Medicines Optimisation Guideline for the Management of Chronic Obstructive Pulmonary Disease (COPD)

(Adapted from NICE Guideline [NG115], updated July 2019)

February 2020

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Contents

Summary: Medicines Management of Stable COPD[1]

Fundamentals of COPD care

All patients should have a diagnosis of COPD, confirmed by post-bronchodilator spirometry.

Offer treatment to support patients to STOP SMOKING

This is an important intervention which slows disease progression. All COPD patients still smoking should be offered help (including drug therapy) at every opportunity. For further information regarding local smoking cessation services, see Appendix 1 for contact details.

Offer pneumococcal and influenza vaccinations

Annual influenza vaccination should be offered to all patients with COPD[1]. In line with national guidance, the pneumococcal vaccination should be offered to patients over 65 years old and younger patients with comorbidities, e.g. chronic heart or lung disease.
Influenza and pneumococcal vaccination decreases the incidence of lower respiratory tract infections[2]

Offer pulmonary rehabilitation (PR) if indicated

Patients who have a MRC score of 3 or more should be referred for PR. PR improves symptoms and quality of life and physical and emotional participation in everyday activities[2]. Early intervention with PR may delay the need to progress to expensive treatments.
For further information regarding local pulmonary rehabilitation services, see Appendix 1.

Develop a personalised self-management plan together with the patient

Patients should be given a self-management plan that encourages them to respond promptly to the symptoms of an exacerbation.
The London Respiratory Network and British Lung Foundation have developed a template Action Plan which can be accessed here:
https://www.networks.nhs.uk/nhs-networks/london-lungs/documents/plan-for-flare-ups-of-copd-editable/file_popview

Optimise treatment for co-morbidities

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These treatments and plans should be revisited at every review (see Appendix 2)

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Start INHALED THERAPIES **only** if: **All** the above interventions have been offered (if appropriate), and inhaled therapies are needed to relieve breathlessness or exercise limitation. See pgs. 5-6 for detailed prescribing information.
For ALL inhaled therapies: Train patients in correct inhaler technique. Review medication, assess inhaler technique & adherence regularly.

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Offer SABA to use if needed. (Offer SAMA if SABA is not tolerated)

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Patient limited by symptoms or has exacerbations despite treatment

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No asthmatic features or features suggesting steroid responsiveness[a]

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Offer LABA + LAMA combination inhaler
(Consider monotherapy if dual therapy is not tolerated or contraindicated)

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Patient still limited by symptoms

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Consider *3 month* trial of LAMA + LABA + ICS[b,c]
(Revert to LABA + LAMA if no improvement)

Asthmatic features or features suggesting steroid responsiveness[a]

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Consider LABA + ICS[b]

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Patient still limited by symptoms or has exacerbations despite using LABA + ICS

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Patient has 1 severe or 2 moderate exacerbations in a year

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Consider / Offer

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LAMA + LABA + ICS[b,c]

If patient is prescribed maximal optimum therapy and is still limited by breathlessness or has frequent exacerbations, seek specialist advice.

[a] **Asthmatic features or features suggesting steroid responsiveness** (see page 5 for further information)
In this context this includes: any previous secure diagnosis of asthma or atopy, a higher blood eosinophil count >0.3x10^9/L^3, substantial variation in FEV1 over time (at least 400 ml) or substantial diurnal variation in peak expiratory flow (at least 20%).
[b] **Be aware of an increased risk of side effects (including pneumonia) in patients who take ICS**
[c] **Document in clinical records the reason for continuing ICS treatment**

PLEASE SEE OVERLEAF FOR INHALER OPTIONS WITHIN EACH CLASS

Key: **SABA** = Short Acting Beta Agonist **SAMA** = Short Acting Muscarinic Antagonist **ICS** = Inhaled Corticosteroid
LABA = Long Acting Beta Agonist **LAMA** = Long Acting Muscarinic Antagonist

Inhaler options within each class of drugs

Choosing the most appropriate inhaler device

- The choice of drug(s) should take into account the patient's response to a trial of the drug, the drug's side effects, potential to reduce exacerbations and cost.
- The device selected should **ALWAYS** be based on the patient's ability to use the device(s) and preference; ensure patients receive training in use of the device and have shown satisfactory technique.
- Before initiating new treatment **ALWAYS check adherence and inhaler technique**. Check again at every review.
- If pMDIs are prescribed, this should always be with a compatible spacer device.
- Where possible minimise the number of inhalers and the number of different types of inhaler used by each person.
- To ensure patients always receive the inhalers they have been trained to use, **always prescribe by brand**.
- Stable patients on existing treatment should not be switched, unless clinically indicated.

Inhaler devices ordered alphabetically. For detailed information on individual inhalers and spacer devices see www.rightbreathe.com

