days of oral steroid.

Ask – why has this patient lost control?

To define severity assess & record:

<table>
<thead>
<tr>
<th>Peak flow (PEF)</th>
<th>Oxygen saturations (SaO2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory examination</td>
<td>Pulse and respiratory rate (RR)</td>
</tr>
</tbody>
</table>
# APPENDIX I - THE DRUG COST TABLE (October 2013)

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>Name</th>
<th>Doses per Device</th>
<th>Cost of Device (Community) (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INHALED SHORT ACTING β-AGONIST</strong></td>
<td>Salbutamol 100mcg Easibreathe</td>
<td>200</td>
<td>6.30</td>
</tr>
<tr>
<td></td>
<td>Salbutamol 100mcg mdi</td>
<td>200</td>
<td>1.46</td>
</tr>
<tr>
<td></td>
<td>Terbutaline 0.5mg Dry powder Inhaler</td>
<td>100</td>
<td>6.92</td>
</tr>
<tr>
<td><strong>NEBULISED SHORT ACTING β-AGONIST</strong></td>
<td>Salbutamol 2.5mg nebulues</td>
<td>20</td>
<td>1.75</td>
</tr>
<tr>
<td></td>
<td>Salbutamol 5mg nebulues</td>
<td>20</td>
<td>2.95</td>
</tr>
<tr>
<td></td>
<td>Terbutaline 5mg / 2ml nebs</td>
<td>20</td>
<td>4.04</td>
</tr>
<tr>
<td><strong>INHALED LONG ACTING β-AGONIST</strong></td>
<td>Salmeterol 25mcg mdi</td>
<td>120</td>
<td>29.26</td>
</tr>
<tr>
<td></td>
<td>Salmeterol 50mcg Accuhaler</td>
<td>60</td>
<td>29.26</td>
</tr>
<tr>
<td></td>
<td>Foradil inhaler 12mcg inhaler</td>
<td>60</td>
<td>23.28</td>
</tr>
<tr>
<td></td>
<td>Oxis 6 turbohaler</td>
<td>60</td>
<td>24.80</td>
</tr>
<tr>
<td></td>
<td>Oxis 12 turbohaler</td>
<td>60</td>
<td>24.80</td>
</tr>
<tr>
<td></td>
<td>Atimos Modulite (Formoterol) 12 mcg mdi</td>
<td>100</td>
<td>30.06</td>
</tr>
<tr>
<td><strong>Leukotriene receptor antagonists</strong></td>
<td>Montelukast tablets 10mg</td>
<td>28</td>
<td>26.97</td>
</tr>
<tr>
<td></td>
<td>Zafirlukast tablets 20mg</td>
<td>56</td>
<td>17.75</td>
</tr>
<tr>
<td><strong>INHALED STEROIDS (small particle cfc free Beclometasone; Qvar)</strong></td>
<td>QVAR 100mcg mdi</td>
<td>200</td>
<td>17.21</td>
</tr>
<tr>
<td></td>
<td>QVAR 100mcg Autohaler</td>
<td>200</td>
<td>17.21</td>
</tr>
<tr>
<td><strong>INHALED STEROIDS (cfc free Beclometasone; Clenil Modulite)</strong></td>
<td>Clenil Modulite 100mcg mdi</td>
<td>200</td>
<td>7.42</td>
</tr>
<tr>
<td>DRUG CLASS</td>
<td>Name</td>
<td>Doses per Device</td>
<td>Cost of Device (Community (£))</td>
</tr>
<tr>
<td>------------</td>
<td>------</td>
<td>------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td><strong>INHALED STEROIDS</strong> <em>(Budesonide)</em></td>
<td>Budesonide 100mcg dry powder</td>
<td>200</td>
<td>11.84</td>
</tr>
<tr>
<td></td>
<td>Budesonide 200mcg dry powder</td>
<td>100</td>
<td>11.84</td>
</tr>
<tr>
<td></td>
<td>Budesonide 400mcg dry powder</td>
<td>50</td>
<td>13.86</td>
</tr>
<tr>
<td><strong>INHALED STEROIDS</strong> <em>(Fluticasone)</em></td>
<td>Fluticasone 125mcg mdi</td>
<td>120</td>
<td>21.26</td>
</tr>
<tr>
<td></td>
<td>Fluticasone 250mcg mdi</td>
<td>120</td>
<td>36.14</td>
</tr>
<tr>
<td></td>
<td>Fluticasone 250mcg Accuhaler</td>
<td>60</td>
<td>21.26</td>
</tr>
<tr>
<td><strong>INHALED STEROIDS</strong> <em>(Ciclesonide)</em></td>
<td>Ciclesonide (Alvesco) 160mcg</td>
<td>60</td>
<td>19.31</td>
</tr>
<tr>
<td><strong>NEBULISED STEROIDS</strong></td>
<td>Budesonide 500mcg/2ml nebs</td>
<td>20</td>
<td>32.00</td>
</tr>
<tr>
<td></td>
<td>Budesonide 1mg/2ml nebs</td>
<td>20</td>
<td>44.64</td>
</tr>
<tr>
<td></td>
<td>Fluticasone 2mg/2ml nebs</td>
<td>10</td>
<td>37.35</td>
</tr>
<tr>
<td><strong>COMBINATION INHALERS</strong> <em>(Budesonide/ formoterol)</em></td>
<td>Symbicort 100/6 Turbohaler</td>
<td>120</td>
<td>33.00</td>
</tr>
<tr>
<td></td>
<td>Symbicort 200/6 Turbohaler</td>
<td>120</td>
<td>38.00</td>
</tr>
<tr>
<td></td>
<td>Symbicort 400/12 Turbohaler</td>
<td>60</td>
<td>38.00</td>
</tr>
<tr>
<td><strong>COMBINATION INHALERS</strong> <em>(Fluticasone / salmeterol)</em></td>
<td>Seretide 100 Accuhaler</td>
<td>60</td>
<td>31.19</td>
</tr>
<tr>
<td></td>
<td>Seretide 125 mdi</td>
<td>120</td>
<td>36.65</td>
</tr>
<tr>
<td></td>
<td>Seretide 250 Accuhaler</td>
<td>60</td>
<td>36.65</td>
</tr>
<tr>
<td></td>
<td>Seretide 250 mdi</td>
<td>120</td>
<td>62.29</td>
</tr>
</tbody>
</table>
These prices are excluding VAT (17.5%) and are based on the direct acquisition cost of the inhaler device / medicinal product in MIMS October 2013.

