Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

All Wales Adult Asthma Management and Prescribing Guideline

December 2021

(August 2022 – correction made to dose frequency listed for 'Seretide Accuhaler (DPI)' in the 'Table of ICS equivalence')

(February 2024 – Added new treatment regime and updated inhaler options

This document has been prepared by the Respiratory Health Implementation Group, and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG)

AWMSG has only endorsed the guideline content. AWMSG has not endorsed the mobile technology application (app) referred to within the document as this falls outside their remit. The responsibility to ensure all regulatory requirements have been investigated in the development of the app, and continue to be adhered to, remains with the app owner.

The National Institute for Care Excellence and the British Thoracic Society are planning to publish asthma guidance in 2024. This All Wales guideline will be reviewed in the light of the publication of that document.

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All Wales Adult Asthma Management and Prescribing Guideline

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
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Y Grŵp Gweithredu ar Iechyd Anadlol
Respiratory Health Implementation Group

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Find out more about this guideline
http://qrinfo.icst.org.uk/adult-asthma-guideline-wales-supporting-notes

CORE PRINCIPLES

- Perform objective tests to confirm a suspected diagnosis of asthma
- All patients should be treated with an inhaled corticosteroid (ICS)
- The **preferred regimen** is a regular ICS/formoterol containing inhaler, with as-needed doses of the same inhaler taken in response to symptoms (maintenance and reliever therapy, or MART)
- In mild asthma with infrequent symptoms, ICS/formoterol can now be used on an **if and when needed basis** (PRN), without regular maintenance dosing. This anti-inflammatory reliever (AIR) approach reduces the risk of exacerbations and unscheduled healthcare attendances compared with daily ICS and PRN SABA
- An alternative regimen is provided. Consider if a patient is stable, with good adherence, infrequent use of SABA (<3 per year) and no exacerbations in the last year on their current therapy. If a patient is poorly controlled they should be **switched to the preferred regimen**.
- Ensure asthma action plan is updated Asthma hub

INHALER PRINCIPLES

- Choice of inhaler is based on patient's preference and technique (use in-check device to assess inspiratory effort)
- Whenever possible choose a device with low global warming potential (GWP) rather than those with high GWP
- If more than one inhaler is prescribed ensure these have the same technique (i.e. do not mix DPIs and MDIs)
- ICS and long-acting beta$_2$ agonists (LABA) MUST be prescribed as a combination product to obviate the risk of patients taking LABA monotherapy (associated with increased risk of mortality)
- MDIs should be used with a spacer device
- Prescribe by brand and specify device (e.g. Fostair NEXThaler)
- At step 3, Fostair and Luforbec are unlicensed options. See page 7 of the supporting notes for further information.

*ASTHMA CONTROL

- Good control is no daytime symptoms, no night time waking, no limitations in activity, no exacerbations
- Before stepping up therapy confirm symptoms are due to asthma and address inhaler technique, adherence and co-morbidity
- Consider stepping down treatment if good control for 3 months

EXACERBATION/EMERGENCY TREATMENT (AIR/MART)

- Administer up to 6 doses of ICS/Formoterol at one minute intervals. Do not go back to SABA therapy.
- If symptoms persist, seek urgent medical advice

Find out more here

Asthmahub

Get your patients to download the AsthmaHub App

RHIG Version: 3.0
Publication date: Feb 2024
Review date: Feb 2025

STEP 1: MILD ASTHMA
Start pathway here if mild, infrequent symptoms (<4-5 days/week)

STEP 2: PERSISTENT ASTHMA
Start pathway here if symptoms most days or waking with asthma ≥1/week

STEP 3: ONGOING POOR CONTROL
Uncontrolled, despite good adherence to low dose ICS/LABA*

STEP 4: ADD-ON THERAPIES
Uncontrolled, despite good adherence to moderate dose ICS/LABA*

Preferred regimen - Maintenance and Reliever Therapy (MART) - Patients use the same anti-inflammatory ICS/Formoterol inhaler for maintenance (BD) and reliever (PRN) doses

	As needed low dose ICS/Formoterol reliever *Maintenance doses - None* *Reliever doses - PRN*	MART low dose ICS/ Formoterol *Maintenance doses - 1 dose BD* *Reliever doses - PRN*	MART moderate dose ICS/ Formoterol *Maintenance doses - 2 doses BD* *Reliever doses - PRN*	Add on LAMA to MART regimen If no benefit after 3 months, remove LAMA from regimen
DPI	LICENSED OPTIONS INCLUDE: **Symbicort Turbohaler 200/6** *1 dose PRN up to 8 doses/day (rarely 12 doses/ day)*	LICENSED OPTIONS INCLUDE: **Symbicort Turbohaler 200/6** *Max doses/day: 12* **Fostair NEXThaler 100/6** *Max doses/day: 8* **Fobumix Easyhaler 160/4.5** *Max doses/day: 12* **DuoResp Spiromax 160/4.5** *Max doses/day: 12* *Other bioequivalent products may be considered*	OPTIONS INCLUDE: **Symbicort Turbohaler 200/6** *Max doses/day: 12* **Fostair NEXThaler 100/6** *Max doses/day: 8 (unlicensed)* **Fobumix Easyhaler 160/4.5** *Max doses/day: 12* **DuoResp Spiromax 160/4.5** *Max doses/day: 12* *Other bioequivalent products may be considered*	LICENSED OPTIONS INCLUDE: Add on **Spiriva Respimat 2.5mcg** *2 doses OD*
	Only Symbicort 200/6 Turbohaler has a licence to be used as a reliever alone without regular ICS/formoterol maintenance doses. *The use of other low dose ICS/formoterol inhalers as reliever alone is unlicenced.*	OR	OR	
MDI		LICENSED OPTIONS INCLUDE: **Fostair MDI + spacer 100/6** *Max doses/day: 8* **Luforbec MDI + spacer 100/6** *Max doses/day: 8* *Other bioequivalent products may be considered*	OPTIONS INCLUDE (UNLICENSED): **Fostair MDI + spacer 100/6** *Max doses/day: 8* **Luforbec MDI + spacer 100/6** *Max doses/day: 8* *Other bioequivalent products may be considered*	
Add-on		AND **Trial of montelukast 10mg at night** (Discontinue if no benefit after 6 weeks)	AND	