BRAND NAME	GENERIC NAME	DEVICE TYPE	DOSE	COST PER INHALER†
SABA				
VENTOLIN or SALAMOL 100mcg	Salbutamol CFC-Free	pMDI	1-2 doses PRN	£1.50
SALBUTAMOL EASYHALER 100mcg	Salbutamol	DPI	1-2 doses PRN	£3.31
VENTOLIN ACCUHALER 200mcg	Salbutamol	DPI	1 dose PRN	£3.60
SAMA (if not tolerant to SABA)				
ATROVENT 20mcg	Ipratropium bromide	pMDI	1-2 doses PRN	£5.56
LAMA				
BRALTUS ZONDA 10mcg* MHRA alert below	Tiotropium	DPI	1 dose OD	£25.80
EKLIRA GENUAIR 322mcg ▼	Aclidinium	DPI	1 dose BD	£32.50
INCRUSE ELLIPTA 65mcg	Umeclidinium	DPI	1 dose OD	£27.50
SEEBRI BREEZHALER 55mcg	Glycopyrronium	DPI	1 dose OD	£27.50
SPIRIVA HANDIHALER 18mcg (for existing patients only)	Tiotropium	DPI	1 dose OD	£34.87
SPIRIVA RESPIMAT 2.5mcg	Tiotropium	SMI	2 doses OD	£23.00
LABA				
ATIMOS MODULITE 12mcg	Formoterol	pMDI	1 dose BD	£30.06
FORADIL 12mcg		DPI	1 dose BD	£28.06
ONBREZ BREEZHALER 150mcg & 300mcg	Indacaterol	DPI	1 dose OD	£32.19
OXIS TURBOHALER 12mcg	Formoterol	DPI	1 dose BD	£24.80
STRIVERDI RESPIMAT 2.5mcg ▼	Olodaterol	SMI	2 doses OD	£26.35
SEREVENT ACCUHALER 50mcg	Salmeterol	DPI	1 dose BD	£35.11
SEREVENT EVOHALER 25mcg		pMDI	2 doses BD	£29.26
LABA + LAMA				
ANORO ELLIPTA 55/22mcg ▼	Umeclidinium + Vilanterol	DPI	1 dose OD	£32.50
DUAKLIR GENUAIR 340/12mcg ▼	Aclidinium + Formoterol	DPI	1 dose BD	£32.50
SPIOLTO RESPIMAT 2.5/2.5mcg ▼	Tiotropium + Olodaterol	SMI	2 doses OD	£32.50
ULTIBRO BREEZHALER 85/43mcg	Glycopyrronium + Indacaterol	DPI	1 dose OD	£32.50
ICS + LABA combination inhalers				
DUORESP SPIROMAX 320/9mcg	Budesonide + Formoterol	DPI	1 dose BD	£27.97
FOSTAIR NEXTHALER 100/6mcg	Beclometasone + Formoterol	DPI	2 doses BD	£29.32
FOSTAIR 100/6mcg		pMDI	2 doses BD	£29.32
RELVAR ELLIPTA 92/22mcg	Fluticasone Furoate + Vilanterol	DPI	1 dose OD	£22.00
SERETIDE ACCUHALER 500mcg (for existing patients only)	Fluticasone + Salmeterol	DPI	1 dose BD	£32.74
SYMBICORT 200/6mcg	Budesonide + Formoterol	pMDI	2 doses BD	£28.00
SYMBICORT TURBOHALER 400/12mcg		DPI	1 dose BD	£28.00
LAMA + LABA + ICS combination inhalers				
TRELEGY ELLIPTA 92/55/22mcg ▼	Fluticasone Furoate + Umeclidinium + Vilanterol	DPI	1 dose OD	£44.50
TRIMBOW 87/5/9mcg	Beclometasone + Formoterol + Glycopyrronium	pMDI	2 doses BD	£44.50

Key: **= Not recommended in SWL** | **LABA** = Long Acting Beta Agonist | **pMDI** = Pressurised Metered Dose Inhaler | **SABA** = Short Acting Beta Agonist | **LAMA** = Long Acting Muscarinic Antagonist | **DPI** = Dry Powder Inhaler | **SAMA** = Short Acting Muscarinic Antagonist | **ICS** = Inhaled Corticosteroid | **SMI** = Soft Mist Inhaler

† Prices from e-drug tariff October 2019[9]

NOTE: All black triangle drugs are subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions on a Yellow Card at www.mhra.gov.uk/yellowcard

***MHRA alert**: Braltus (tiotropium): risk of inhalation of capsule if placed in the mouthpiece of the inhaler

For further information on any drugs, see current BNF or Summary of Product Characteristics (SmPC) [www.emc.medicines.org.uk]

Inhaler options within each class of drugs

Inhaler devices ordered alphabetically. For more information on individual inhalers, see www.rightbreathe.com

SABA	SAMA	LAMA	LABA	LABA + LAMA	ICS + LABA	LAMA + LABA + ICS
 Salbutamol (pMDI)	 Ipratropium (pMDI)	 Braltus Zonda (DPI)	 Atimos Modulite (pMDI)	 Anoro Ellipta▼ (DPI)	 DuoResp Spiromax (DPI)	 Trelegy Ellipta▼ (DPI)
 Salbutamol Easyhaler (DPI)		 Eklira Genuair ▼ (DPI)	 Foradil (DPI)	 Duaklir Genuair▼ (DPI)	 Fostair NextHaler (DPI)	 Trimbow (pMDI)
 Ventolin Accuhaler (DPI)		 Incruse Ellipta (DPI)	 Onbrez Breezhaler (DPI)	 Spiolto Respimat▼ (SMI)	 Fostair (pMDI)	
		 Seebri Breezhaler (DPI)	 Oxis Turbohaler (DPI)	 Ultibro Breezhaler (DPI)	 Relvar Ellipta (DPI)	
		 Spiriva Handihaler (DPI)	 Striverdi Respimat▼ (SMI)		 Seretide Accuhaler (DPI)	
		 Spiriva Respimat (SMI)	 Serevent Accuhaler (DPI)		 Symbicort (pMDI)	
			 Serevent Evohaler (pMDI)		 Symbicort Turbohaler (DPI)	

