





Respiratory Health | The Pharmacist's Role

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Known as 'The Pharmacist Coach,' Rachel has 25 years experience in diverse areas of Pharmacy Practice – community, hospital, business – coaching and leading pharmacists and their teams. She coaches leaders across 6 continents to put their own oxygen masks on first, thrive as a person and be a leader who inspires others to be and do their best.

In addition to being a seasoned Pharmacist, Rachel is an International Coaching Federation Master Certified Individual and Team Coach (IMCI) and a Board Certified Health and Wellness Coach (NBC-HWC). She is also a certified Yoga and Breathwork Teacher and Mental Fitness Coach.










4Front's 6Ps of Positive Practice

PERSONAL	PURPOSE	PROFESSIONAL
PEOPLE	PRODUCT/ SERVICE	PROSPERITY




What to Expect

- ▶ Be an Active Participant
- ▶ Make notes for yourself
- ▶ Use Chat
- ▶ 90 min session
- ▶ Ask Questions in Chat



Aim


To empower you, as a pharmacist, to play a proactive role in promoting respiratory health, both in your professional practice and in your personal life.



Agenda

At the end of this session, you will be able to

1. **Outline** normal functioning of the respiratory system as well as common dysfunctions and pathophysiological processes that can affect respiratory health.
2. **Identify** how respiratory health directly affects overall health, wellbeing and performance.
3. **Structure** respiratory health interventions using SIMPLES framework, incorporating inhaler technique
4. **Apply** insights to optimise your own respiratory health, as well as empowering your patients to do the same.



What do YOU most want to learn?

Given the session aims and outcomes outlined, I invite you to type into CHAT what you are most curious to explore deeper in this session and WHY that is important to you.

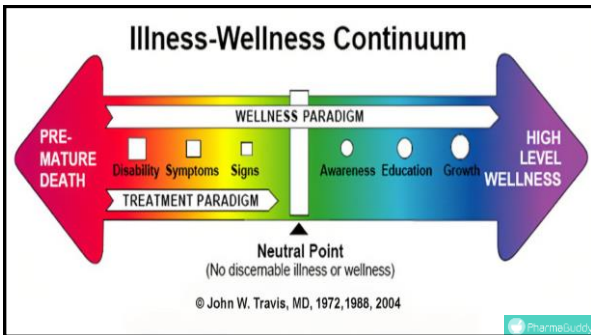
On a Scale of -10 to +10, where 0 = neutral,

How **proactive** are you in promoting respiratory health in your professional practice?

1. **Outline** normal functioning of the respiratory system as well as common dysfunctions and pathophysiological processes that can affect respiratory health.

WHO Definition of Health 1948

‘Health is a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity’.



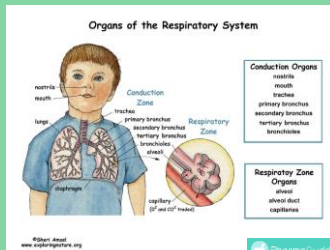
Respiration

- ▶ Physiological Respiration
- ▶ Cellular Respiration

Respiratory System



- What does the respiratory system do?
- Besides helping you inhale (breathe in) and exhale (breathe out), it:
- Allows you to talk and to smell.
- Warms air to match your body temperature and moisturises it to the humidity level your body needs.
- Delivers oxygen to the cells in your body.
- Removes waste gases, including carbon dioxide, from the body when you exhale.
- Protects your airways from harmful substances and irritants.



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Respiratory System Dysfunction



- Asthma
- COPD
- Infection
- Allergies
- Aging
- Inelastic respiratory muscles

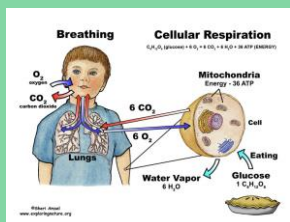
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Cellular Respiration



Generates usable ATP energy through metabolic process

1. Glycolysis
2. Pyruvate oxidation
3. Krebs's Cycle
4. Electron Transport Chain



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Cellular Respiration Dysfunction



- Oxygen Availability
- Respiratory or Cardiovascular System Disorders
- Metabolic Disorders
- Chronic Inflammation
- Mitochondrial Stressors
- Nutrient Intake
- Exposure to toxins
- Age
- Sedentary Lifestyle
- Certain Medications

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2. **Identify** how respiratory health directly affects overall health, wellbeing and performance.