DID YOU KNOW?

NHS Wales has set a target to reduce the proportion of high global warming potential (GWP) inhalers from more than 70% to less than 20% by 2025

PRESCRIBE A DPI PREFERENTIALLY UNLESS THE PATIENT CANNOT USE ONE

Learn more here

STEP 5: CONSIDER REFERRAL

Consider trial of high-dose ICS/LABA and referral to secondary care for asthma phenotyping +/- biological therapy

INDICATIONS FOR REFERRAL:
- Diagnostic uncertainty
- Complex comorbidity
- Suspected occupational asthma
- Poor control following treatment at Step 4
- ≥2 courses of oral steroids/ year

Trial of high dose ICS/ Formoterol

Discontinue if no benefit after 3 months. Issue steroid warning card.

High dose ICS/LABA can only be used as part of fixed dose regime **with PRN SABA.**

Not to be used as per MART.

WITHOUT LAMA	WITH LAMA
Symbicort Turbohaler 400/12 *2 doses BD* **Fostair NEXThaler 200/6** *2 doses BD* **DuoResp Spiromax 320/9** *2 doses BD* **Fobumix Easyhaler 320/9** *2 doses BD* **Atectura Breezhaler 125/260mcg** *1 dose OD* **Relvar Ellipta 184/22** *1 dose OD*	*High dose ICS/ Formoterol with add on* **Spiriva Respimat 2.5mcg** *2 doses OD* *Or switch from high dose ICS/LABA to triple therapy containing high dose ICS/LABA/LAMA* **Enerzair Breezhaler 114/46/136** *1 dose OD*
OR	OR
Fostair MDI + *spacer* **200/6** *2 doses BD* **Luforbec MDI** + *spacer* **200/6** *2 doses BD*	*If already on MDI:* **Switch to Trimbow MDI 172/5/9** *2 doses BD*
AND	AND
As needed SABA reliever	

Alternative (more traditional) regimen - patients use a different inhaler for maintenance (OD or BD) and reliever (PRN)

	Regular low dose ICS AND As needed SABA Reliever	Regular low dose ICS/LABA AND As needed SABA Reliever	Regular moderate dose ICS/LABA AND As needed SABA Reliever	Add on trial of LAMA Discontinue if no benefit after 3 months
DPI	LICENSED OPTIONS INCLUDE: • Budesonide Easyhaler 200mcg 1 dose BD • Flixotide Accuhaler 100mcg 1 dose BD	LICENSED OPTIONS INCLUDE: • Relvar Ellipta 92/22 1 dose OD • Atectura Breezhaler 125/62.5mcg 1 dose OD • Fostair NEXThaler 100/6 1 dose BD • Symbicort Turbohaler 200/6 1 dose BD • Fobumix Easyhaler 160/4.5 1 dose BD • DuoResp Spiromax 160/4.5 *1 dose BD*	LICENSED OPTIONS INCLUDE: • Relvar Ellipta 92/22 1 dose OD • Atectura Breezhaler 125/127.5mcg 1 dose OD • Fostair NEXThaler 100/6 2 doses BD • Symbicort Turbohaler 200/6 2 doses BD • Fobumix Easyhaler 160/4.5 2 doses BD • DuoResp Spiromax 160/4.5 2 doses BD	*If already on a DPI device:* Add on Spiriva Respimat 2.5mcg *2 doses OD*
	OR	OR	OR	OR
MDI	LICENSED OPTIONS INCLUDE: • Clenil Modulite 200mcg + spacer 1 dose BD • Soprobec 200mcg + spacer 1 dose BD • Qvar Easi-Breathe (BAI) 100mcg 1 dose BD	LICENSED OPTIONS INCLUDE: • Fostair MDI 100/6 + spacer 1 dose BD • Luforbec MDI 100/6 + spacer 1 dose BD	LICENSED OPTIONS INCLUDE: • Fostair MDI 100/6 + spacer 2 doses BD • Luforbec MDI 100/6 + spacer 2 doses BD	Switch to Trimbow MDI 87/5/9 2 doses BD *(Triple therapy containing* ***moderate dose*** *ICS/ LABA/LAMA)*
	AND	AND	AND	AND
Reliever	LICENSED OPTIONS INCLUDE: • Ventolin Accuhaler 200mcg 1 dose PRN • Salbutamol Easyhaler 100mcg 1-2 doses PRN • Salamol MDI 100mcg + spacer 1-2 doses PRN			
	AND	AND		
Add-on	Trial of montelukast 10mg at night (Discontinue if no benefit after 6 weeks)			