Key:				
	SABA = Short Acting Beta Agonist	**SAMA** = Short Acting Muscarinic Antagonist	**LABA** = Long Acting Beta Agonist	**LAMA** = Long Acting Muscarinic Antagonist
	ICS = Inhaled Corticosteroid	**pMDI =** Pressurised Metered Dose Inhaler	**DPI =** Dry Powder Inhaler	**SMI =** Soft Mist Inhaler

NOTE: All black triangle drugs are subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions on a Yellow Card at www.mhra.gov.uk/yellowcard

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Management of Chronic Obstructive Pulmonary Disease (COPD)

Medicines Management of Stable COPD

The main treatment goals are to reduce exacerbations, reduce hospital admissions and to improve patient's quality of life. For further information on the management of COPD, refer to NICE guidelines[1] and Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019.[2]

Smoking Cessation

- Document an up-to-date smoking history, including pack years smoked (number of cigarettes smoked per day, divided by 20, multiplied by the number of years smoked) for everyone with COPD.[1]
- At every opportunity, advise and encourage every person with COPD who is still smoking (regardless of their age) to stop, and offer them help to do so.
- Unless contraindicated, offer nicotine replacement therapy, varenicline or bupropion as appropriate to patients who want to stop smoking, combined with an appropriate support programme to optimise smoking quit rates for patients with COPD.[1]

Pulmonary Rehabilitation

Pulmonary rehabilitation (PR) is an effective and cost effective intervention for stable and post exacerbation COPD patients.

National guidance and quality standards state that PR should be offered to all COPD patients with a functional restriction due to dyspnoea. Importantly it should be considered and presented to patients as a fundamental part of COPD management and not seen as an add-on to medical management.

Long term follow up has shown a reduction in admissions, bed days and mortality in those patients who complete PR. This is in addition to the comprehensive benefits gained in exercise tolerance, dyspnoea, health status and psychological state.

- Offer PR to all people who view themselves as functionally disabled by COPD.
- Consider referring all patients with dyspnoea MRC Score of $\geq$ 3 (2 or more for Wandsworth & Croydon patients) for PR. See appendix 1 for contact details.
- PR can be adapted to suit the patients existing comorbidities. Only those with recent cardiac events, uncontrolled cardiac conditions or those who will not be safe in a group environment should be excluded at the point of referral.

Inhaled Therapy

Short-acting beta-2 agonists (SABA) and short-acting muscarinic antagonists (SAMA)

Use short acting bronchodilators e.g. salbutamol (SABA) or ipratropium (SAMA) as the initial empirical treatment to relieve breathlessness and exercise limitation.[1]

Assess patients for asthmatic features or features suggesting steroid responsiveness (see below).

Asthmatic features or features suggesting steroid responsiveness[1]

1. Any previous, secure diagnosis of asthma or of atopy OR
2. A higher blood eosinophil count (>0.3x10^9/L) OR
3. Substantial variation in FEV1 over time (at least 400 ml) OR
4. Substantial diurnal variation in peak expiratory flow (at least 20%).

Seek specialist advice for patients who have recently had an episode of significant pneumonia. ICS therapy in this patient cohort may not be appropriate despite having features suggesting steroid responsiveness.

Inhaled combination therapy

Choose between the following two options accordingly:

Option A: Offer a **LABA + LAMA combination inhaler*** to patients who:

1. Have spirometrically confirmed COPD **AND**
2. Do NOT have asthmatic features or features suggesting steroid responsiveness (see box above) **AND**
3. Remain breathless or have exacerbations despite:
    a. Having used or been offered smoking cessation treatment if they smoke **AND**
    b. Optimised non-pharmacological management and relevant vaccinations **AND**
    c. Using a short-acting bronchodilator

*NICE have reviewed the evidence for inhaled therapies in COPD and have concluded that, compared with other dual therapy combinations and with monotherapy, the combination of long-acting muscarinic antagonists and long-acting beta2 agonists (LAMA+LABA): provides the greatest benefit to overall quality of life, is better than other inhaled treatments for many individual outcomes (such as reducing the risk of moderate to severe exacerbations) and is the most cost-effective option.[1]

Option B: Consider an **ICS + LABA combination inhaler** for patients who:

1. Have spirometrically confirmed COPD **AND**
2. Have asthmatic features or features suggesting steroid responsiveness (see box below) **AND**
3. Remain breathless or have exacerbations despite:
    a. Having used or been offered smoking cessation treatment if they smoke **AND**
    b. Optimised non-pharmacological management and relevant vaccinations **AND**
    c. Using a short-acting bronchodilator

Triple therapy (LAMA + LABA + ICS)

Before starting LAMA+LABA+ICS, conduct a clinical review to ensure that:

- non-pharmacological COPD management is optimised and the patient has used or been offered treatment for tobacco dependence if they smoke
- acute episodes of worsening symptoms and/or the symptoms adversely impacting on the patient's quality of life are caused by COPD exacerbations and not by another physical or mental health condition

For people with COPD who are taking LABA+ICS:

- offer LAMA+LABA+ICS if their day-to-day symptoms continue to adversely impact their quality of life or they have a severe exacerbation (requiring hospitalisation) or they have 2 moderate exacerbations within a year.

For people with COPD who are taking LAMA+LABA either:

- consider LAMA+LABA+ICS if they have a severe exacerbation (requiring hospitalisation) or they have 2 moderate exacerbations within a year

OR

- consider a **TRIAL** of LAMA+LABA+ICS, lasting for **3 MONTHS** if the patient's day-to-day symptoms adversely impact their quality of life
    - after 3 months, conduct a clinical review to establish whether or not LAMA+LABA+ICS has improved their symptoms.
    - if symptoms have not improved, **STOP** LAMA+LABA+ICS and switch back to LAMA+LABA
    - if symptoms have improved, continue with LAMA+LABA+ICS.