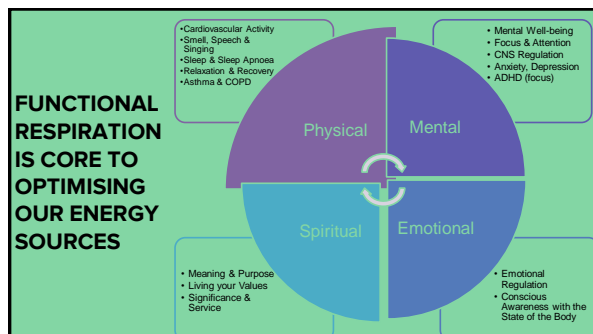


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Psycho-Social Factors Affecting Respiratory Function

- ▶ Posture (while sitting, driving, working)
- ▶ Stress
- ▶ Anxiety, Worry or Depression
- ▶ Fear of Breathlessness
- ▶ Panic Attacks

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3. **Structure** respiratory health interventions using **SIMPLES** framework, incorporating inhaler technique



SIMPLES Structured Review For Respiratory Consultations

- S** - Smoking
- I** - Inhalers
- M** - Monitoring
- P** - Pharmacotherapy
- L** - Lifestyle
- E** - Education
- S** - Support

Review Respiratory Case Study

- S** - Ms JR is a 29 year old, DPS asthma patient
- I** - Her 6/12 repeat prescription (on file for the past two months) includes Salbutamol PRN and Seretide® 250 Diskus BD
- M** - In the past two months, she has been dispensed 4 Salbutamol inhalers and NO Seretide® (On each occasion she stated she "has enough" Seretide® to keep her going)
- L** - She has presented today with a prescription for antibiotics and oral prednisolone

Smoking and Respiratory Health

- S** - **Mortality:** WHO Smoking is responsible for 8 million deaths annually
- I** - **Lung Cancer:** Smoking 15-30 times more likely to develop lung cancer than non-smokers
- M** - **COPD, Chronic Bronchitis, Emphysema:** 80-90% of cases attributed to smoking
- P** - **Asthma:** 1 in 5 asthma deaths – active smokers. Exposure to smoke (1st or 2nd hand) triggers asthma attacks and increases risk of dying from asthma
- L** - **Respiratory Infections:** Increased susceptibility to respiratory infections and increased risk of prolonged and more severe illness.
- E** - **Sleep:** Increased risk of Snoring, Sleep Apnoea and Insomnia

Smoking | Pharmacists' Role

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- Pharmacists & staff should:
 - Open smoking cessation conversation at every opportunity
 - Offer ongoing support to people trying to quit
 - Combine behavioural support & counselling with pharmacotherapy to enhance efficacy
- How effective is your team currently in "making every contact count"?





Inhaler Technique

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- Critical for efficacy
 - NRAD – Only 49% of people had inhaler technique checked in year before death
 - Only 7% HCP could demonstrate ALL the correct steps for a MDI – Thorax (2010)

How would you rate your competency?