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Respiratory Health Implementation Group

Y Grŵp Gweithredu ar Iechyd Anadlol

All Wales Adult Asthma Diagnosis and Management Guidelines

Supporting notes

THE ALL WALES ASTHMA DIAGNOSIS GUIDELINE

allwales.icst.org.uk/guidelines/all-wales-adult-asthma-diagnostic-guidelines/

THE ALL WALES ASTHMA MANAGEMENT & PRESCRIBING GUIDELINE

allwales.icst.org.uk/guidelines/all-wales-adult-asthma-management-guidelines/

FOREWORD FROM THE NATIONAL ASTHMA CLINICAL LEAD

The diagnosis and management of asthma is complicated by many factors. Objective investigations are key in ensuring an accurate diagnosis but are not available in all healthcare settings. Poor concordance with medication is common. Co-morbidity causing breathlessness is common and may complicate asthma. The main guidelines for asthma all differ slightly in their approach.

Originally published in August 2020, the All Wales asthma guideline aimed to improve asthma outcomes and reduce variation in inhaler prescribing in the management of adult asthma. It was based on recommendations from the British Thoracic Society (BTS), National Institute for Health and Care Excellence (NICE) and Global Initiative for Asthma (GINA).

The 2021 update encouraged consideration of the NHS Wales decarbonisation agenda. The 2024 update follows the Global Initiative for Asthma approach in recommending anti-inflammatory reliever therapy as the preferred regimen for managing mild-moderate asthma. In the Spring of 2023 ICS/formoterol was approved as a reliever therapy in addition to its pre-existing licence as a preventer or MART therapy. This has allowed the development of the All Wales guidelines which when implemented should improve asthma care; reducing reliance on short acting bronchodilators, reducing the risk of asthma exacerbations and improving the respiratory carbon footprint of the NHS. This approach has been endorsed by the primary care respiratory society (PCRS). In the UK this new therapy has not yet been incorporated in national guidelines with the joint British Thoracic Society/NICE guidelines currently being under development.

I hope that the 2024 update is embraced by healthcare professionals in Wales and encourage anyone who would like further support to seek out their local respiratory specialists in order to apply this guideline to practice.

Dr Katie Pink
Consultant Respiratory Physician
National Adult Asthma Clinical Lead, NHS Wales

ACKNOWLEDGEMENTS

Thank you to the Respiratory Health Implementation Group (RHIG), the wider network of Adult Asthma clinicians who have contributed towards these guidelines, and for all the support to disseminate these guidelines to GP practices and community pharmacies across NHS Wales.

DIAGNOSIS

The diagnosis of asthma is a clinical diagnosis supported by tests of airway hyper-responsiveness and airway inflammation. All patients with suspected asthma should undergo objective testing including spirometry/reversibility and peak flow diary monitoring to document evidence of variable airflow obstruction. Exhaled nitric oxide (where available) is a simple breath test that can identify airway inflammation that is likely to respond to inhaled corticosteroids. An elevated exhaled nitric oxide level (FeNO) is supportive (but not diagnostic) of asthma[1,2]. The Respiratory Health Implementation Group (RHIG) has produced a consensus document on the use of FeNO[3].

It should be usual practice to perform objective testing prior to starting therapy for asthma. If inhalers have already been prescribed, these will need to be withheld prior to performing bronchodilator reversibility testing. Most inhaled corticosteroid/long-acting $beta_2$agonists (ICS/LABAs) will need to be withheld for >12h however once daily preparations (e.g. Relvar) will need to be withheld for >24h. Short acting $beta_2$ agonists (SABAs) need to be withheld for >4h and long acting anti-muscarinic agents (LAMAs) for >36h. Inhalers do not need to be withheld prior to performing FeNO however levels of FeNO will be reduced by inhaled corticosteroids. Ideally objective tests should be performed prior to starting inhaled therapy.

Reversibility to either inhaled or oral corticosteroids could also be considered if initial spirometry is obstructive (forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] ratio < 0.7 or below lower limit of normal). A change in FEV_1 of >12% and 200ml confirms reversibility and supports an asthma diagnosis. Some patients with Chronic Obstructive Pulmonary Disease (COPD) also show reversibility and asthma and COPD can coexist (asthma/COPD overlap syndrome [ACOS]).
https://allwales.icst.org.uk/programmes/making-a-diagnosis-of-asthma/

Clinical history is important in distinguishing asthma from COPD.

When diagnostic uncertainty remains, or both COPD and asthma are present, use the following findings to help identify asthma:

- A large (over 400 ml) response to bronchodilators
- A large (over 400 ml) response to 30mg oral prednisolone daily for 2 weeks
- Serial peak flow measurements showing 20% or greater diurnal or day-to-day variability.

Clinically significant COPD is not present if the FEV1 and FEV1/FVC ratio return to normal with drug therapy[4].

GENERAL PRINCIPLES OF MANAGEMENT

The aims of asthma management are to achieve good symptom control and to minimise the future risk of asthma exacerbations, mortality, persistent airflow obstruction and side effects of treatment.

