Manchester PCT

Guideline on the Management of Stable Asthma

Developed in line with the **British Guideline on the Management of Asthma** 2003[1] and updated in line with the 2004-2009[2] Updates/Revisions.

Introduction

As healthcare professionals we have a wide variety of drugs and devices available for the treatment of asthma. The following guideline has been developed to help simplify and rationalise treatment selection at each step in the management of asthma.

Pharmacological Management

Please refer to the charts for the stepwise management of asthma, using the chart appropriate for the patient's age.

Aim of asthma management is control of the disease. Control of asthma is defined as:

- no daytime symptoms
- no night-time awakening due to asthma
- no need for rescue medication
- no exacerbations
- no limitations on activity including exercise
- normal lung function (in practical terms FEV_1 and/or PEF>80% predicted or best) with minimal side effects.

- Use a stepwise approach to control symptoms quickly, starting treatment at the level most likely to achieve this
- Aim for early control by stepping up treatment as necessary and stepping down when control is good
- Use the lowest step that controls symptoms - consider stepping-down every 3 months, reducing the dose of inhaled corticosteroid gradually by 25-50% each time
- If a trial of an add-on treatment is ineffective, stop the drug (or in the case of increased dose of inhaled steroid, reduce to the original dose)
- Before changing a patient's treatment due to poor control, check their concordance and inhaler technique and try to eliminate any possible trigger factors
- Review inhaler use periodically (ideally every 3-6 months)
- Try to engage and educate patients regarding their own asthma management, including the need for regular reviews (Personalised asthma action plans)

Key changes detailed in the revised BTS/SIGN Guidelines 2008/9[2]

Secondary prophylaxis

Recommended

- Subcutaneous immunotherapy for patients who cannot avoid a clinically significant allergen
- Buteyko breathing technique for symptom control

Not recommended

- Sublingual immunotherapy
- Probiotics
- Air ionisers

Comparison of inhaled corticosteroids

Most evidence is available for beclometasone (BDP), budesonide and fluticasone. **Mometasone** appears to provide equal clinical activity to beclometasone and budesonide at half the dosage. Its relative safety is not established. **Ciclesonide** trials suggest it has less systemic activity and fewer local oropharyngeal side effects than conventional inhaled steroids. The clinical benefit of this is not clear as the exact efficacy to safety ratio compared with other ICS has not been fully established.

Add-on therapy

Long acting B_2 agonists (LABAs) should only be started in patients who are already on inhaled corticosteroids. Monotherapy with salmeterol or formoterol alone has been associated with significant adverse events, and therefore **LABAs should only be used in conjunction with an ICS**.

SMART therapy

In selected adult patients at step 3 who are poorly controlled or in selected adult patients at step 2 (above BDP 400mcg/day who are poorly controlled), the use of budesonide/formoterol combination inhaler as rescue medication may be effective instead of a short-acting B_2 agonist (in addition to regular use) provided careful patient education is employed.
GMMMG does not recommend the *routine* use of a single inhaler for maintenance and relief of asthma. See Combination Inhalers for further details.

Omalizumab

Due to lack of comparative studies, omalizumab has not been placed in the stepwise guidelines. It should only be initiated in specialist centres. See section below.

Difficult asthma

In this new section, difficult asthma is defined as persistent symptoms and/or frequent exacerbations despite treatment at step 4 or 5. Assessment of such patients should be facilitated through a multidisciplinary difficult asthma service provided by an experienced team who will identify the mechanism of persistent symptoms through systematic evaluation and assess adherence to therapy.

- Refer such patients to Dr Rob Niven, University Hospital South Manchester, Dr Jon Miles, North Manchester General Hospital, Dr Chris Hardy, Central Manchester Hospital or Dr Ronan O'Driscoll, Salford Royal Hospital.