MDI Inhaler Technique

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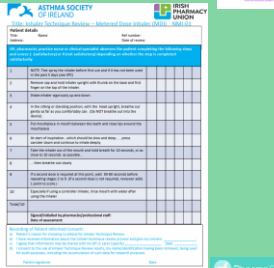
How to use a metered dose inhaler


- Remove cap and shake inhaler
- Breathe out gently
- Put mouthpiece in mouth between the teeth and close lips, press canister down and inhale deeply
- Hold breath for 10 seconds, or as long as possible, then breathe out
- Wait for 30-60 seconds before repeating steps 2-4 for a second dose

Demonstrate your inhaler technique to your GP, nurse, pharmacist or clinical specialist at every opportunity

Asthma Society of Ireland | Asthma Action Plan 2022 | 44 of 64







Inhaler Devices

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- Pressurised Metered Dose Inhalers
- Breath Actuated Inhalers
- Dry Powder Inhalers
- Spacer Devices
- Nebulisers

Poster from Asthma Society of Ireland





Inhaler Technique Counselling

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- Check inhaler technique at EACH visit
- Know how to counsel patients on the full range of inhalers you dispense
 - “Slow and Deep” for metered dose inhaler
 - “Forcefully and Deep” for turbobhaler
 - “Steady and Deep” for diskus





Inhaler Technique | Pharmacists' Role

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- Clear opportunity to improve outcomes
 - HCP with most patient contact
 - Medicines experts
- Pharmacist Resources
 - Patient Information Leaflet
 - Placebo inhalers & training
 - Video library www.asthma.ie

Inhaler Technique Videos | Asthma Society of Ireland





Monitoring – Tools to Support Pharmacist/Patient Partnerships

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- Spirometry
- Peak Expiratory Flow (PEF) Monitoring
- Six Minute Walk Test
- Wearable Health Technology
 - Pulse Oximetry
 - Respiratory Rate Monitoring
 - Heart Rate Variability (HRV)
- Symptom Tracking
- Body Oxygen Level Test (BOLT) / Control Pause Test
- Pollen Tracker

Monitoring – Pharmacists' Role Assessment of Asthma Symptom Control

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In the past 4 weeks, has the patient had:	Yes/No	Well Controlled	Partly Controlled	Uncontrolled
Daytime symptoms more than twice/week?		None of these	1-2 of these	3-4 of these
Any night-time waking due to asthma?				
Reliever needed more than twice/week?				
Any activity limitation due to asthma?				

Self-Monitoring Tools for Patient

Pharmacotherapy

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National Clinical Care Programme for Respiratory includes

- ▶ **Asthma** [2023 GINA Main Report - Global Initiative for Asthma - GINA](https://www.ginasthma.org) ([ginasthma.org](https://www.ginasthma.org))
- ▶ **COPD** [2023 GOLD Report - Global Initiative for Chronic Obstructive Lung Disease - GOLD](https://www.goldcopd.org) ([goldcopd.org](https://www.goldcopd.org))

Respiratory Infections

- ▶ [Antibiotic Prescribing - HSE.ie](#)
- ▶ [Immunisation - HSE.ie](#)
- ▶ [Acute Respiratory Infection - Health Protection Surveillance Centre \(hpsc.ie\)](#)

Pharmacotherapy | Asthma

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GINA 2023 – Adults & adolescents 12+ years

Personalised asthma management for individual patient needs

TRACK 1: PROGRESSIVE CONTROLLER ICS AND RELIEVER
Using ICS formoterol as the preferred controller for Step 1, 2, 3, 4, and 5. An add-on long-acting beta₂-agonist (LABA) is added at Step 2, 3, 4, and 5. LABA should not be used as a sole controller.

TRACK 2: Asthma CONTROLLED WITH RELIEVER
Using SABA as the preferred reliever. If the patient is unable to achieve control with SABA, consider Step 1 treatment.

RELIEVER: As needed low-dose ICS-formoterol*

RELIEVER: As needed ICS-SABA*, or as-needed SABA

*Not recommended for patients with severe asthma.