Asthma is an inflammatory condition and recent guidelines (British Thoracic Society and Scottish Intercollegiate Guidelines Network 2019[1], NICE 2017[2], and GINA 2023[5]) have highlighted the need to treat all individuals symptomatic of asthma with inhaled corticosteroids. The practice of using a short acting bronchodilator (SABA) as monotherapy is now outdated and reports such as the National Review of Asthma Deaths (NRAD)[6] have highlighted the potential dangers of this practice with underuse of inhaled corticosteroids and over reliance on beta-agonists a contributory factor in a number of deaths.

For individuals with **mild, intermittent asthma** there is now good evidence for the use of ICS/formoterol on an 'if and when required' (PRN) basis in response to symptoms (no need for maintenance therapy). This is referred to as anti-inflammatory reliever therapy (AIR). Symbicort Turbohaler 200/6 is the first inhaler to receive a licence from the MHRA for use in this way (in addition to its role as a preventer and MART therapy). The evidence supporting this approach is with low dose budesonide-formoterol. Other ICS-formoterol preparations have not been studied but the use of beclomethasone-formoterol is supported in GINA guidelines[5]. This is now the preferred option for individuals with mild asthma (defined as symptoms less than 4-5 days per week). In trials, low dose ICS/formoterol taken on a PRN basis resulted in a two-thirds reduction in asthma exacerbations compared to SABA alone[7]. In addition, use of PRN low dose ICS/formoterol resulted in a reduction in emergency department visits and hospitalisations compared to regular ICS[8,9].

The use of PRN ICS/formoterol in this way allows patients to titrate the dose of inhaler to their symptoms. In this way more is used when symptoms are worse (for example during an upper respiratory tract infection or high pollen counts), and less when symptoms are well controlled. It is important patients do not revert back to their SABA inhaler during exacerbations as this is when the anti-inflammatory effect of the ICS/formoterol is most beneficial. Studies have shown an improvement in asthma outcomes and an overall reduction in the average daily dose of ICS with this approach[8].

For individuals with **persistent** asthma the use of a regular, maintenance formoterol containing ICS/LABA with the same inhaler used as a reliever is the preferred option. This maintenance and reliever therapy (MART) approach has been shown to reduce exacerbations compared to conventional asthma treatments (see later section on MART)[10].

It is recognised that the strong preference for anti-inflammatory reliever medication and a move away from short acting bronchodilator therapy represents a significant change from older asthma guidelines. The UK is late to this approach with it already being used widely throughout Europe and New Zealand. The evidence is now clear that this approach is better for patients with a reduction in asthma exacerbations and risk of hospitalisation. It is anticipated that some patients will find the switch difficult and will need a clear explanation of the benefits.

An alternative (more traditional) regimen is provided. For those patients who are very stable on their current preventer inhalers with good adherence, no exacerbations and rare use of SABA (<3 SABA inhalers a year) there is no need to change management. If patients are poorly controlled or experience exacerbations on the traditional regimen they should be switched to the preferred regimen. This will usually be done at the same treatment step, but in very poor control a step up may be required.

If a well controlled patient wishes to switch to the preferred regimen (e.g. for simplicity of single inhaler) they can be switched at the same treatment step.

ASTHMA CONTROL

An objective measure of asthma control and risk of adverse outcomes should be recorded during each consultation. This would usually include a symptom score, such as the 'asthma control test' [ACT] or the Royal College of Physicians [RCP] 'three questions', a measure of airflow obstruction (peak flow or spirometry) and an assessment of exacerbation risk based on ICS adherence, reliever use and any requirement for oral steroids.

Reliever inhalers should not be required more than twice per week. This is particularly relevant for patients using SABA reliever therapy. The risk of severe exacerbations and mortality increases incrementally with higher SABA use, independent of treatment step. Prescribing three or more 200 dose SABA inhalers per year is associated with an increased risk of severe exacerbations and mortality, and reflects very poorly controlled asthma[5].

For those patients using anti-inflammatory reliever therapy (or MART) each extra dose taken provides additional controller medication and hence helps to prevent exacerbations. The cut off of >2 doses of reliever therapy a week indicating poor control does not therefore apply for the preferred regimen. The average frequency of reliever doses of ICS/formoterol over a 4 week period should be considered. If persistent rescue doses beyond the maintenance dose are required (as a guide >7 per week), this should be considered when reviewing the necessary maintenance dose and need for add on therapy[17].

LEVELS OF ASTHMA CONTROL AND EXACERBATION RISK[5]

<table>
<tr><td colspan="4">Assessment of current clinical control (over last 4 weeks)</td></tr>
<tr><td>Characteristic</td><td>Completely Controlled</td><td>Partly Controlled</td><td>Uncontrolled</td></tr>
<tr><td>Daytime symptoms more than twice per week</td><td rowspan="4">None of these</td><td rowspan="4">1-2 of these</td><td rowspan="4">3-4 of these</td></tr>
<tr><td>Limitation on activities</td></tr>
<tr><td>Nocturnal symptoms/ awakening</td></tr>
<tr><td>SABA reliever more than twice per week (if on traditional regimen)</td></tr>
<tr><td>Asthma Control Test</td><td>21-25 well controlled</td><td>16-20 poorly controlled</td><td>0-15 very poorly controlled</td></tr>
<tr><td colspan="4">Additional risk factors for future exacerbation</td></tr>
<tr><td>Previous exacerbation/asthma attack</td><td colspan="3">Especially within last 12 months, intubation/intensive care admission (ever)</td></tr>
<tr><td>Medication adherence</td><td colspan="3">Increased risk if poor ICS adherence (<80%), poor inhaler technique, and high SABA use (increased risk of exacerbation if ≥3 SABA/year and mortality if >1 SABA inhaler/month)</td></tr>
<tr><td>Lung function (Peak flow or FEV_1)</td><td colspan="3">Increased risk if reduced lung function, especially if <60% predicted</td></tr>
<tr><td>Co-morbidities</td><td colspan="3">Smoking, obesity, gastro-oesophageal reflux disease, pregnancy, chronic rhino-sinusitis, anxiety, depression, confirmed food allergy, socioeconomic problems</td></tr>
<tr><td>Type 2 inflammatory biomarkers</td><td colspan="3">Higher eosinophils and FeNO</td></tr>
</table>