Key recommendations added in earlier revisions:

Long-acting B_2-agonists (LABA)

- **Step 3:** Use of other treatments, particularly LABA, before stepping up to high dose inhaled corticosteroid in adults and children ≥ 5 years

Inhaled Corticosteroids (ICS)

- Start ICS at a level appropriate to asthma severity
- ICS should be introduced in milder cases than previously recommended: ICS should be considered in patients:
    - Using inhaled B_2 agonists three times a week or more
    - Exacerbation of asthma in the last 2 years
    - Symptomatic three times a week or more, or waking one night a week.
- ICS should be titrated to the lowest dose at which effective control of asthma is maintained
- Higher doses of ICS may be required for smokers or ex-smokers
- No longer recommended to double the dose of ICS for an exacerbation

Children

- Any child treated with **≥800mcg** per day of beclometasone or equivalent should receive specific written advice about steroid replacement in the event of a severe intercurrent illness as part of their management plan. Any child on this dose should be under the care of a specialist paediatrician for the duration of the treatment.
- **Leukotriene receptor antagonists** can be used as an alternative to steroids in children <5 years (If ICS cannot be used)

Asthma action plans

- People with asthma should receive education and a written action plan. Those admitted with severe asthma should receive a personalised action plan on discharge from a clinician with expertise in asthma management.
  Free copies of the *Self-management 'Be in control' asthma action plan* can be obtained from Asthma UK:
  http://www.asthma.org.uk/all_about_asthma/controlling_your_asthma/resources_to_help_you/personal_asthma_acti.html

Diagnosis

The diagnosis of asthma is not always simple. Some of the symptoms of asthma are shared with other diseases/disorders. The BTS/SIGN guideline has a useful section to aid diagnosis. If diagnosis is unclear refer for a specialist opinion, (e.g. wheezy infants). The guideline revision recommends assigning a probability of asthma of low, intermediate or high on the basis of symptoms and spirometry.[2]

Regular Patient Review and Follow-up

Asthma is best monitored by routine clinical review on at least an annual basis. Symptomatic asthma control is best monitored using validated tools such as the Asthma Control Questionnaire, the Asthma Control Test or the RCP '3 questions', as follows:

In the last week or month

1. Have you had difficulty sleeping because of your asthma symptoms? (including cough)
2. Have you had your usual asthma symptoms during the day? (breathlessness, wheeze, cough, chest tightness, etc)
3. Has your asthma interfered with your usual activities? (housework, work/school, etc)

- **A telephone review may be undertaken by a nurse, pharmacist or doctor with appropriate training, however inhaler technique can not be monitored and therefore this does not fulfil QOF requirements**
- **Other monitoring parameters are listed in the BTS/SIGN Guideline 2009[2]**
- **The review should incorporate an individual written action plan**

Devices

- Ideally MDI + spacer
- Patient preference must be considered in order to aid treatment and compliance

NICE Guidance:

Inhaler devices in children <5 yrs with chronic asthma[3]

1. MDI + spacer (facemask where necessary)
2. If this is not effective consider dry powder inhalers (DPI) in children aged 3-5 years
   (N.B. young children may not generate sufficient inspiratory flow for DPI)
   OR alternatively consider nebulised therapy as a last resort

Inhaler devices in older children (5-15 yrs) with chronic asthma[4]

1. MDI + spacer
2. If adherence is poor change to alternative device (be flexible with choice of bronchodilator)

- **A MDI + spacer is useful to have in the event of an acute exacerbation**

Inhaled corticosteroids in adults and children[5,6]

- **Prescribe the least costly ICS product that is suitable, within its licence**

Steroid Dose Equivalence

The following table (BTS/SIGN) applies to ICS when given by MDI (dosage equivalents are approximate and will depend on other factors such as inhaler technique and inhaler or spacer device):

Inhaled corticosteroid	Equivalent dose/mcg	CFC-free
CFC beclometasone	400	✗
Clenil Modulite	400	✓
Qvar	200 - 300	✓
Fostair (BDP + formoterol)	200	✓
Budesonide	400	✓
Fluticasone	200	✓
Mometasone	200	✓
Ciclesonide	200 - 300	✓