Pharmacotherapy | COPD

Description	Treatment Recommendations
Rescue	Short Acting Beta-2 Agonist (SABA) or Short Acting Anti-Muscarinic (SAMAs) prn
Confirmed Stable COPD with ongoing resp symptoms	Combination Long-Acting Bronchodilators (LAMA/LABA) improve FEV1 and reduce exacerbation frequency
Asthma/COPD Overlap Syndrome and Moderate to Severe COPD	Triple Inhaled Therapy ICS/LABA/LAMA Combination improves lung function, symptoms and reduces exacerbations over monotherapy or duo-therapy
Exacerbations	ICS 40mg OD x 5 days for all patients. Oral antibiotics , as per local bacterial resistance patterns or individual's sputum microbiology.
Severe COPD with two treated exacerbations	Prophylactic use of azithromycin for a year (with caveats)

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[management-of-copd-nccc-guideline-no-27.pdf](#) 2021 ([hse.ie](https://www.hse.ie))

COPD | Pharmacotherapy Cautions

Description	Recommendations
ICS	Offering an inhaled corticosteroid (ICS) to patients with confirmed stable COPD as first line therapy is not routinely recommended. Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease and should be considered before considering addition of ICS in such patients.
Antioxidants and mucolytics	Their in routine practice for management of patients with COPD is not recommended, due to insufficient evidence of benefit.
Leukotriene antagonists	A role for leukotriene receptor antagonists in the management of patients with COPD is not recommended.
Inhaler Technique	Inhaler technique and adherence to therapy should be assessed before concluding that current therapy is insufficient and a change in therapy considered.

management-of-copd-ncec-guideline-no-27.pdf (hse.ie) 2021

Respiratory Infections | Treatment

In many cases the Preferred Antibiotic is No Antibiotic

Preferred Antibiotics in Community

Respiratory Infections	Urinary Tract Infections	Skin and Soft Tissue Infections
Amoxicillin	Trimethoprim* (Only for lower UTI)	Flucloxacillin
Doxycycline*	Clarithromycin	Clarithromycin* (second)
Penicillin V (phenoxymethylpenicillin)	Fluoroquinolone* (Only for lower UTI)	Levofloxacin* (second)

Antibiotics To Be Avoided First Line in Community

Oral penicillins	Risks: C-DR	Quinolones	Risks: C-DR, drug interactions, tendinopathy & other tendon, prolongation of QT interval, severe nausea/throwing
Amoxicillin or amoxicillin/clavulanic acid	• Claforan®	• Levofloxacin®	• Clarithromycin®
Amoxicillin/clavulanic acid	• Augmentin®	• Moxifloxacin®	• Clarithromycin®
Amoxicillin/clavulanic acid (oral suspension)	• Augmentin®	• Moxifloxacin®	• Clarithromycin®
Amoxicillin/clavulanic acid (oral suspension)	• Augmentin®	• Moxifloxacin®	• Clarithromycin®
Amoxicillin/clavulanic acid (oral suspension)	• Augmentin®	• Moxifloxacin®	• Clarithromycin®

Antibiotic Prescribing - HSE.ie

Respiratory Infections | The Pharmacists' Role Promote Vaccination

Respiratory Infections Against Which Vaccination is Recommended	
COVID-19	Vaccination Recommended as NIAC classifies those with chronic respiratory disease as 'very high risk' for severe disease.
Influenza	Children 2-17, Adults Over 65, At Risk including HCW and Respiratory Disease
Pneumococcal Disease	Primary Childhood Vaccination Schedule (PCVS), Everyone over 65, Everybody aged 2 years and over with chronic lung disease
Pertussis (As Tdap vaccine)	Primary Childhood Vaccination Schedule, School (Junior Infants and First Year), Pregnancy.
Respiratory Syncytial Virus (RSV)	Vaccines licensed but not yet included in PCVS

Immunisation - HSE.ie

Lifestyle – Manage Modifiable Risk Factors

- Environmental factors e.g. allergens, air pollution, occupational exposure, second-hand smoke etc.
- Co-morbidities e.g. obesity, rhino-sinusitis, food allergy
- Nutrition e.g. Dietary potassium and magnesium
- Regular exercise to increase cardiopulmonary capacity
- Medication e.g. Adherence, Inhaler Technique and Identifying Iatrogenic Disease (trigger medications)
- Vaccinations against respiratory infections
- Breathing Technique and Exercises

Breathing Techniques and Exercises

Benefits

- ▷ improve respiratory function
- ▷ reduce stress & anxiety
- ▷ induce relaxation & emotional regulation
- ▷ increase cellular energy & mitochondrial function
- ▷ enhance focus & reduce distraction
- ▷ improve sleep quality and quantity
- ▷ improve recovery - reduce resting heart rate and increase Heart Rate Variability (HRV)

Breathing for Rest & Recovery Insomnia. Stress. Anxiety.