<table>
<thead>
<tr>
<th></th>
<th>Product</th>
<th>Quantity</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Fluticasone / formoterol)</td>
<td>Seretide 500 Accuhaler</td>
<td>60</td>
<td>40.92</td>
</tr>
<tr>
<td></td>
<td>Flutiform 125</td>
<td>120</td>
<td>29.62</td>
</tr>
<tr>
<td></td>
<td>Flutiform 250</td>
<td>120</td>
<td>45.56</td>
</tr>
<tr>
<td>COMBINATION INHALERS (Beclomethasone (fine particle) / formoterol)</td>
<td>Fostair 100/6</td>
<td>120</td>
<td>29.32</td>
</tr>
</tbody>
</table>
APPENDIX II – ALLERGEN AVOIDANCE MEASURES

House Dust Mite:

Several measures can be considered, though their individual clinical efficacy is limited. Selected individuals may derive some benefit from combinations of;

1. Encase bedding (mattress, duvet and pillows) in mite-proof covers.
2. Hot wash bed linen (55-60 °C).
3. Replace carpets with hard flooring.
4. Use vacuum cleaners with integral HEPA filter and double thickness bags.
5. Hoover the mattress once a fortnight.
6. Damp dusting in the bedroom.
7. Keeping bedroom windows open for a couple of hours a day.

Pets:

Pet allergens are ubiquitous and are seen outside the home in workplaces, schools and on public transport. Several measures can be considered, though their individual clinical efficacy is limited. Selected individuals may derive some benefit from combinations of;

1. Remove pet from the home. Note that even after removal from the home, pet allergen levels may remain elevated for many months. Removal has to be balanced against the potential upset that could result!
2. Keep the pet away from main living areas (e.g. bedrooms).
3. Wash the pet.
4. Replace carpets with hard flooring.
5. Use vacuum cleaners with integral HEPA filter and double thickness bags.

Pollens:

Pollens are impossible to avoid completely. Exposure may be reduced by;

1. Closing doors and windows and remaining indoors when pollen levels are highest (e.g. early mornings and early evenings).
2. Wear sunglasses when pollen levels are high.
3. During the pollen season check the pollen count to guide potential exposure.
APPENDIX III - RESOURCES & KEY REFERENCES

Resources – self management plans

Self management plans are shown to decrease morbidity and mortality from asthma and can be obtained from:
Asthma UK:  http://www.asthma.org.uk/Sites/healthcare-professionals/pages/self-management-materials

Key References:


APPENDIX V - AUTHORS & APPROVALS

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Approvals:
These guidelines have been reviewed and approved by the Southampton, Winchester, Portsmouth, Isle of Wight and Basingstoke Respiratory Groups.