In COPD patients who do not have asthmatic features or features suggesting steroid responsiveness, document the reason for continuing ICS use in clinical records e.g. frequent exacerbations and review at least annually as part of their annual COPD review.

Environmental impact of inhalers

The NHS has committed to reducing its carbon footprint by 51% by 2025 to meet the target in the Climate Change Act, including a shift to dry powdered inhalers (DPI) to deliver a reduction of 4%.
Pressurised metered dose inhalers (pMDI) use a propellant, which is a greenhouse gas that contributes to global warming.
Dry powder inhalers (DPI), which use no propellant, are less harmful to the environment. However, DPIs require people to have an adequate inspiratory flow rate for effective delivery of the medicine.

The NHS aims to use more dry powdered inhalers, where clinically appropriate.

Reviewing patients prescribed inhaled therapies who no longer fit the updated NICE guidance

Patients using long-acting bronchodilators outside of the NICE recommendations (NG 115), (i.e. LABA or LAMA monotherapy) and who are stable, may continue with their current treatment until both they and their NHS healthcare professional agree it is appropriate to change[1].

There will be patients who are prescribed ICS but who do not meet the current NICE criteria, e.g. the patient does not have asthmatic features or features suggesting steroid responsiveness and is not symptomatic or exacerbating. Consideration could be given to using the COPD annual review to assess appropriateness of ICS use and stepping down and withdrawing the ICS element of their current treatment. **Appendix 3: Evaluation of appropriateness of ICS therapy on COPD and guidance on ICS withdrawal** provides some practical suggestions as to how the ICS component of their therapy can be withdrawn. Please seek specialist advice as necessary.

Nebulisers

The majority of patients can be taught to use handheld inhaler devices. However, the few patients with distressing or disabling breathlessness despite maximal therapy with inhalers should be referred to the Respiratory Specialist Team for formal assessment and provision of a compressor if appropriate.

Nebulised therapy should be reviewed two weeks after initiation and only continued if 1 or more of the following occurs:

- a reduction in symptoms
- an increase in the ability to undertake activities of daily living
- an increase in exercise capacity
- an improvement in lung function.

Spacers

Provide patients with a spacer that is compatible with the person's metered-dose inhaler[1]. See www.rightbreathe.com for guidance on selecting an appropriate spacer.

Advise patients to use a spacer with a metered-dose inhaler in the following way[1]:

- administer the drug by single actuations of the metered-dose inhaler into the spacer,
- inhaling after each actuation
- there should be minimal delay between inhaler actuation and inhalation
- normal tidal breathing can be used as it is as effective as single breaths
- repeat if a second dose is required

Advise patients how to clean their spacer[1]:

- Hand wash spacers using warm water and washing-up liquid, and allow the spacer to air dry
- Don't clean the spacer more than monthly. More frequent cleaning affects their performance because of a build-up of static

Oral Therapy

Oral corticosteroids (maintenance)

Maintenance use of oral corticosteroids is not normally recommended. In cases where maintenance therapy cannot be withdrawn, the lowest possible dose should be used. Patient response to oral corticosteroids cannot be used to predict response to inhaled corticosteroid therapy and should not be used to identify patients suitable for inhaled corticosteroids.

Osteoporosis prophylaxis

- Calcium and Vitamin D should be considered for patients requiring frequent courses or a maintenance dose of oral corticosteroids.
- Consider bone scan and bisphosphonates, if indicated and appropriate.

Theophylline

- Theophylline has a limited place in therapy and should only be initiated by a respiratory specialist.
- It should only be used after a trial of SABA and LABA inhalers or in patients who are unable to use inhaled therapies.
- Prescribe by brand name only and be aware of drug interactions (check current BNF) and monitor/adjust doses as necessary.
- Levels need to be monitored every 6-12 months or more often if toxicity is suspected.
- Measure trough level immediately pre-dose, Levels should be between 10-20mg/litre.
- Refer to BNF for further information on monitoring and side effects.

Mucolytics

- Oral mucolytics should not be routinely used for prevention of an exacerbation in patients with stable COPD.
- A 4-week trial of mucolytics e.g. carbocysteine (tablet or sachets) can be considered in patients with a chronic productive cough of sputum.
- Treatment should only be continued if there is symptomatic improvement (e.g. reduction in cough frequency or sputum). Treatment with mucolytic agents has shown a small but significant reduction in acute exacerbations and total number of days disability. Evidence suggests that if patients take mucolytics regularly through the winter months; it could result in a 20% reduction in exacerbations, which in turn may prevent hospitalisations. They are safe and well tolerated.[5]
- Anti-tussives should not be used to manage cough in COPD as there is no conclusive evidence of benefit.

Oral prophylactic antibiotic therapy

- Prophylactic antibiotics e.g. azithromycin (usually 250mg 3 times a week[1]) **should only be started following respiratory consultant assessment and advice and can be continued in primary care. The specialist should advise on duration of therapy**.
- Before starting azithromycin, ensure the patient has had an electrocardiogram (ECG) to rule out prolonged QT interval, sputum sampling (microscopy, cultures and sensitivities (MC&S) for acid-fast bacillus (AFB) to rule out mycobacterium) and baseline liver function tests. A CT scan of the thorax may be requested where required, to rule out bronchiectasis and other lung pathologies. These tests should be completed by secondary care and results communicated to the GP, where relevant.
- When prescribing azithromycin, advise patients about the small risk of hearing loss and tinnitus and tell them to contact a healthcare professional if this occurs.
- A review is advised after the first 3 months and then at least every 6 months. Only continue treatment if the continued benefits outweigh the risks. If required, seek specialist advice.