- When given in equivalent doses, beclometasone, budesonide and fluticasone are equally effective and cause comparable systemic effects
- Monitor asthma control whenever a change is made to the type of inhaler device used (e.g. A patient may receive a different dose when they inhale from a MDI compared to a DPI)

CFC-free Prescribing

CFC-containing steroid inhalers are being phased out and patients will need to be transferred to a CFC-free device or dry powder inhaler (DPI). Ensure that patients transferring between devices are aware that their asthma control may change and that a subsequent review is arranged. Inhaler technique should be checked whenever there is any change in device.

- See table above
- To avoid confusion prescribe beclometasone CFC-free inhalers by BRAND
- Doses for CFC-free steroid inhalers may be different from those that contain CFCs
- **Qvar MDI** is compatible with the Aerochamber and is also available as an Autohaler or Easi-breathe inhaler
- **Qvar** is not licensed in children under the age of 12
- **Clenil Modulite MDI** is compatible with the Volumatic
- **Clenil Modulite** is licensed in children.
- The CFC-free combination inhaler **Fostair** also contains beclometasone. See below for dose equivalence.

Adverse Effects of Inhaled Corticosteroids

In addition to local adverse effects like candidiasis, clinically significant systemic adverse effects may arise at licensed doses: adrenal suppression, osteoporosis, growth retardation, cataracts and glaucoma. It is evident that for drugs with a high degree of first-pass effect (e.g. fluticasone and budesonide), such systemic effects are caused by absorption of the drug from lung tissue, rather than what is swallowed and absorbed from the gastro-intestinal tract.[7]

Using a spacer increases the proportion of the dose reaching the lung and may therefore increase systemic absorption. Fluticasone reaches its maximum effect at doses of 500mcg daily (90% of benefit is seen at 100-250mcg daily).[8] It is important to review any patients taking higher doses. If the patient is able to use the inhaler/delivery device correctly they are likely to develop adverse effects rather than any additional benefit from higher doses.

The balance between benefits and risk should be assessed for each patient. Take account of topical steroid therapy when assessing systemic risk.

Adrenal Suppression

- Evidence suggests significant adrenal suppression occurs at doses around 1.5mg/day beclometasone/budesonide and 0.75mg/day fluticasone[7]
- Patients receiving ICS doses at or above this level should be given a steroid card
- The Commission on Human Medicines (CHM) advices that ICS higher than in the current guidelines should only be prescribed by specialist physicians

Children

- The BTS guideline advises monitoring height on a regular basis. Initially, children may have slower growth rates, but eventually catch up providing the ICS dose used is within those recommended. Refer to a General Paediatrician if concerned about a child's height.
- Consider the possibility of adrenal insufficiency in any child on ICS presenting with decreased level of consciousness. Blood glucose levels should be checked urgently. Consider whether IM hydrocortisone is required. See above for management of children treated with ≥800mcg per day of beclometasone or equivalent.
- Steroid cards should be given to children using high doses of inhaled corticosteroids. See current BNF for definitions of 'high dose'.
- MDI inhalers: Fluticasone not licensed in children <4 years. Budesonide and Clenil are not licensed in children <2 years.
- The BTS guideline also suggests the possibility of more rapid dose reduction in children with milder asthma who have a clear seasonal pattern during their 'good' season.

Oral steroids

Patients on long term steroid tablets (e.g. >3 months) or requiring frequent courses (e.g. 3 to 4 per year) will be at risk of systemic side effects.

- Consider bone protection
- Monitor for diabetes and hypertension
- Screen for cataracts in children

Combination Inhalers

BTS/SIGN state that: 'There is no difference in efficacy in giving inhaled steroid and long-acting B_2 agonist in combination or in separate inhalers.'

