Stepwise Management of Asthma: Inhaled Therapy in Adults
Following BTS guidelines 2016 / NICE guidelines 2017

(Refer to Manufacturer SPC for full details www.medicines.org.uk)

Key:
- SABA = Short-acting B2 agonist
- LABA = Long-acting B2 agonist
- ICS = Inhaled Corticosteroid
- MDI = Metered Dose Inhaler
- DPI = Dry Powder Inhaler
- BDP = Beclometasone Dipropionate or equivalent

Step 2: Symptomatic Asthma: Start Low Dose ICS 200 – 400 micrograms BDP or equivalent daily
(Higher doses may be needed in Smokers and ex-smokers)

ICS dose response curve: 90% of effect is seen at daily doses of 400 micrograms BDP or equivalent
(Masoli M et al. Thorax 2004; 59:16-20)

MDI Treatment Options:
- Clenil Modulate MDI 100mcg 1-2P BD
- Qvar Easi-Breathe 50-100mcg 1P BD
- Fluticasone MDI 50mcg 1-2P BD

DPI Treatment Options:
- Budesonide Turbohaler 100mcg 1-2P BD
- Fluticasone Accuhaler 50-100mcg 1P BD

Step 3A: Remains Symptomatic / Uncontrolled:
Either - Add LABA (best given in combination inhaler to avoid non-compliance)
Or - Trial of LTRA (leukotriene receptor antagonists) 4-8 weeks – discontinue if no benefit

*Symbicort 100/6, Symbicort 200/6, DuoRespSpiromax 160/4.5 and Fostair pMDI 100/6 can be used as maintenance and reliever therapy
MART (See page 5)

MDI Treatment Options Change to:
- Fostair MDI 100/6 1P BD*
- Flutiform MDI 50/5 2PBD

DPI Treatment Options Change to:
- DuoRespSpiromax 160/4.5 1P BD*
- Fostair NEXThaler 100/6 1P BD
- Relvar Ellipta 92/22 1P OD
- Symbicort 100/6 Turbohaler 1-2P BD*
- Symbicort 200/6 Turbohaler 1P BD*

STEP 3B: Increase ICS to 800 – 1000 micrograms BDP or equivalent daily
If control still inadequate consider trial of other therapies e.g. SR theophylline

MDI Treatment Options Change to:
- Flutiform MDI 125/5 2P BD
- Fostair MDI 100/6 2P BD
- Give Steroid Card

DPI Treatment Options Change to:
- DuoRespSpiromax 160/4.5 2P BD*
- DuoRespSpiromax 320/9 1P BD
- Fostair NEXThaler 100/6 2P BD
- Relvar Ellipta 92/22 1P OD
- Symbicort 200/6 Turbohaler 2P BD*
- Symbicort 400/12 Turbohaler 1P BD
- Give Steroid Card

STEP 4: Consider adding in Tiotropium Respimat 2.5mcg 2P OD via spacer,
Then increase ICS up to 2000 micrograms daily AND refer to Secondary care
If control still inadequate add 4th drug e.g. SR theophylline if not already taking

MDI Treatment Options Increase to:
- Flutiform MDI 250/10 2P BD
- Fostair MDI 200/6 2P BD
- Give Steroid Card

DPI Treatment Options Increase to:
- DuoRespSpiromax 160/4.5 4P BD*
- DuoRespSpiromax 320/9 2P BD
- Fostair NEXThaler 200/6 2P BD
- Relvar 184/22 1P OD
- Symbicort 200/6 Turbohaler 4P BD
- Symbicort 400/12 Turbohaler 2P BD
- Give Steroid Card

STEP 5: Refer to Secondary Care

Inhaled SABA PRN

Reliever device should be chosen on basis of patient preference & technique, not cost, as with good control fewer devices should be required. LABEL WITH WHEN TO REFER TO GP (see page 3)

Refer to the specific inhaler Summary of Product Characteristics for full prescribing information

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**Brand Specific Step-Down Suggestions**

(Each step down represents an ~50% reduction in ICS dose)