DEVICE SELECTION

Always involve the patient when choosing the device. Take into account individual preference, ease at which the device can be used and prior success or failure with different preparations, as well as the environmental impact of the inhaler. Ensure continuity of device for individual patients so that only one inhaler technique is required. Whenever possible do not mix Metered Dose Inhalers (MDIs) and Dry Powder Inhalers (DPIs) as they require radically different inhaler techniques (slow and gentle vs forceful and deep). Current (poor) practice is that many patients are prescribed MDI SABA reliever despite being on a DPI preventer. This should be addressed by switching patients to the preferred regimen.

A patient decision aid has been produced by NICE which may be useful in guiding device selection[11]. MDIs have a higher carbon footprint than dry powder devices and British Thoracic Society (BTS) guidelines recommend that inhalers with low global-warming potential should be used when they are likely to be equally effective[1]. MDIs currently contribute an estimated 3.5% of the carbon footprint of the NHS. MDIs comprise 70% of all inhalers prescribed in the UK, but only 14% in Sweden. The default option should be to prescribe a DPI, unless a patient has a better technique, or prefers, an MDI. Patients should also be encouraged to use any locally available inhaler recycling and recovery schemes. Patients can return empty or unused inhalers to their community pharmacy.

Ventolin (salbutamol) MDI has been omitted from the guidelines as it is an MDI with a very high carbon footprint (>25 kg $CO2_e$ per inhaler). Salamol in comparison has a lower carbon footprint (<10 kg $CO2_e$ per inhaler) although is still classed as a high global warming potential inhaler in comparison to DPIs.

DPIs require inspiratory flow rates of 30-90 l/min. The In-Check DIAL device or training whistles can be used to check patients can achieve this. MDIs should be used with a spacer device (Aerochamber flow-vu or Volumatic) to improve technique and lung deposition. The Flo-Tone device is also useful to optimise MDI technique. It is important to teach patients that they need to wait 30 seconds between activations of their MDI devices to allow time for the canister to recharge before administering a second dose.

Full instruction on the inhaler technique for specific devices can be found on the Right-Breathe app or asthma UK website, **www.asthma.org.uk/advice/inhaler-videos**. The NHS AsthmaHub app contains educational videos on inhaler technique (**www.healthhub.wales/asthmahub/**)

Inhaled corticosteroids and long-acting bronchodilators MUST be prescribed as a combination product to obviate the risk of patients inadvertently taking the LABA as mono-therapy, which has been associated with increased risk of mortality. All inhalers should also be prescribed by brand to prevent the wrong inhaler device being inadvertently issued by the pharmacy.

The costs of the inhaler devices have not been included on the guidelines as these are prone to changes over time. As stated previously the most important factor in choosing an inhaler is selecting a device the patient is able to and is willing to use. Where there is a choice of inhalers the lowest cost item should be preferred. An increasing number of bioequivalent inhalers are coming to market. These can be considered but will involve a face to face review with the patient to explain differences in how to use the device.

STEPPING UP THERAPY

It is important to check and address factors known to be associated with poor asthma control at every opportunity including when considering a step up in treatment. The following factors should be considered:

- Diagnosis - is there good evidence for the asthma diagnosis?
- Inhaler technique
- Adherence with asthma medication. This can be checked by an open conversation with the patient - it is important to be non-judgemental and explore barriers to adherence with medication (e.g. dislike of device, side effects, chaotic lifestyle). The prescription 'fill rate' should be reviewed (i.e. the actual number of preventative inhalers collected [issued] in a 12 month period compared with the number that should have been collected [issued]). This is a surrogate measure of adherence and can prompt a conversation with a patient.
- Smoking status (including vaping) and referral to smoking cessation services
- Triggers and trigger avoidance (including occupation)
- Co-morbid conditions – e.g. weight management, obstructive sleep apnoea, dysfunctional breathing pattern, rhinitis

Asthma control should be re-assessed within 3 months of a change in therapy[2].

MAINTENANCE AND RELIEVER THERAPY (MART)

A number of combination inhalers are licensed for use in a variable dosing regime termed MART (Maintenance And Reliever Therapy). These include Fostair 100/6 MDI and NEXThaler, Symbicort 200/6 Turbohaler, Fobumix 160/4.5, DuoResp Spiromax 160/4.5, and Wockair 160/4.5. The higher strength preparations are not licensed for this use.

The patient should take twice daily maintenance therapy and then also use the same product and device as a reliever medication if required. This enables the amount of inhaled steroid to be titrated against symptoms. Do not prescribe a separate reliever inhaler if a patient is on this regime. MART regimes can help overcome poor adherence with ICS inhalers and historic over reliance on beta$_2$ agonist reliever therapy as well as reducing exacerbation frequency.