Oral phosphodiesterase-4 inhibitors

Roflumilast▼ is recommended for COPD (NICE TA461).[4] This is a **hospital only drug** in South West London, and therefore should not be prescribed in primary care.

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For further information on any drugs, see current BNF or Summary of Product Characteristics (SmPC) [www.emc.medicines.org.uk]

Oxygen

Long-term and ambulatory oxygen therapy in hypoxic patients is recommended for patients meeting the necessary criteria[1]:

- very severe airflow obstruction (FEV1 below 30% predicted)
- cyanosis (blue tint to skin)
- polycythaemia
- peripheral oedema (swelling)
- a raised jugular venous pressure
- oxygen saturations of 92% or less breathing air

Refer patients to the Community Respiratory Specialist team or Home Oxygen Service and Review (HOSAR) for assessment and appropriate initiation of oxygen therapy. See appendix 1 for contact details.

Be aware that inappropriate oxygen therapy in patients with COPD may cause respiratory depression.

COPD Responsible Prescribing Advice

Medication Review – see appendix 2 for further details

- All patients with mild/moderate COPD should be reviewed at least annually
- Patients with severe/very severe COPD should be reviewed at least twice per year
    1. Review the symptom control and number of COPD exacerbations in last 12 months.
    2. Activities of daily living and exercise capacity should be reviewed using the MRC dyspnoea scale.
    3. Before changing treatment, check adherence and inhaler technique.

Inhaled corticosteroids (ICS)

- There is evidence from randomised trials that ICS use is associated with oral candidiasis, hoarse voice, skin bruising and non-fatal pneumonia. Care must be taken in patients treated with high dose ICS; the risks should be discussed with the patient.
- The potential risk of developing systemic side effects such as adrenal suppression and osteoporosis with high dose ICS should also be considered and prophylaxis provided if appropriate (see below).
- The London Respiratory Network developed guidance for healthcare professionals on inhaled corticosteroids. See link: fhttps://www.networks.nhs.uk/nhs-networks/london-lungs/documents/inhaled-corticosteroids-in-adults/file_popview
- When prescribing high dose inhaled corticosteroids (>1000mcg BDP equivalent), ensure that the patient is issued an inhaled steroid safety card. See link: https://www.networks.nhs.uk/nhs-networks/london-respiratory-network/key-documents/responsible-respiratory-prescribing/LRT%20Inhaled%20steroid%20safety%20card.pdf
  Cards may be purchased using the following form: https://www.networks.nhs.uk/nhs-networks/london-lungs/documents/high-dose-inhaled-corticosteroid-alert-card-order-form
- Withdrawal of ICS - Review steroid treatment in patients who have developed pneumonia on ICS, to reduce risks of further episodes. Seek specialist advice as necessary.

Rescue antibiotics and steroids

- Consider offering patients a short course of oral corticosteroids and a short course of oral antibiotics to keep at home as part of their exacerbation plan if:
    - They have had an exacerbation within the last year and remain at risk of exacerbation
    - They understand and are confident about when and how to take these medicines
    - They know to tell their healthcare professional as soon as they start taking their medicines and to ask for replacements
    - They know to seek medical help if symptoms worsen rapidly or significantly, or do not improve within 2 to 3 days
    - Refer to local antimicrobial guidelines for antibiotic choice and duration.
    - Prednisolone 30mg OM for 5 days[1]
- The decision to prescribe should be at GP's discretion in appropriate patients.
- See Medicines Management of Acute COPD for prescribing information (pg.11)
- Follow up with a review.
- For patients who have used 3 or more courses of oral corticosteroids and/or oral antibiotics in the last year, investigate the possible reasons for this.
- For patients who are taking prophylactic azithromycin and are still at risk of exacerbations, provide a non-macrolide antibiotic to keep at home as part of their exacerbation plan. Recommendations can be found in NICE Guidance 114

Unlicensed use

Some patients may require unlicensed doses or devices and this should be decided on an individual basis, with specialist input.

QT interval prolongation and bronchodilators

- Combinations such as salbutamol inhaler + clarithromycin need not be avoided. Such combinations have been used uneventfully for many years.[6]
- Prescribing software has been updated to highlight the possible increased risk of torsade de pointes if a medicine that can cause hypokalaemia is co-prescribed with a medicine that can prolong the QT interval.
- Inhaled beta$_2$ agonists are unlikely to cause hypokalaemia; it is an adverse effect more commonly associated with oral or parenteral administration.
- Hypokalaemia is a rare adverse effect of inhaled corticosteroids; it is more commonly associated with oral or parenteral administration.

Long acting muscarinic antagonists - Special warnings and precautions for use

- Consistent with their anticholinergic activity, all inhaled LAMAs should be used with caution in patients with bladder outflow obstruction, paradoxical bronchospasm, prostatic hyperplasia or susceptibility to angle-closure glaucoma.
- LAMAs should be used with caution in patients with recent myocardial infarction (<6 months), unstable or life-threatening arrhythmias, heart failure resulting in hospitalisation in the last year and unstable ischaemic heart disease. Refer to individual product SPCs for full details.
- Tiotropium should only be used in patients with a creatinine clearance of ≤50 mL/min if the expected benefits outweigh the risk of accumulation[7].
- Glycopyrronium should only be used in patients with eGFR <30 mL/minute if the potential benefit outweighs the risk[7].

