GIG CYMRU NHS WALES

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/

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 FEV$_1$ and FEV$_1$/FVC ratio return to normal with drug therapy [4].

GENERAL PRINCIPLES OF MANAGEMENT

Asthma is an inflammatory condition and recent guidelines (British Thoracic Society and Scottish Intercollegiate Guidelines Network 2019[1] and NICE 2017[2]) have highlighted the need to treat all individuals symptomatic of asthma with inhaled corticosteroids. The practice of using a short acting bronchodilator as monotherapy is now outdated and reports such as the National Review of Asthma Deaths (NRAD)[5] 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 increasing support for the use of inhaled corticosteroid taken together with short acting bronchodilators on an 'if and when required' basis (PRN). This is only recommended for individuals with symptoms less than twice per month. If an individual has more frequent symptoms they should take regular inhaled corticosteroid to reduce their risk of exacerbation and asthma related death. The GINA strategy 2019 supports this approach.[6]

ASTHMA CONTROL

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

Reliever inhalers should not be required more than twice per week. 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, corresponding to daily use, is associated with an increased risk of severe exacerbations and mortality and reflects very poorly controlled asthma[6]. As an initial step patients prescribed more than 6 SABA reliever inhalers per year should be invited for **urgent review** of their asthma control.

- **Do not prescribe repeat SABAs without also prescribing an inhaled corticosteroid.**

LEVELS OF ASTHMA CONTROL AND EXACERBATION RISK

Assessment of current clinical control (over last 4 weeks)[6]

<table>
<tr><th>Characteristic</th><th>Completely Controlled</th><th>Partly Controlled</th><th>Uncontrolled</th></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>Need for reliever/rescue treatment more than twice per week</td></tr>
<tr><td>Asthma Control Test</td><td>25</td><td>20-24</td><td><20</td></tr>
<tr><td colspan="4">Additional risk factors for future exacerbation</td></tr>
<tr><td colspan="2">Previous exacerbation/asthma attack</td><td colspan="2">Especially within last 12 months
Intubation/intensive care admission (ever)</td></tr>
<tr><td colspan="2">Medication adherence</td><td colspan="2">Increased risk if poor ICS adherence (<80%) and high SABA use (increased risk of mortality if >1 SABA inhaler/month)</td></tr>
<tr><td colspan="2">Lung function (Peak flow or FEV_1)</td><td colspan="2">Increased risk if reduced lung function, especially if <60% predicted</td></tr>
<tr><td colspan="2">Co-morbidities</td><td colspan="2">Smoking, obesity, gastro-oesophageal reflux disease, pregnancy, chronic rhino-sinusitis, anxiety, depression, confirmed food allergy</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. 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 practice is that many patients are prescribed MDI SABA reliever despite being on a DPI preventer. Addressing the overuse of SABA MDI devices will have a significant impact on the overall carbon footprint from inhaled therapy. There may be some patients who can be prescribed a DPI SABA but may need an MDI for emergency treatment. Ventolin (salbutamol) MDI has been omitted from the guidelines as it is an MDI with a very high carbon footprint (>25 kg CO2e per inhaler). Salamol in comparison has a lower carbon footprint (<10 kg CO2e per inhaler) although is still classed as a high global warming potential inhaler in comparison to DPIs.

A patient decision aid has been produced by NICE which may be useful in guiding device selection[7]. **Metered dose inhalers 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**. MDIs currently contribute an estimated 3.5% of the carbon footprint of the NHS[1]. MDI's 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 inhalers to their community pharmacy.**

DPIs require inspiratory flow rates of 30-90 l/min. The In-Check DIAL device or training whistles should be used to check patients can achieve this. Metered dose inhalers (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.

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:

- 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 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 and DuoResp Spiromax 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. There is no need to 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. There is also evidence these regimes can reduce exacerbation frequency.

LICENSED MART INHALERS

Fostair NEXThaler or MDI MART	100/6 – 1 dose twice daily plus PRN	Max. daily dose 8 doses
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
Symbicort Turbohaler MART	200/6 – Either 1 dose twice daily plus PRN or 2 doses twice daily plus PRN	Max. daily dose 12 doses
Luforbec MDI MART	100/6 – 1 dose twice daily plus PRN	Max. daily dose 8 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 and Symbicort Turbohaler 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. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice and their maintenance therapy should be reconsidered.

Even in patients using a MART regime the persistent requirement for PRN doses of their inhaler more than twice per week indicates poor asthma control and should prompt a review of therapy.

ADD-ON THERAPIES

STEP 3

Montelukast may be particularly helpful in those with exercise-induced asthma and in asthma associated with allergic rhinitis. If patients do not benefit from a 6 week trial of this agent it should be discontinued.

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

STEP 5

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[8,9]. This therapy may be of particular benefit in patients who have both asthma and COPD.

There are now three options available for clinicians and patients: add-on Spiriva Respimat (tiotropium) or combination inhalers Trimbow MDI (beclometasone dipropionate/formoterol/glycopyrronium) and Enerzair Breezhaler (indacaterol/ glycopyrronium/ mometasone). Of note the triple therapy inhalers (Trimbow/Enerzair Breezhaler) contain different strengths of inhaled corticosteroid and caution is needed to ensure that the required dose of ICS is not inadvertently stepped up or down when commencing a triple therapy inhaler.

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

Within primary care it is envisaged that most patients will be on a moderate dose of ICS when a LAMA is considered. Of note, Trimbow is only available as a MDI device and therefore those who are using dry powder devices will be better managed with separate ICS/LABA and Spiriva Respimat inhalers (this combination also offers the lowest global warming impact).