LICENSED MART INHALERS

DuoResp Spiromax MART	160/4.5 – Either 1 dose twice daily plus PRN or 2 doses twice daily plus PRN	Max. daily dose 12 doses *
Fobumix Easyhaler MART	160/4.5 – Either 1 dose twice daily plus PRN or 2 doses twice daily plus PRN	Max. daily dose 12 doses *
Fostair NEXThaler or MDI MART	100/6 – 1 dose twice daily plus PRN	Max. daily dose 8 doses
Luforbec MDI MART	100/6 – 1 dose twice daily plus PRN	Max. daily dose 8 doses
Symbicort Turbohaler MART	200/6 – Either 1 dose twice daily plus PRN or 2 doses twice daily plus PRN	Max. daily dose 12 doses *
Wockair MART	160/4.5 – Either 1 dose twice daily plus PRN or 2 doses twice daily plus PRN	Max. daily dose 12 doses *

The maximum recommended number of doses of an inhaler differs depending on which inhaler is used as part of the MART regime.

* With DuoResp Spiromax, Fobumix Easyhaler, Symbicort Turbohaler and Wockair it is recognised that a total daily dose of more than 8 doses is not normally needed, however a total daily dose of up to 12 doses could be used for a limited period (usually 2-3 days).

If a patient is deteriorating or has failed to respond to an increase in as-needed doses of ICS/formoterol over 2-3 days they should seek medical advice and may need treatment for an exacerbation. If a patient is needing more than 12 puffs in a 24hr period they should seek urgent (same day) medical advice.

As a guide 2-7 doses of PRN inhaler use a week is acceptable. If an individual persistently requires more than 7 doses the reason for this should be established and may need their maintenance therapy stepped up. Always check inhaler technique, comorbidity and consider alternate causes of breathlessness prior to stepping up therapy.

If less than 2 doses are regularly required consider whether the maintenance dose can be stepped down.

Fostair and Luforbec are only licensed at a dose of 1 dose twice daily plus PRN. They been included in the All Wales Guidelines as an unlicensed option at step 3 (2 doses twice daily plus PRN) in order to allow a MDI option for those who need this, whilst still receiving the benefits of anti-inflammatory reliever therapy. The total maximum daily dose is unchanged (8 doses). Further information on the use of unlicensed medication can be found on the All Wales Therapeutics and Toxicology Centre website Understanding unlicensed medicines - All Wales Therapeutics and Toxicology Centre (nhs.wales)

ADD-ON THERAPIES

Montelukast

Montelukast can be trialled at step 2 or 3 of the treatment pathway dependent on patient phenotype and choice. It may be particularly helpful in those with exercise induced asthma, aspirin exacerbated asthma and in asthma associated with allergic rhinitis. We would usually recommend a trial in such individuals prior to stepping up to step 3.

Always treat co-existing allergic rhinitis with a separate nasal steroid +/- antihistamines to prevent asthma triggering from nasal inflammation.

LAMA

The addition of a long acting antimuscarinic agent (LAMA) is an option for adult patients who are on maintenance moderate dose ICS/LABA who experience one or more asthma exacerbations in the previous year[12,13]. This therapy may be of particular benefit in patients who have both asthma and COPD.

Add-on Spiriva Respimat (tiotropium) allows patients to continue with their moderate strength ICS/LABA MART regime and is the LAMA of choice. For those on the traditional regimen using MDi devices the alternative is to switch to the triple therapy inhaler, low strength Trimbow MDI (beclometasone dipropionate 87mcg/ formoterol 5mcg/glycopyrronium 9mcg).

For individuals at step 5 on high strength ICS/LABA who need a LAMA there are three options available: add on Spiriva Respimat (tiptropium) or switching to Enerzair Breezhaler (DPI - indacaterol/ glycopyrronium/ mometasone) or high strength Trimbow (MDI - beclometasone dipropionate 172mcg/formoterol 5mcg/ glycopyrronium 9mcg).

	Spiriva Respimat	Trimbow MDI 87/5/9	Trimbow MDI 172/5/9	Enerzair Breezhaler
ICS strength	LAMA only Separate ICS/LABA to be prescribed	Moderate strength ICS (plus LABA/LAMA)	High strength ICS (plus LABA/LAMA)	High strength ICS (plus LABA/LAMA)
Dose	2 doses OD	2 doses BD (via spacer)	2 doses BD (via spacer)	1 dose OD
Device	Soft mist inhaler (spacer can be used if preferred)	MDI	MDI	Breezhaler (DPI)

Oral theophylline is a further add-on therapy that can be trialled at step 5 (usually done on recommendation of secondary care).

Always review response to add-on therapies and discontinue if ineffective.

REFERRAL/SPECIALIST THERAPY

Patients who remain uncontrolled despite moderate dose ICS/LABA +/- additional controller agents have difficult to control or severe asthma. A proportion of these will have an alternative or co-existent condition that is contributing to their symptoms. Objective and structured evaluation can help identify and treat these conditions. Patients with suspected occupational asthma should be referred.

Some individuals will have severe eosinophilic/TH2 high asthma and will require high dose ICS/LABA combination inhalers. Others may have neutrophilic asthma and may benefit from treatments such as azithromycin.

Patients receiving 2 or more courses of oral steroids in a 12 month period despite adherence with optimised therapy should be referred.