Medicines Management of Acute COPD

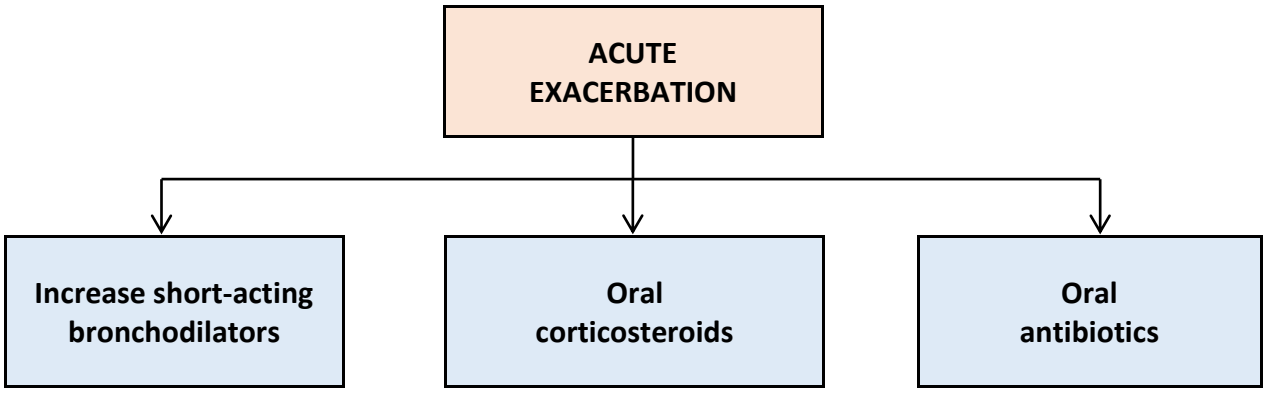
An exacerbation is a sustained worsening of the patient's symptoms from their usual stable state which is beyond normal day-to-day variations and is acute in onset.

Commonly reported symptoms are:

- worsening breathlessness
- cough
- increased sputum production and change in sputum colour

The change in these symptoms often necessitates a change in medication

A range of factors (including viral infections and smoking) can trigger an exacerbation and many exacerbations (including some severe exacerbations) are not caused by bacterial infections so will not respond to antibiotics



Short Acting Bronchodilators

- Increase frequency of short-acting bronchodilator (SABA) use. Use 2 puffs up to a max of 10 doses.
- Consider using a spacer if appropriate.
- Consider using nebulised treatment if not responding to inhaled SABA.
- *Nebulised doses:* 2.5mg/2.5ml QDS and increase up to 6 times per day, if necessary

Oral Corticosteroids

- Prednisolone 30mg daily for 5 days
- For all patients with significant increase in breathlessness, sputum or cough and all patients admitted to hospital, unless contraindicated.
- Patients should be made aware of the adverse effects of prolonged steroid therapy
- Osteoporosis prophylaxis should be considered for patients requiring frequent courses of oral corticosteroids
- Routine use of oral steroids in stable COPD is NOT recommended

Oral Antibiotics [8]

- Treat with antibiotics if purulent sputum and increased shortness of breath and/or increased sputum volume
- See local antimicrobial guidelines for recommended antibiotic choices and duration.
- Change antibiotic if there is no improvement in symptoms on first choice taken for at least 2-3 days. Choice should be guided by sensitivities when available.
- If a patient is receiving antibiotic prophylaxis, treatment should be with an antibiotic from a different class. It is not necessary to stop prophylactic azithromycin during an acute exacerbation of COPD.

References

1. National Institute for Health and Clinical Excellence. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE guideline no. 115. December 2018. See link (Accessed 24/09/2019)
2. GOLD 2019: Global Strategy for the Diagnosis, Management and Prevention of COPD 2019. See link
3. Cazzola M, Rogliani P, Calzetta L, et al. Triple therapy versus single and dual long-acting bronchodilator therapy in COPD: a systematic review and meta-analysis. Eur Respir J 2018; 52: 1801586
4. National Institute for Health and Clinical Excellence. Roflumilast for treating chronic obstructive pulmonary disease. Technology Appraisal Guidance no. 461. July 2017. See link (Accessed 14/12/2018)
5. The Cochrane Library 2006 Issue 3. Poole P and Black P. Mucolytic agents for chronic bronchitis or chronic obstructive pulmonary disease (review). The Cochrane Library Issue 3. 2006
   Article No. CD001287.DOI:10.1002/14651858.CD001287.pub2. (Accessed 23/2/2018)
6. Specialist Pharmacy Service. Drug interactions with senna or salbutamol increasing the risk of torsade de pointes. January 2018. See link (Accessed 27/08/2019)
7. British National Formulary Online. See link. (Accessed 04/10/2019)
8. National Institute for Health and Clinical Excellence. Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing. NICE guideline no. 114. December 2018. See link (Accessed 14/12/2018)
9. NHS Business Services Authority Drug Tariff Online. October 2019. See link (Accessed 07/10/2019)
10. EMIS Web Chronic Disease Management – COPD consultation template.