- **It is essential to ensure the patient has benefited from LABA before prescribing a combination inhaler**

NICE guidance[5,6]

- Applicable to adults and children
- The decision on whether to use two agents separately or a combination should be made on an individual basis taking into account therapeutic need and the likelihood of treatment adherence
- **The least costly device suitable for the individual should be chosen.**

Advantages

- Reduce number of different inhalers - compliance (one prescription fee)
- Patient is aware of deterioration immediately, if they discontinue the combination

Disadvantages

- Not all patients benefit from long-acting B_2 agonists
- Lack of flexibility with Seretide (fluticasone+salmeterol) – the patient can't increase their steroid dose without receiving too much salmeterol (without changing inhaler)

SMART (Symbicort Maintenance and Relief Therapy)

- Symbicort (budesonide+formoterol) DPIs 100/6 and 200/6 are licensed in adults >18y as single maintenance and reliever therapies, i.e. a short-acting B_2 agonist is not required
- SMART may be of benefit in selected patients:
    - At step 3 who are poorly controlled or at step 2 who are poorly controlled with BDP above 400mcg/day
    - who have demonstrated a good response to inhaled B_2-agonist therapy (i.e. no history of excessive B_2-agonist use)
    - with adequate cognitive ability to use the treatment properly (e.g. awareness of worsening asthma)
- The dose is 2 puffs per day [as either 2 puffs once daily or 1 puff twice daily (2 puffs twice daily may be appropriate for some patients)]. Patients should take 1 additional puff as needed in response to symptoms up to max 6 puffs at a time; max 8 puffs daily; up to 12 puffs daily can be used for a limited time..
- Prescribe "budesonide/formoterol 200/6, one puff twice daily plus as needed."
- Adequate patient education must be provided, including advice on maximum doses and action if there is a lack of response. Patients taking rescue budesonide/formoterol once a day or more should have their treatment reviewed.

Fostair

- CFC-free MDI containing 120 actuations of beclometasone 100mcg + formoterol 6mcg
- Licensed for regular treatment of asthma in adults >18y where use of a combination product is appropriate (Step 3) at a dose of 1 or 2 puffs twice daily
- Fostair contains extra-fine BDP (same as Qvar), so 100mcg of beclometasone in Fostair is equivalent to 200-250mcg beclometasone in other beclometasone-containing products (BNF)
- 100mcg beclometasone in Fostair is equivalent to 100mcg fluticasone and 200-250mcg budesonide (BNF)
- **Fostair is less expensive than Seretide or Symbicort at equivalent doses**

Oral Therapies

Leukotriene receptor antagonists have some beneficial clinical effect in some patients

1st Choice Montelukast tablets (chewable tablets or granules for children) given as a single daily dose at bedtime: 6 months-5 years 4mg daily, 6-14 years 5mg daily, adults 10mg daily. It is metabolised by the cytochrome P450 enzyme system, so caution is necessary in patients also taking enzyme inducers such as phenytoin, phenobarbitone and rifampicin.
(Zafirlukast is not licensed in children under 12 years of age. It inhibits the cytochrome P450 enzyme system and may interact with drugs such as theophylline, warfarin and erythromycin.)
They should not be used to treat acute asthma attacks, during pregnancy or lactation (unless considered clearly essential) or in unstable asthma. Currently, they should not be used to reduce doses of inhaled or oral corticosteroids (Risk of Churg-Strauss syndrome).

Theophyllines have some beneficial clinical effect in some patients
(Side effects and interactions are more common, and monitoring of plasma levels is required.)

Theophylline MR tablets (prescribe by **brand**) Adult dose: 200-400mg twice daily.
Uniphyllin Continus is stocked by local hospitals and is available in a range of doses.
Theophylline is also available as a liquid formulation.
Common drug interactions include erythromycin, ciprofloxacin and oral contraceptives.