**Important**

- Patients should be maintained on the lowest dose of ICS that controls symptoms\(^1\)
- If incorrect inhaler technique and / or concordance with therapy is contributing to lack of control address and correct
- **Attempt step down in patients who have achieved complete asthma control for at least 12 weeks** \(^1\) Stepping down before 12 weeks can lead to exacerbations and hospital admissions. Table 1 (page 3) defines the levels of asthma control.
- Patients who have found it very difficult to achieve control, or in whom previous step-down attempts have resulted in repeated exacerbations, may need to continue current treatment for a more prolonged period of time.
- **Exclude** patients who are symptomatic, oral steroids in last 3 months, under specialist review or pregnant
- Make sure the patient has an **up-to-date written asthma action plan**
- Step down by 25-50% every 3 months and **review patients regularly as they step down**.
- Keep device changes to a minimum and consider the beclometasone dipropionate (BDP) equivalence of different inhaler devices.\(^1,2\)

### Metered Dose Inhalers (via Spacer)

<table>
<thead>
<tr>
<th>BTS Step</th>
<th>Flutiform MDi</th>
<th>Fostair MDi</th>
<th>Seretide MDi</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 4</strong></td>
<td>Flutiform 250/10 2P BD</td>
<td>Fostair 200/6 2P BD</td>
<td>Seretide 250/25 2P BD</td>
</tr>
<tr>
<td><strong>Step 3B</strong></td>
<td>Flutiform 125/5 2P BD</td>
<td>Fostair 100/6 2P BD</td>
<td>Seretide 125/25 2P BD</td>
</tr>
<tr>
<td><strong>Step 3A</strong></td>
<td>Flutiform 50/5 2P BD</td>
<td>Fostair 100/6 1P BD*</td>
<td>Seretide 50/25 2P BD</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td>Flixotide 50mcg MDi1P BD</td>
<td>Qvar 50mcg 2P BD</td>
<td>Flixotide 50mcg MDi2P BD</td>
</tr>
</tbody>
</table>

### Dry powder Inhalers

<table>
<thead>
<tr>
<th>BTS Step</th>
<th>Seretide DPI</th>
<th>Symbicort DPI</th>
<th>Fostair DPI (NEXThaler)</th>
<th>DuoResp DPI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 4</strong></td>
<td>Seretide 500/50 1P BD</td>
<td>Symbicort 400/12 2P BD</td>
<td>Fostair 200/6 2P BD</td>
<td>DuoResp 320/9 2P BD</td>
</tr>
<tr>
<td><strong>Step 3B</strong></td>
<td>Seretide 250/50 1P BD</td>
<td>Symbicort 400/12 1P BD or Symbicort 200/6 2P BD</td>
<td>Fostair 100/6 2P BD</td>
<td>DuoResp 320/9 1P BD or DuoResp 160/4.5 2P BD</td>
</tr>
<tr>
<td><strong>Step 3A</strong></td>
<td>Seretide 100/50 1P BD</td>
<td>Symbicort 200/6 1P BD*</td>
<td>Fostair 100/6 1P BD*</td>
<td>DuoResp 160/4.5 1P BD*</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td>Flixotide 100mcg Accuhaler 1P BD</td>
<td>Pulmicort Turbohaler 100mcg 1P BD</td>
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</tbody>
</table>

* LABA dose in ICS/LABA combination at 50% of the recommended treatment dose

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Refer to the specific inhaler Summary of Product Characteristics for full prescribing information

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STEPPING DOWN

Why Step down?
As with all medicines, the well-recognised benefits of Inhaled Corticosteroids (ICS) need to be balanced against the potential risks. Patients should be maintained on the lowest possible dose of ICS. High dose ICS carry a risk of systemic side-effects e.g. adrenal suppression, growth retardation, decrease in bone mineral density, cataract and glaucoma.1, 3–5 Clinicians should ensure patients are aware of the benefits and risks associated with high dose ICS

What do the guidelines say about stepping-down?
The decision to step-down therapy should be jointly made between the clinician and the patient. Reductions should be considered every three months, but only if patients have complete asthma control1. When reducing inhaled corticosteroids (ICS) clinicians should remember that patients deteriorate at different rates. If asthma is controlled with a combination of ICS/long-acting beta₂ agonist (LABA), the preferred approach is to reduce the ICS in increments of approximately 50% whilst continuing the LABA at the same dose.2

If control is maintained after stepping-down, further reductions in the ICS should be attempted until a low dose of ICS is reached, when the LABA may be stopped.2 The patients’ previous asthma severity and how hard it has been to achieve control should be considered before any treatments are withdrawn.