Appendix 1: Local Contact Details

Stop Smoking Services

NHS Croydon CCG
Website: https://www.justbecroydon.org/be-smoke-free/ Also available via DXS
Tel: 020 8604 7719
Email: livewell@croydon.gov.uk

NHS Kingston CCG
Website: http://www.kick-it.org.uk/
Tel: 0203 434 2500 or text KICK IT to 07800 000 264
Email: info@kick-it.org.uk

NHS Merton CCG
Website: https://www.live-well.org.uk/merton/health/i-want-to-stop-smoking.aspx
Tel: 0208 251 0606 (living well program) or 0208 973 3545 (ONEYOU Merton)
Email: livewell@hrch.nhs.uk

NHS Richmond CCG
Website: http://www.richmond.gov.uk/stop_smoking
Tel: 0800 011 4558
Email: stopsmoking@richmond.gov.uk

NHS Sutton CCG
Face to face support: please advise patients to drop into one of the pharmacies listed on this map of Sutton
Pan-London Helpline: Phone 0300 123 1044 for telephone support to quit smoking or visit stop smoking London portal

NHS Wandsworth CCG
Website: https://www.wandsworth.gov.uk/stopsmoking
Freephone (24 hour): 0800 389 7921
Email: StopSmokingteam@richmondandwandsworth.gov.uk

Pulmonary Rehabilitation Services

NHS Croydon CCG
Generic Referral Form: https://www.croydonhealthservices.nhs.uk/a-to-z-of-services/service/pulmonary-rehabilitation-149/
Tel: 020 8274 6495
Email: ch-tr.crt@nhs.net
Website: https://www.croydonhealthservices.nhs.uk/a-to-z-of-services/service/pulmonary-rehabilitation-149/

NHS Kingston CCG
Referral: Please fax discharge summary and write 'referral to Kingston Respiratory Community Team' and specify service needed e.g. Pulmonary rehab, LTOT assessment, home nebs assessment. Please also telephone to confirm receipt.
Tel: 0208 274 7088
Fax: 0208 390 6923
Email: KINCCG.YourhealthcareSPA@nhs.net

NHS Merton CCG
Tel: 0333 241 4242
Email: CLCHT.MertonRespiratory@nhs.net
Website: https://clch.nhs.uk/health-professionals/merton

NHS Richmond CCG
Referral form: https://www.hrch.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5550
Tel: 0208 973 3450
Email: hownslowandrichmond.spa@nhs.net
Website: https://www.hrch.nhs.uk/our-services/services-directory/services-in-richmond/respiratory-care-team/

NHS Sutton CCG
Referral: Sutton-GP-referral-form.docx
Tel: 020 8661 3908
Email: esth.shc-referrals@nhs.net
Website: https://www.suttonhealthandcare.nhs.uk/respiratory-service

NHS Wandsworth CCG
Referral form available here: https://www.stgeorges.nhs.uk/wp-content/uploads/2019/08/Pulmonary-Rehab-Referral-Form-2019.docx
Please email BOTH sheets of the referral form to Respiratory Liaison Physiotherapy
Tel: 020 8725 3016
Email: Stgh-tr.nmskpathwayhub@nhs.net
Website: https://www.stgeorges.nhs.uk/service/chest-medicine/pulmonary-rehabilitation/

Home Oxygen Services

NHS Croydon CCG
Generic Referral Form accessible here: https://www.croydonhealthservices.nhs.uk/download.cfm?doc=docm93jijm4n1139.rtf&ver=1855
Tel: 020 8401 3963
Email: ch-tr.crt@nhs.net

NHS Kingston CCG
Referral to respiratory specialist via DXS – Home Oxygen Referral Form and Home Oxygen Order Form
Tel: 0800 111 333

NHS Merton CCG
Tel: 0333 241 4242
Email: CLCHT.MertonRespiratory@nhs.net

NHS Richmond CCG
Referral form: https://www.hrch.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5550
Tel: 0208 973 3450
Email: hownslowandrichmond.spa@nhs.net
Website: : https://www.hrch.nhs.uk/our-services/services-directory/services-in-richmond/respiratory-care-team/

NHS Sutton CCG
Tel: 020 8661 3908
Email: karen.rix@nhs.net

NHS Wandsworth CCG
For COPD & bronchiectasis patients contact CLCH respiratory nurse team:
Team Administrator - Tel: 07990 352 598 Email: valeriealexander@nhs.net
For pulmonary hypertension and interstitial lung disease patients contact SGH respiratory nurses:
Tel: 0208 725 1329 / 0208 725 1956 / 0208 725 3458.
Email: stgh-tr.referrals@nhs.net or stgh-tr.StGeorgesRespiratoryNurses@nhs.net

Appendix 2: Annual COPD Review

Patients with COPD should be reviewed at least once per year and more frequently if indicated.

An annual COPD review should ideally cover all of the following points[1,10]

Observations
Measure height, weight and calculate BMI
Record blood pressure, respiratory rate, heart rate & rhythm
Measure peripheral oxygen saturation (SpO2)

Smoking
Document Smoking status (including use of electronic cigarettes, cannabis use or other recreational drug use), previous quit attempts and motivation to quit.
Calculate Smoking pack years
Offer smoking cessation advice and make onwards referral to stop smoking services if appropriate

Spirometry
Measure and record VC, FEV1, FEV1 % predicted, FVC, FEV1/FVC ratio and peak expiratory flow rate (PEFR)

Consultation
Discuss number of A&E attendances and emergency admissions related to COPD since last review
Document the number of COPD exacerbations in the last year
Assess adequacy of symptom control:

- Cough
- Wheeze
- Breathlessness
- Sleep disturbance
- exercise tolerance
- Sputum – type, colour, thickness, presence of blood

Record MRC dyspnoea score
Carry out COPD Assessment Test (CAT). See link: https://www.catestonline.org/hcp-homepage/clinical-practice.html
Complete depression screen and assess impact on social factors e.g. employment/housing
Assess Inhaler technique

Management
Vaccinations – annual influenza vaccination, pneumococcal vaccination
Complete a COPD education and self-management plan
Review prescribed medication

- frequency of bronchodilator use
- inhaler compliance (check prescription issue frequency)
- appropriateness of continued ICS use (see pg.6 for further details)
- use of spacer device
- home nebuliser use
- Use of rescue antibiotics and steroids
- Issue high dose inhaled corticosteroid card if appropriate.