- Give a trial of montelukast or theophylline therapy for **2 months** and stop if ineffective

Omalizumab[9]

Omalizumab is licensed as add-on therapy for adults and children aged 6 or over for severe persistent allergic asthma. It is given by subcutaneous injection every 2 or 4 weeks. NICE recommends omalizumab as a possible treatment when all the following apply:

- Confirmation of IgE-mediated allergy to a perennial allergen confirmed by clinical history and allergy skin testing
- A full trial of, and documented compliance with, high dose ICS and long-acting B2-agonists, in addition to leukotriene receptor antagonists, theophyllines, oral corticosteroids and oral B2-agonists
- The patient is a non-smoker
- The patient has had at least two exacerbations of asthma within the past year that have resulted in hospital admission, or three or more exacerbations within the past year, one of which has required hospital admission and the other two requiring treatment in an emergency department.
- Omalizumab should be initiated and monitored by a physician experienced in allergy and respiratory medicine in a specialist centre. Omalizumab should be discontinued at 16 weeks if an inadequate response is shown.
- Eligible patients should be referred to Dr Rob Niven, University Hospital South Manchester, Dr Jon Miles, North Manchester General Hospital, Dr Chris Hardy, Central Manchester Hospital or Dr Ronan O'Driscoll, Salford Royal Hospital.

Nebulisers

Treatment with inhaled therapies should be maximised before considering nebulised treatment. A referral should be made to a Consultant Respiratory Physician for assessment and if appropriate a nebuliser/compressor will be supplied with appropriate support.

Spacer Devices

- Reduce poor inhaler technique with MDIs (increased airway deposition)
- Reduce the oral absorption of inhaled steroids (less candidiasis)
- MDI + spacer is at least as effective as a nebuliser in adults and children ≥ 2
- Check the patient uses their spacer device

Use and Care of Spacers

- The drug should be administered by repeated **single** actuations of the inhaler into the spacer, each followed directly by inhalation
- Different spacers may change the amount of drug recovered
- The spacer should be compatible with the MDI being used (check SPC)
- The build-up of electrostatic charge causes the drug to stick to the surface and thereby reduces drug delivery
- Wash monthly in detergent and allow to air dry
- **Replace every 6-12 months**

The British Guideline on the Management of Asthma[2] also contains guidance on:

- Management of acute asthma (useful flow charts in Annex)
- Exercise-induced asthma
- Asthma in pregnancy
- Occupational asthma
- Difficult asthma
- Patient education and self-management

A new section: Asthma in adolescents will be included in the 2010 update.

References

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Summary of stepwise asthma management in children under 5

-Review patients every 3-6 months to ensure that the level of treatment they receive remains optimum
-Step up or down as necessary

STEP 4 Persistent poor control

- **Refer to Respiratory Paediatrician**

STEP 3 Initial add-on therapy

- Consider trial of montelukast therapy (licensed from 6 months)
- In those taking montelukast alone, consider addition of an inhaled steroid 200-400mcg/day
- In children under 2 years, consider proceeding to step 4

STEP 2 Regular preventer therapy– Add inhaled steroid 200-400mcg/day*^

START AT DOSE APPROPRIATE TO SEVERITY

1st Beclometasone MDI (Clenil®) + spacer +/- face mask (licensed from 2 years)
2nd Budesonide MDI + spacer +/- face mask (licensed from 2 years)
Consider montelukast therapy if inhaled steroid cannot be used (licensed from 6 months)
Consider referral to a General Paediatrician before considering fluticasone (unlicensed in this age group)

STEP 1 Mild intermittent asthma– Inhaled short-acting β_2-agonist as required

1st Salbutamol MDI + spacer (plus appropriate face mask when necessary)

- N.B. Children <5 find it difficult to generate sufficient inspiratory flow for dry powder inhalers
- Very occasionally salbutamol does not work in infants under 12-15 months, first check compliance and if necessary consider a trial of ipratropium bromide (consider alternative diagnosis)

* Beclometasone or equivalent
^ Higher doses may be required if drug delivery is difficult