- ▷ 4-7-8 Breathing
- ▷ Diaphragmatic Breathing
- ▷ Bhamari Pranayama Breathing

Breathing for Focus

Inattention. Distraction.

- ▷ Box Breathing
- ▷ Alternate Nostril Breathing



Breathing for Energy

Increase alertness & productivity

- ▷ Kapalabhati Breathing
- ▷ Bhastrika Pranayama (Bellows Breath)
- ▷ Wim Hof Method



Resonant Breathing

Snoring.

- ▷ Nose Breathing
- ▷ Respiratory Rate 5-6 breaths per min
- ▷ Alternate Nostril Breathing



Breathing for Self-Regulation

Emotional Regulation

- ▷ Breath Counting
- ▷ Breath Shifting
- ▷ Sensory Breathing



Education

- S** • S: Smoking Cessation
- I** • I: Inhaler Technique
- M** • M: Chronic Disease Self-Management Plans
- P** • P: Reliever, Controller, Emergency OCS
- L** • L: Exercise, Avoid triggers, Vaccination
- E** • E: Signpost resources (see next slide)
- S** • S: Support



Education

- Signpost resources such as
- S** • **Smoking Cessation Supports** <https://www.hse.ie/eng/about/who/tobaccocontrol/cessation/>
 - I** • **Inhaler Technique Videos** | [Asthma Society of Ireland](#)
 - M** • **Managing Winter Illnesses** [Common illnesses - HSE.ie](#)
 - P** • **Patient Information Leaflets** [The Health Products Regulatory Authority \(hpra.ie\)](#)
 - L** • **Information about Immunisation** [Public Information - HSE.ie](#)
 - E** • **Living Well With a Chronic Condition Self Management Programme** [Self-Management Support - HSE.ie](#)
 - S** • **Resources for People living with a Long-term Health Condition - HSE.ie** including **Managing Exacerbations** e.g. asthma attack, acute COPD
 - **Pulmonary rehabilitation - exercise and education programme - HSE.ie**



Support Post-Exacerbation



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Review patient/carer understanding of:

- Signs & symptoms of worsening condition
- Factors that precipitated the exacerbation
- How to avoid/manage modifiable risk factors
- Purpose of medications
- Demonstration of inhaler technique skills
- Referral to education resources e.g. Pulmonary Rehab, Living Well Programme
- Written Self-Management Plan, including emergency response
- Address Health Beliefs – e.g. adherence with ICS and OCS may fall to 50% within a week after discharge
 - Attitudes to antibiotics
 - Steroid phobia
 - Fear of becoming “immune” over time
 - “Unnaturalness” of medicines



Support Special Populations



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Children & Teenagers:

- School Teachers
- Parents
- Children
- Teenagers
- Pharmacy Respiratory Health / Smoking Cessation Clinics

Adults:

- Pregnancy & breast-feeding
- Elderly
- COPD
- Allergic rhinitis
- Occupational risks
- Sport & respiratory health

How can we best support these patients to follow their treatment plans?



Supporting Treatment Adherence



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Pharmacist & Patient co-create alliance to address:

- Medication adherence including inhaler technique
- Adherence to written management plan
- Attendance at follow-up appointments
- Trigger factor avoidance
- Peak flow monitoring
- Breathing Techniques
- Nutrition and Exercise

What else could you do when you see evidence of non-adherence?



4. **Apply** insights to optimise your own respiratory health, as well as empowering your patients to do the same.