<table>
<thead>
<tr>
<th>Table 1: LEVELS OF ASTHMA CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of current clinical control (preferably over 4 weeks)</td>
</tr>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>RCP 3 Questions</td>
</tr>
<tr>
<td>Daytime symptoms</td>
</tr>
<tr>
<td>Limitation on activities</td>
</tr>
<tr>
<td>Nocturnal symptoms/awakening</td>
</tr>
<tr>
<td>Need for reliever/rescue treatment</td>
</tr>
<tr>
<td>Lung function (PEF or FEV₁)</td>
</tr>
</tbody>
</table>

Adapted from MeReC Bulletin 2008; 13(2) and BTS/SIGN Asthma Guideline 2016

Management Considerations

Salbutamol MDi doses and labelling (Asthma only)
As salbutamol is for symptomatic relief and not a treatment for Asthma, is it important that these medications are labelled to allow the patient to understand when they need to seek medical advice. The current standard label of; ONE – TWO puffs FOUR times a day, when required. Does not indicate to patients when their Asthma control is deteriorating. From the National Review of Asthma Deaths, 45% of patients that died, failed to seek medical help. Therefore new label recommendation: ONE-TWO puffs, up to every FOUR hours, when required for cough, wheeze, breathlessness. SEEK MEDICAL HELP IF NO RELIEF, IF RELIEF DOES NOT LAST FOR 4 HOURS, OR YOU HAVE SIGNIFICANTLY INCREASED THE AMOUNT YOU USE.

N.B. All patients must be counselled on MDi use and instructed to allow enough time between actuations (min 15 seconds). If this is not done then subsequent doses will not be adequate to relieve symptoms.

Peak Flow Meter Variation
There is a documented variation between peak flow meters of up to 20%. Therefore it is advised that patient, (where possible), use their own peak flow meter for Asthma monitoring, rather than different devices.

Refer to the specific inhaler Summary of Product Characteristics for full prescribing information
Assess Control
- RCP 3 questions (Table 1 Page 3)
- PEF or Spirometry
- Number of reliever inhalers collected in previous 12 months
- Number of exacerbations in last 12 months
- Only attempt step down in completely controlled patients
- Consider results of previous step-down attempts

Controlled inhalers/year (SABA)

Partly controlled or uncontrolled inhalers/year

Completely controlled - consider step down
1. Check and correct inhaler technique
2. If technique is a problem consider spacer or alternative device at the same step. Eg move from MDI to DPI
3. Identify which ICS inhaler, (strength and current dose) the patient is using, and locate where this is positioned in the flowchart (page 1)
4. Follow the arrow and step down to next recommended ICS inhaler(s)
5. Step down from LTRA is also recommended

Note: If patient is prescribed add on therapies (e.g. Theophylline, oral prednisolone) these should be stopped one by one before attempting to reduce the ICS dose.

Uncontrolled or partial control – do not step down
1. Check and correct inhaler technique – consider spacer or alternative device
2. Are there any issues affecting compliance e.g. dexterity?
3. Check concordance with therapy and consider any issues which may affect compliance. (Collection of 75% or less ICS prescriptions over the last 12 months may indicate poor concordance, but also consider other contributory factors to number of inhalers ordered. E.g. community pharmacy repeats ordering services).
   If these have been excluded, step up therapy

Clinicians should consider:
Patients achieve complete asthma control at different rates. Clinicians should have a discussion with the patient to decide whether to trial the current therapy for longer or to step up again.