Summary of stepwise asthma management in children aged 5-12

-Review patients every 3-6 months to ensure that the level of treatment they receive remains optimum
-Step up or down as necessary

STEP 5 Oral steroids

- Maintain high dose inhaled steroid at 800mcg/day* and **refer** to Respiratory Paediatrician
- Use daily steroid tablets at lowest dose to maintain control

STEP 4 Persistent poor control

- Try increasing inhaled steroid up to 800mcg/day* and consider referral

STEP 3 Initial add-on therapy- Trial of long-acting β_2-agonist (LABA)

Choose device according to patient's ability to use and existing inhalers:
MDI or accuhaler–salmeterol turbohaler–formoterol (child over 6 years)
(See advice regarding use of combination inhalers)

- **Good response** – continue LABA
- **Some benefit but still inadequate** – continue LABA and increase steroid to 400mcg/day*
- **No response** – stop LABA and increase steroid to 400mcg/day*, consider trial of montelukast, with referral to a General Paediatrician if lack of response

STEP 2 Regular preventer therapy– Add inhaled steroid 200-400mcg/day*

(Consider other preventer drug (montelukast) if inhaled steroid cannot be used.)
START AT DOSE APPROPRIATE TO SEVERITY
200mcg/day* is an appropriate starting dose for many patients

1st Beclometasone MDI (Clenil®) + spacer device
2nd Dry powder inhaler budesonide turbohaler OR fluticasone accuhaler

STEP 1 Mild intermittent asthma– Inhaled short-acting β_2-agonist as required

1st Salbutamol MDI + spacer device
2nd Dry powder inhaler terbutaline turbohaler OR salbutamol accuhaler

*Beclometasone or equivalent

Summary of stepwise asthma management in adults and children >12

-Review patients every 3-6 months to ensure that the level of treatment they receive remains optimum
-Step up or down as necessary

STEP 5 Oral steroids

- Maintain high dose inhaled steroid at 2000mcg/day* and **refer** to specialist
- Use daily steroid tablets at lowest dose to maintain control
- Consider other treatments to minimise steroid use

STEP 4 Persistent poor control - Consider trials of:

- Increasing inhaled steroid up to 2000mcg/day*
- Addition of montelukast, theophylline MR or β_2 agonist tablet depending on previous therapy
- Consider referral

STEP 3 Initial add-on therapy - Trial of long-acting β_2-agonist (LABA)

Choose device according to patient's ability to use and existing inhalers:
Formoterol is available as MDI or turbohaler. Only use salmeterol if accuhaler is device of choice.
See advice regarding use of combination inhalers and formulary choices.
Based on cost: 1. Fostair® MDI, 2. Symbicort® turbohaler, 3. Seretide® accuhaler

- **Good response** – continue LABA
- **Some benefit but still inadequate** – continue LABA and increase steroid to 800mcg/day*
- **No response** – stop LABA and increase steroid to 800mcg/day*, if necessary trial either montelukast, branded theophylline e.g. Uniphyllin MR or β_2 agonist tablet (for 2 months)

STEP 2 Regular preventer therapy - Add inhaled steroid 200-800mcg/day*

START AT DOSE APPROPRIATE TO SEVERITY
400mcg/day* is an appropriate starting dose for many patients

1st	Beclometasone MDI (Clenil® or Qvar®) + spacer device	
2nd	Breath-actuated inhaler	beclometasone (Qvar® easibreathe or autohaler)
	Dry powder inhaler	budesonide turbohaler or fluticasone accuhaler

STEP 1 Mild intermittent asthma - Inhaled short-acting β_2-agonist as required

1st	Salbutamol MDI +/- spacer device	
2nd	Breath-actuated inhaler	salbutamol (easibreathe or autohaler)
	Dry powder inhaler	terbutaline turbohaler or salbutamol accuhaler

*Beclometasone or equivalent (Qvar 100mcg is approx. equivalent to 200-250mcg of Clenil or budesonide and 100mcg of fluticasone.) (BNF)