Review and Action Steps



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1. What does **SIMPLES** acronym mean?
2. Referring back to your -10 to +10 number, how has **SIMPLES** approach impacted your proactivity in promoting respiratory health?
3. How might **SIMPLES** equip you to have a more impactful pharmacy consultation with patients like Ms JR?
4. What steps will you take to implement the **SIMPLES** principles in your pharmacy practice?



Summary



At the end of this session, are you able to

1. **Outline** normal functioning of the respiratory system as well as common dysfunctions and pathophysiological processes that can affect respiratory health?
2. **Identify** how respiratory health directly affects overall health, wellbeing and performance?
3. **Structure** respiratory health interventions using SIMPLES framework, incorporating inhaler technique?
4. **Apply** insights to optimise your own respiratory health, as well as empowering your patients to do the same?



Review Respiratory Case Study

- S**
- I**
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- S**
- Ms JR is a 29 year old, DPS asthma patient
 - Her 6/12 repeat prescription (on file for the past two months) includes Salbutamol PRN and Seretide® 250 Diskus BD
 - In the past two months, she has been dispensed 4 Salbutamol inhalers and NO Seretide® (On each occasion she stated she "has enough" Seretide® to keep her going)
 - She has presented today with a prescription for antibiotics and oral prednisolone



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ADDITIONAL RESOURCES

Not included in oral presentation

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Short Acting Beta-Agonists (SABA)

Medications	Salbutamol, Terbutaline
Mode of Action	Relaxes the muscles of the airways thus relieves broncho-constriction (B2-agonist)
Indication	<ul style="list-style-type: none"> Immediate relief of reversible airways obstruction Prophylaxis of exercise/allergen induced bronchospasm
Counselling Points	<ul style="list-style-type: none"> Every asthma patient should carry a reliever inhaler Inhaler technique & use of spacer device Indicators of worsening control (use >twice/week) Management of acute exacerbation Caution: hyperthyroidism, diabetes, CVD, hypertension Referral criteria
Potential Side-effects	Hypokalaemia, hypomagnesaemia, fine tremor, nervous tension, headache, muscle cramps, palpitation



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Inhaled Corticosteroids-ICS

Medications	Beclomethasone, Budesonide, Ciclesonide, Fluticasone, Mometasone
Mode of Action	Reduces airway inflammation
Indication	<ul style="list-style-type: none"> Asthma prophylaxis when patient requires SABA >twice per week
Counselling Points	<ul style="list-style-type: none"> MOST effective anti-inflammatory medication for asthma REGULAR use reduces risk of exacerbations Alleviation of symptoms within 3-7 days Inhaler technique. Rinse mouth after use Use spacer device Steroid card for high dose ICS
Potential Side-effects	Candidiasis, hoarseness, throat irritation High dose ICS over prolonged time may induce adrenal suppression, osteoporosis Use minimum effective dose
Steroid Equivalence (Beclomethasone dipropionate is reference standard)	ICS differ in their potency Total daily dose ICS: Low <800mcg, Med 800-1,000mcg, High >1,000mcg e.g. Qvar®=Becotide® (due to smaller particle size)



PharmaBuddy

Long Acting Beta-Agonists (LABA)

Medications	Formoterol, Salmeterol, Vilanterol, Indacaterol
Mode of Action	Relaxes the muscles in the airways thus relieves broncho-constriction (B2-agonist)
Indication	<ul style="list-style-type: none"> First line add-on therapy to ICS in step 3 & 4 Formoterol ONLY – licensed for short term symptom relief
Counselling Points	<ul style="list-style-type: none"> Inhaler technique Dose, frequency & max. number of inhalations in 24 hours should be stated explicitly to patient Use with ICS - use of LABA without ICS in asthma is associated with ↑ risk of adverse outcomes Asthma patients using salmeterol or vilanterol MUST carry a SABA inhaler for acute asthma
Potential Side-effects	Tachycardia, headache, cramps



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LABA/ICS Combination Products