Suggested action/discussion points with patient:
1. Is the patient exposed to trigger factors e.g. smoking, pets, pollen or stress?
2. Are there any lifestyle points to consider where asthma suitability is crucial e.g. impending exam?
3. How long did it take the patient to achieve complete asthma control last time?
4. What would be the potential consequences of an exacerbation and does the patient know what to do if this occurs?
5. Has the patient got a written self-management plan?
6. What would the patient prefer to do?

Action:
Clinicians should use their professional judgement to decide whether to continue trialling the current therapy or step up again. If continuing on the current therapy for longer, the patient should be advised to monitor their symptoms and reliever use, and review the patient in 1 month. Patients should be advised to return to the clinic if their symptoms become problematic within this time.

Refer to a specialist if necessary – for patients who remain poorly in control at Step 4 or at Step 5
If concordance or inhaler technique corrected on this occasion, review again in 3 months.

Repeat prescriptions should routinely be for one month’s treatment.
Patients on the SMART regime or Fostair maintenance and reliever regime regularly requiring more than one inhaler per month should trigger a review.

Refer to the specific inhaler Summary of Product Characteristics for full prescribing information
Maintenance and Reliever Therapy (MART)

There are currently only three combination inhalers that have a licence for Maintenance and Reliever Therapy (MART). These are Symbicort (200/6 and 100/6) DPI, Fostair 100/6 MDi and Duoresp 160/4.5 DPI. Symbicort is licenced from 12 years of age, with Fostair and Duoressp from 18 years of age. MART therapy should be considered for patients that are non-compliant with their ICS inhalers and are using large amounts of reliever therapy. Consideration should be given to the patients’ ability to use either a DPI or MDi (via a spacer) before deciding on a choice of therapy.

Patients requiring regular use of ‘when required’ rescue inhalations should be strongly recommended to seek medical advice to have their maintenance therapy reviewed.

Licensed dosing table for MART in adults (BNF March 2018)

<table>
<thead>
<tr>
<th>Inhaler device</th>
<th>Starting maintenance dose</th>
<th>Maximum maintenance dose</th>
<th>When required inhalations per day</th>
<th>Maximum total daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duroresp 160/4.5 DPI</td>
<td>1 puff twice daily</td>
<td>2 puffs twice daily</td>
<td>6 puffs</td>
<td>8 puffs (12 puffs may be used for a limited time with medication assessment)</td>
</tr>
<tr>
<td>Symbicort 100/6 DPI</td>
<td>1 puff twice daily</td>
<td>-</td>
<td>6 puffs</td>
<td>8 puffs (12 puffs may be used for a limited time with medication assessment)</td>
</tr>
<tr>
<td>Symbicort 200/6 DPI</td>
<td>1 puff twice daily</td>
<td>2 puffs twice daily</td>
<td>6 puffs</td>
<td>8 puffs (12 puffs may be used for a limited time with medication assessment)</td>
</tr>
<tr>
<td>Fostair 100/6 MDi via spacer</td>
<td>1 puff twice daily</td>
<td>-</td>
<td>6 puffs</td>
<td>8 puffs</td>
</tr>
</tbody>
</table>

N.B. One MART inhaler per month provided the starting maintenance dose, plus 60 extra PRN doses

Should these patients have an emergency salbutamol MDi as an acute issue on request?

It has always been advised that patients on MART therapy do not have a regular reliever inhaler on repeat every month. The reliever should come from the MART use of their preventer inhaler. During an exacerbation the amount of reliever required may go over the maximum permitted 24 hour dose. Therefore for patients with a self-management plan, a restricted number of salbutamol MDI inhalers per year should be permitted, to be used during exacerbations when the need for a reliever inhaler is increased. By issuing a salbutamol MDi and a spacer, the administration of the medication using “Tidal” breathing can be achieved.

References

Key Notes to Consider When Assessing Inhaler Technique

When and why we need to assess patients
An assessment of a patient’s ability to correctly use their inhaler devices should be undertaken at every available opportunity (and at least once a year). Patients who use their inhaler device incorrectly can reduce the amount of drug that is administered by up to 75%. Correct inhaler use can prevent the need for stepping up to high inhaled corticosteroid doses in many patients.