There are a number of biological therapies now licenced for severe asthma for individuals experiencing three or more exacerbations requiring oral steroids a year. These can be prescribed where appropriate following review by a specialist in severe asthma, and discussion in the All Wales Difficult Asthma MDT.

STEPPING DOWN

All asthma guidelines recommend a step wise approach including the need to consider stepping down therapy once control is achieved and maintained[1,2]. High-dose ICS carries a risk of systemic side effects (adrenal suppression, growth retardation, decrease in bone mineral density and cataracts) and these risks should be balanced against the benefits.

Reductions in asthma therapy should be considered if a patient has had complete asthma control over a three month period. A decision to step down should take into account how difficult it was to achieve stability and also whether previous step down attempts have resulted in exacerbations. Seasonal variation in symptoms should also be considered. Stop or reduce dose of medicines in an order that takes into account the clinical effectiveness when the medicine was introduced, side effects and the person's preference. It is recommended that the dose of ICS is reduced by no more than 50% each time. The risks and benefits of dose reduction should be discussed with patients and their carers.

SELF MANAGEMENT & ASTHMA ACTION PLANS

The importance of supported self-management is highlighted in national guidelines[1,2]. This should include a written personalised asthma action plan containing advice on how to recognise a loss of asthma control (peak flow monitoring or symptoms) and what action to take to regain control, including when to start oral steroids and seek emergency advice. Patients should be encouraged and supported to download the Asthmahub app. A recent survey has identified that regular app users improved their respiratory health with 36% of users reducing their visits to the GP and 19% reducing their visits to A&E.

Patients should be prescribed a peak flow meter to aid self-management. **Best peak flow should be ascertained when treatment is optimised and symptoms are stable. Best peak flow is more accurate than predicted peak flow. Trigger points should be individualised but as a guide oral steroids are usually required when peak flow reaches ≤60% of best and emergency review is usually necessary when peak flow reaches ≤50% of best**.

There is evidence that quadrupling ICS dose when asthma control starts to deteriorate (peak flow ≤80% best) can reduce the risk of an exacerbation[14]. In those individuals prescribed anti inflammatory reliever/ MART therapy this will be achieved through increased use of PRN reliever doses of their ICS/formoterol inhaler.

EXACERBATIONS/ EMERGENCY TREATMENT (AIR/MART)

For emergency treatment of acute asthma patients can take up to 6 puffs of their ICS/Formoterol containing inhaler at one minute intervals. If 6 puffs do not relieve the symptoms urgent medical advice should be sought. Patients should NOT go back to short acting bronchodilator therapy during exacerbations as this is the time the anti-inflammatory reliever therapy will have the most benefit.

In rare situations some select individuals on the preferred regimen may have a MDI SABA reserved for emergency use only. However most individuals should use their ICS/formoterol inhaler.

For those individuals on the traditional regime one puff of SABA should be administered as a reliever every 60 seconds up to 10 puffs.

Routine prescription of antibiotics is not indicated unless bacterial infection is suspected.

ORAL CORTICOSTEROID STEWARDSHIP

Oral corticosteroids are highly effective for the treatment of acute asthma exacerbations however evidence suggests indiscriminate use is common. It is now recognised that even a single course of oral corticosteroids is associated with significant adverse effects. Within 30 days of a course of oral corticosteroids there is an increased risk of fractures, venous thromboembolism and sepsis. The long-term side effects are well known and include osteoporosis, diabetes, cataracts, weight gain and adrenal insufficiency.

A loss of asthma control requiring a course of oral corticosteroids is a significant event and requires urgent follow up to identify the reasons for the loss of control and to take steps to prevent this from happening again. Patients should not be issued recurrent courses of oral corticosteroids without review, and they should not be prescribed ‘just in case’. If a patient with asthma has a respiratory infection with no evidence of bronchospasm this can be treated with antibiotics alone.

Refer patients requiring two or more courses of oral corticosteroids despite optimising asthma therapy. No-one should be started on regular oral corticosteroids in primary care for asthma.

TEMPLATE FOR ASTHMA REVIEW

All individuals with asthma should receive a review at least annually. This will need be more frequent if poor control is identified and will need to be face to face. All patients should be reviewed after an emergency admission or exacerbation.

- Assess asthma control (e.g. RCP 3 questions, Asthma Control Test)
- Check peak flow and/or spirometry
- Review medication including use of reliever medication, adherence with preventer therapies (check prescription fill rate)
- Number of exacerbations in last 12 months/since last review
- Review risk factors for asthma death (e.g. previous near fatal asthma, admission in last 12 months, heavy use of SABA, poor adherence, failure to attend reviews, alcohol/drug misuse)
- Review inhaler technique and consider if patient would benefit from and be willing to switch to a low global warming potential inhaler (DPI)
- Review triggers e.g. pets, occupation, NSAIDs, Beta-blockers
- Smoking status – refer to smoking cessation if required
- Reinforce need for annual flu vaccination and check has received COVID vaccine
- Review asthma action plan and ensure patient knows how to manage an exacerbation and when to seek advice
- If well controlled for >3 months consider stepping down therapy
- If poorly controlled consider and address reasons behind this (e.g. poor inhaler technique, adherence) – if no reversible factors can be identified then consider stepping up therapy.
- Refer to secondary care if poor control despite moderate-dose therapies or if required ≥2 courses oral corticosteroids/year

NATIONAL STEROID TREATMENT CARDS

A National Steroid Treatment Card should be given to all patients prescribed high dose inhaled corticosteroids. In addition, steroid cards should be considered for people using other glucocorticoids (including potent/very potent topical glucocorticoids, intra-articular injection, regular nasal glucocorticoids) alongside medium dose inhaled steroids. Further information on steroid treatment cards can be found in the Welsh Health Circular June 21[16]. The NHS Wales Adult Emergency Steroid Card can also be provided as a supplement to, but not a replacement for, the National Steroid Treatment Card. This is important for those patients who are steroid dependent (i.e. on long term/ regular prednisolone). Copies of both cards are available on the Welsh Endocrine and Diabetes Society website (**www.weds-wales.co.uk/steroid-therapy/**).