Medications	Symbicort®, Flutiform®, Seretide®, Relvar Ellipta®, Bufomix®, Airflusal®, Duo-Resp® Forspiro®, Aerivio®
Pros	Ensures LABA admin with ICS (as per guidelines)
Cons	Reduced flexibility to adjust each component
Factors affecting choice	<ul style="list-style-type: none"> Inhalation device – patient preference Price Onset and duration of action Licensed for prophylaxis +/- symptom relief Age of patient Symptom severity
Symbicort® SMART Protocol	Licensed for prophylaxis AND symptom relief If patient requires RELIEVER >1/day, refer
Seretide®	Evohaler and Diskus NOT interchangeable – dose ratio
Relvar Ellipta®	Combination product licensed for one inhalation, once daily Indicated aged 12 years and over Discard six weeks after opening

Long Acting Muscarinic Antagonists (LAMA)

Medications	Tiotropium, Glycopyrronium, Umeclidinium, Acclidinium
Mode of Action	Blocks acetylcholine from binding with the muscarinic receptors in the bronchi, reducing broncho-constriction
Indication	COPD first line. Asthma, second line. See Guidelines
Counselling Points	<ul style="list-style-type: none"> Inhaler technique Age >18 years Two puffs, ONCE daily Check expiry date from first opening – short! Ensure patient can prime inhaler prior to first use
Potential Side-effects	Anti-cholinergic side effects such as dry mouth, constipation, difficulty passing urine, blurred vision

Triple Inhaled Therapy Products LABA/LAMA/ICS

Medications	Trelegy Ellipta®
Pros	Ensures LABA/LAMA/ICS combination (as per guidelines)
Cons	Reduced flexibility to adjust each component Six week expiry once device has been opened
Factors affecting choice	<ul style="list-style-type: none"> Inhalation device – patient preference Price Onset and duration of action Symptom severity

Oral Corticosteroids (OCS)

Medications	Prednisolone, Betamethasone
Mode of Action	Reduce airway inflammation (and hence reduce oedema and secretion of mucus into the airway)
Indication	<ul style="list-style-type: none"> Short term treatment (5 days) is important in early treatment of severe acute exacerbations OCS preferred and is as effective as IM/IV in preventing relapse Long-term OCS may be required in severe asthma (step 5)
Counselling Points	Take as a single dose, mane, with food Effects seen after 4-6 hours Tapering required only if treatment duration >2 weeks Steroid Treatment Card for long-term therapy
Potential Side-effects	Short-term: Hyperglycaemia, hypokalaemia, GI side effects, mood changes, insomnia Long-term: Cataract, glaucoma, osteoporosis, adrenal suppression, hypertension, immunosuppression

Leukotriene Receptor Antagonists (LTRA)

Medications	Montelukast, Zafirlukast
Mode of Action	Target one part of the inflammatory pathway in asthma (the effects of cysteinyl LT in the airways)
Indication	2 nd line asthma prophylaxis <ul style="list-style-type: none"> Symptomatic relief of seasonal allergic rhinitis in patients with asthma (montelukast only) Exercise induced asthma
Counselling Points	Take montelukast in evening (may cause drowsiness) Dose dependent on age
Potential Side-effects	Montelukast: abdominal pain, thirst, headache, drowsiness, hyperkinesia in children Zafirlukast: GI disturbances, headache, respiratory infection, insomnia, sleep disturbances, malaise

Methylxanthines

Medications	Theophylline, Aminophylline
Mode of Action	Bronchodilator
Indication	2 nd line option, narrow therapeutic index
Counselling Points	<ul style="list-style-type: none"> Plasma (theophylline) measured 5 days after initiation and 3 days after any dose adjustment Drug interactions Changes in smoking & alcohol Do NOT substitute different brands SR theophylline
Potential Side-effects	<ul style="list-style-type: none"> GI upset (nausea, vomiting, diarrhoea) Hypokalaemia (palpitations, tachycardia, arrhythmias) CNS stimulation (headache, insomnia, convulsions)