Choice of Metered Dose inhaler (MDI) vs Dry Powder inhaler (DPI)

MDIs
Require a minimum amount of inspiratory effort from the patient, as the propellant produced by the device dose all of the work. It is therefore very common (>85%) for patients to breath in too fast for these devices. If this is the case than the first line option should be to convert the patient to a dry powder inhaler device (provided they have sufficient inspiratory flow to achieve good lung deposition). Inspiratory flow for each DPI can be assessed using an In-Check dial.

Spacer devices
If a patient is unable to breathe in with sufficient force for a DPI and does not have a slow enough technique, or the coordination for an MDi, then a spacer device should be used. This allows the patient to focus on their inspiratory flow rather than their coordination. It is worth noting that the use of a DPI is preferential to an MDi + spacer, in patients who may forget to use the spacer.

DPIs
Contain no propellant and so require the patient to have sufficient inspiratory flow to obtain the dose from the device. As most patients breathe in forcefully when using all inhalers a DPI will be suitable for most patients.

Keeping all inhaler devices the same
Once an appropriate inhaler device is identified for a patient, all additional inhaled medications should be prescribed via the same device where possible.

Dose adjustments when changing inhaler devices
For patients who are using specific inhaler devices incorrectly, consideration should be given to the dose of the medication in the inhaler when switching to a different device.

By changing to a device that the patient is actually able to use we are effectively increasing the dose of the medication by 2 or even 4 fold. Therefore the dose of medication for a stable patient should be halved in the first instance at the point at which the device is changed and the patients’ asthma control reassessed the following month.

Smoking
Patients who smoke have, in general an increased requirement for inhaled corticosteroids. This is due to a combination of decreased adsorption and also increased metabolism linked to smoking. In this group of patients it is advisable to start at the higher end of the stated range. i.e. STEP 2, start at Clenil Modulite (beclometasone dipropionate) 400mcg rather than 200mcg.
**SPACERS**

**Use and Care of Spacers**

- All pMDI’s should be used via a spacer, as this ensures the best drug deposition to the lung and minimises risk of oral candidiasis.

- The spacer should be compatible with the pMDI being used.

- The drug should be administer as a single actuation of the metered dose inhaler into the spacer, followed by inhalation, and with at least 15 seconds before the next dose is released into the spacer.

- There should be minimal delay between pMDI actuation into the spacer and inhalation.

- Tidal breathing is the preferred technique (5 breaths in and out).

- All spacers should be cleaned weekly as per manufacturer’s recommendations or performance is adversely affected.

- A Volumatic should be washed in detergent and allowed to dry in air. The mouthpiece should be wiped clean of detergent before use.

- The AeroChamber Plus Flow Vu can be washed in the dishwasher (on the top shelf).

- Drug delivery via the Volumatic may vary significantly due to static charge.

- Plastic spacers should be replaced at least every 12 months but some may need changing at six months.

  *British Guideline on the Management of Asthma; BTS/SIGN May 2008, revised September 2016*

**Comparison of Spacers**

<table>
<thead>
<tr>
<th></th>
<th>AeroChamber Plus Flow Vu</th>
<th>Volumatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airomir® MDi</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Alvesco®</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Clenil Modulite®</td>
<td>a</td>
<td>✓</td>
</tr>
<tr>
<td>Flixotide Evohaler®</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Flutiform®</td>
<td>✓</td>
<td>a</td>
</tr>
<tr>
<td>Fostair® MDi</td>
<td>✓</td>
<td>a</td>
</tr>
<tr>
<td>Qvar MDi®</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>Salbutamol (generic) MDi</td>
<td>✓</td>
<td>a</td>
</tr>
<tr>
<td>Seretide Evohaler®</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Tiotropium Respimat®</td>
<td>a</td>
<td>x</td>
</tr>
<tr>
<td>Ventolin® Evohaler</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Key**

- ✓ = Fits in this spacer and is licensed for use
- × = Does not fit in this spacer
- a = Fits in this spacer but is not licensed

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