TABLE OF ICS EQUIVALENCE

The table below shows the available inhalers used to treat asthma and their inhaled steroid dose equivalents. It is recognised that generic versions of many of the combination inhalers are now available and not all have been included in this table.

	Dose		
ICS	Low	Medium	High *(steroid treatment card)*
Clenil Modulite (MDI) (Beclometasone dipropionate)	 200mcg 1 dose BD	 200mcg 2 doses BD	 200mcg 4 doses BD
Soprobec (MDI) (Beclometasone dipropionate)	 200mcg 1 dose BD	 200mcg 2 dose BD	 200mcg 4 doses BD
Qvar Easi-Breathe (breath actuated MDI) (Beclometasone dipropionate)	 100mcg 1 dose BD	 100mcg 2 doses BD	 100mcg 4 doses BD
Budesonide Easyhaler (DPI) (Budesonide)	 200mcg 1 dose BD	 200mcg 2 doses BD	 400mcg 2 doses BD
Pulmicort Turbohaler (DPI) (Budesonide)	 100mcg 2 doses BD	 200mcg 2 doses BD	 400mcg 2 doses BD
Alvesco (MDI) (Ciclesonide)	 80mcg 2 doses OD	 160 mcg 2 doses OD	 160mcg 2 doses BD
Flixotide Accuhaler (DPI) (Flixotide)	 100 mcg 1 dose BD	 250 mcg 1 dose BD	 500mcg 1 dose BD
ICS/LABA			
Fostair (NEXThaler DPI) (Beclometasone dipropionate/ formoterol)	 100/6 1 dose BD	 100/6 2 doses BD	 200/6 2 doses BD
Fostair (MDI) (Beclometasone dipropionate/ formoterol)	 100/6 1 dose BD	 100/6 2 doses BD	 200/6 2 doses BD
Luforbec (MDI) (Beclometasone dipropionate/ formoterol)	 100/6 1 dose BD	 100/6 2 doses BD	N/A
Symbicort Turbohaler (DPI) (Budesonide/ formoterol)	 200/6 1 dose BD	 200/6 2 doses BD	 400/12 2 doses BD
Fobumix Easyhaler (DPI) (Budesonide/ formoterol)	 160/4.5 1 dose BD	 160/4.5 2 doses BD	 320/9 2 doses BD
DuoResp Spiromax (DPI) (Budesonide/ formoterol)	 160/4.5 1 dose BD	 160/4.5 2 doses BD	 320/9 2 doses BD
Relvar Ellipta (DPI) (Fluticasone furoate/ vilanterol)	 92/22 1 dose OD		 184/22 1 dose OD
Atectura Breezhaler (DPI) (Indacaterol acetate/mometasone furoate)	125/62.5 1 dose OD	125/127.5 1 dose OD	125/260 1 dose OD
Flutiform (MDI) (Fluticasone propionate/ formoterol)	125/5 1 dose BD	125/5 2 doses BD	250/10 2 doses BD
Seretide (MDI) (Fluticasone propionate/ salmeterol)	125/25 1 dose BD	125/25 2 doses BD	250/25 2 doses BD
Seretide Accuhaler (DPI) (Fluticasone propionate/ salmeterol)	100/25 1 dose BD	250/50 1 dose BD	500/50 1 dose BD
WockAIR (DPI) (Budesonide/ formoterol)	160/4.5 1 dose BD	160/4.5 2 doses BD	320/9 2 doses BD
ICS/LABA/LAMA			
Trimbow (MDI) (beclometasone dipropionate/ formoterol/ glycopyrronium)	N/A	87/5/9 2 doses BD	172/5/9 2 doses BD
Enerzair Breezhaler (DPI) (indacaterol/glycopyrronium/ mometasone)	N/A	N/A	114/46/136 1 dose OD

SHORT-ACTING RELIEVER INHALERS

The table below shows the available short-acting reliever inhalers used to offer short-term symptom relief. The use of SABA reliever inhaler more than twice per week indicates poor asthma control. Using ≥3 SABA inhalers per year is associated with increased risk of exacerbations and patients should be switched to the 'preferred regimen' (AIR) on the All Wales Guideline.

Short-acting bronchodilator	
Salbutamol Accuhaler (DPI) (Salbutamol)	 200mcg 1 dose PRN
Salbutamol Easyhaler (DPI) (Salbutamol)	 100mcg 1-2 doses PRN
Salamol Easi-Breathe (MDI) (Salbutamol)	 100mcg 1-2 doses PRN
Salamol (MDI) (Salbutamol)	 100mcg 1-2 doses PRN

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