Oral theophylline is a further add-on therapy that can be trialled at step 5.

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 asthma and will require high dose ICS/LABA combination inhalers. Others may have neutrophilic asthma and may benefit from additional bronchodilator therapy such as Spiriva Respimat.

In addition 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. 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 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[10]. In those individuals prescribed MART therapy this will usually be achieved through increased use of PRN reliever doses of their ICS/LABA inhaler.

In those individuals at step 1, it is relatively easy to achieve the required increase of ICS dose by quadrupling the use of their ICS inhaler. In those individuals on a fixed ICS/LABA regime (e.g. Relvar 92/22), prescribing an additional ICS inhaler may be required as part of an asthma management plan. For example if taking Relvar 92/22 OD prescribe additional fluticasone 250 accuhaler to take 3 doses BD in addition to Relvar as part of action plan when peak flow ≤80%, for maximum of 14 days – see table below. If an individual is already taking high dose ICS/LABA (step 5) the evidence for increasing ICS is less clear and is not currently routinely recommended.

It is recognised that this approach does require a motivated patient and will not be appropriate in all cases. In some cases an action plan proceeding immediately to oral steroids will be more appropriate.

HOW TO ACHIEVE A QUADRUPLING IN ICS AS PART OF PERSONALISED ACTION PLAN IN PATIENTS ON A FIXED DOSE COMBINATION INHALER

ICS/LABA	Maintenance Dose	Method of achieving increase in ICS	Additional ICS *(for use with action plan in addition to maintenance dose ICS/LABA)*
Fostair (MDI) (Beclometasone dipropionate with formoterol)	100/6 1 dose BD	Increase maintenance dose to 4 doses BD	N/A
	100/6 2 doses BD	Provide additional ICS	Clenil 200mcg 6 doses BD
Luforbec (MDI) (Beclometasone dipropionate with formoterol)	100/6 1 dose BD	Increase maintenance dose to 4 doses BD	N/A
	100/6 2 doses BD	Provide additional ICS	Clenil 200mcg 6 doses BD
Fostair NEXThaler (DPI) (Beclometasone dipropionate with formoterol)	100/6 1 dose BD	Increase maintenance dose to 4 doses BD	N/A
	100/6 2 doses BD	Provide additional ICS	Beclometasone Easyhaler 200mcg 6 doses BD
Symbicort (DPI) (Budesonide with formoterol)	200/6 1 doses BD	Increase maintenance dose to 4 doses BD	N/A
	200/6 2 doses BD	Provide additional ICS	Budesonide Turbohaler 200mcg 6 doses BD
Fobumix (DPI) (Budesonide with formoterol)	160/4.5 1 dose BD	Increase maintenance dose to 4 doses BD	N/A
	160/4.5 2 dose BD	Provide additional ICS	Budesonide Easyhaler 200mcg 6 doses BD
DuoResp Spiromax (DPI) (Budesonide with formoterol)	160/4.5 1 dose BD	Increase maintenance dose to 4 doses BD	N/A
	160/4.5 2 doses BD	Provide additional ICS	Budesonide Turbohaler or Easyhaler 200mcg 6 doses BD
Relvar (DPI) (Fluticasone furoate with vilanterol)	92/22 1 doses OD	Provide additional ICS	Fluticasone Accuhaler 250mcg 3 doses BD
Atectura Breezhaler (DPI) (Indacaterol acetate/ mometasone furoate)	125/62.5 1 dose OD	Provide additional ICS	
	125/127.5 1 dose OD	Provide additional ICS	
Trimbow (MDI) (beclometasone dipropionate/formoterol/ glycopyrronium)	87/5/9 2 doses BD	Provide additional ICS	Clenil 200mcg 6 doses BD

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

Computer based asthma annual review templates have been developed through RHIG.

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[11]. 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.

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

REFERENCES

1. British Thoracic Society and Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. 2019. Available at **https://www.brit-thoracic.org.uk/quality-improvement/guidelines/asthma/**

2. Asthma: diagnosis, monitoring and chronic asthma management. NICE guideline [NG80]. National Institute for Health and Care Excellence. November 2017. Available at **https://www.nice.org.uk/guidance/ng80/chapter/Recommendations#initial-clinical-assessment**

3. Consensus statement on FeNO testing- Respiratory Health Implementation Group. April 2018.

4. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE guideline [NG115]. National Institute for Health and Care Excellence. July 2019. Available at **https://www.nice.org.uk/guidance/ng115/chapter/Recommendations#diagnosing-copd**

5. The National Review into Asthma Deaths. Royal College Physicians. May 2014. Available at **https://www.rcplondon.ac.uk/projects/outputs/why-asthma-still-kills**

6. Asthma Management and Prevention. Global Initiative for Asthma (GINA) 2021. **https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf**

7. Patient decision aid: Inhalers for asthma. May 2019. Available at **https://www.nice.org.uk/guidance/ng80/resources/patient-decision-aid-pdf-6727144573**

8. All Wales Medicines Strategy Group. Final Appraisal Recommendation Spiriva Respimat. November 2018. Available at **https://awmsg.nhs.wales/files/appraisals-asar-far/final-recommendation-tiotropium-spiriva-respimat-1882/**

9. All Wales Medicines Strategy Group. Final Appraisal Recommendation. Enerzair Breezhaler. May 2021. Available at **https://awmsg.nhs.wales/files/appraisals-asar-far/final-recommendation-indacaterol-enerzair-Breezhaler-3141/**

10. McKeever et al. Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations. NEJM. March 2018. 378:902-910

11. Welsh health Circular June 21. Available at **https://gov.wales/sites/default/files/publications/2021-05/revised-national-steroid-treatment.pdf**