Assess need for pulmonary rehabilitation and/or oxygen therapy – refer as necessary

Use of the In-Check DIAL as a measure of inhaler technique

The In-Check DIAL may be used as part of an inhaler technique check during a patient's annual COPD review.

The effectiveness of a powdered drug when inhaled depends on the inspiratory flow rate generated by the patient and on the turbulence produced by the intrinsic resistance of the DPI[1]. The level of turbulence and resistance in each device is dependent on its design, there are higher, medium and low resistance devices. With low-resistance DPIs, the disaggregation and micro-dispersion of the drug is highly dependent on the patient's inhalation airflow rate, because the role of turbulence is negligible[1]. DPI's with low resistance therefore require a higher inspiratory airflow rate and effort, which patients suffering from a disease-induced airflow limitation may not be able to achieve. When patients use DPIs with medium or high resistance the inspiratory

flow-rate dependency is minimised in the presence of a sufficient regimen of turbulence as in the case of medium-resistance DPIs.

The In-Check DIAL assesses peak inspiratory flow rate, and can simulate the resistance characteristics of certain inhalers, providing the device is set on the correct setting. The patient can then be trained to inhale at a flow rate known to be suitable for their personal DPI or pMDI. This device should not however be used as the sole measure of a patient's inhaler technique and there are limitations to be aware of:

1. Inhaler resistance & drug molecules – The In-Check DIAL is not able to completely reflect the resistance and turbulence profile of all inhalers. Optimal flow rates are mainly justified on in vitro delivery data that does not always reflect the dose response behavior of the drug in vivo[2].
2. Mouth piece size – The size of the In-Check DIAL mouthpiece is larger than all inhalers currently on the market. Patients increase their inspiratory pressure by purse lip breathing and breathing in through a small mouthpiece generates the force required much more easily than breathing in through a tube with a mouthpiece the size of a 10p piece.

Other tools or device features can also be used to assess a patient's ability to use an inhaler. For example: Turbohaler® - inspiratory flow training whistles are available, Genuair® – the window changes colour when dose has been delivered, Nexthaler® – makes a clicking sound, etc.

It is also important to consider clinical outcomes when assessing the suitability of a particular device for a patient. The Handihaler® is the highest resistance inhaler currently available on the market and many patients use this device successfully with good clinical outcomes.

*The above advice regarding the use of In-Check DIALs is supported by Dr Anna Murphy – consultant respiratory pharmacist at University Hospitals of Leicester NHS Trust***.**

References

1. Dal Negro RW. Dry powder inhalers and the right things to remember: a concept review. Multidiscip Respir Med 2015; 10(1):13
2. Pedersen S, Hansen OR, and Fuglsang G. Influence of inspiratory flow rate upon the effect of a Turbuhaler. Arch Dis Child. 1990 Mar; 65(3): 308–310

Appendix 3: PCRS – Evaluation of appropriateness of inhaled corticosteroid (ICS) therapy in COPD and guidance on ICS withdrawal

Primary Care Respiratory Society

Evaluation of appropriateness of inhaled corticosteroid (ICS) therapy in COPD and guidance on ICS withdrawal

This guide provides an algorithm to identify people with chronic obstructive pulmonary disease (COPD) who might benefit from ICS treatment and those in whom it may not be appropriate, and an approach to withdrawing ICS in patients in whom it is not needed.

- In symptomatic patients with COPD at low risk of exacerbation, bronchodilation should be the first-line treatment. [GOLD 2017]. In symptomatic patients on monotherapy, treatment can be stepped up to a combination long-acting β2-agonist plus long acting muscarinic antagonist (LABA+ LAMA), and for patients with severe breathlessness (CAT score 10 or MRC grade 2) initial therapy with LABA+LAMA may be considered [GOLD 2017].
- In patients with symptoms (CAT score <10 or MRC grade <2) at high risk of an exacerbation,

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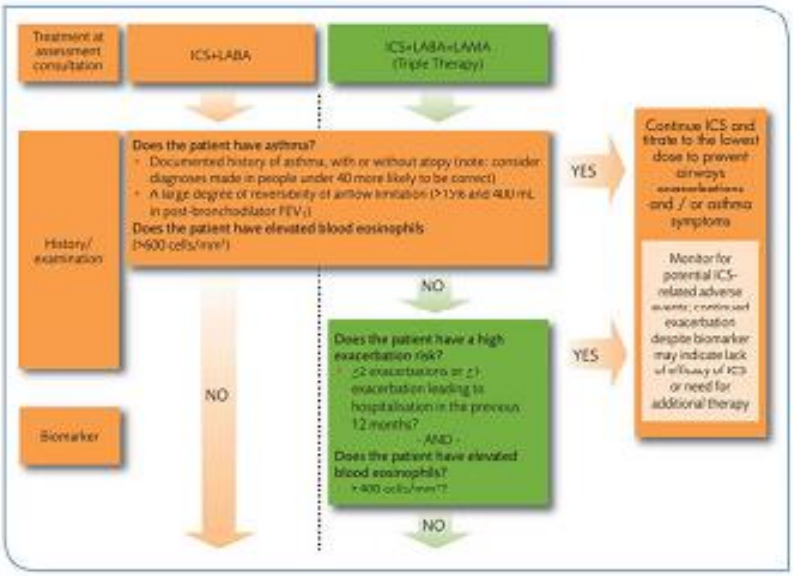

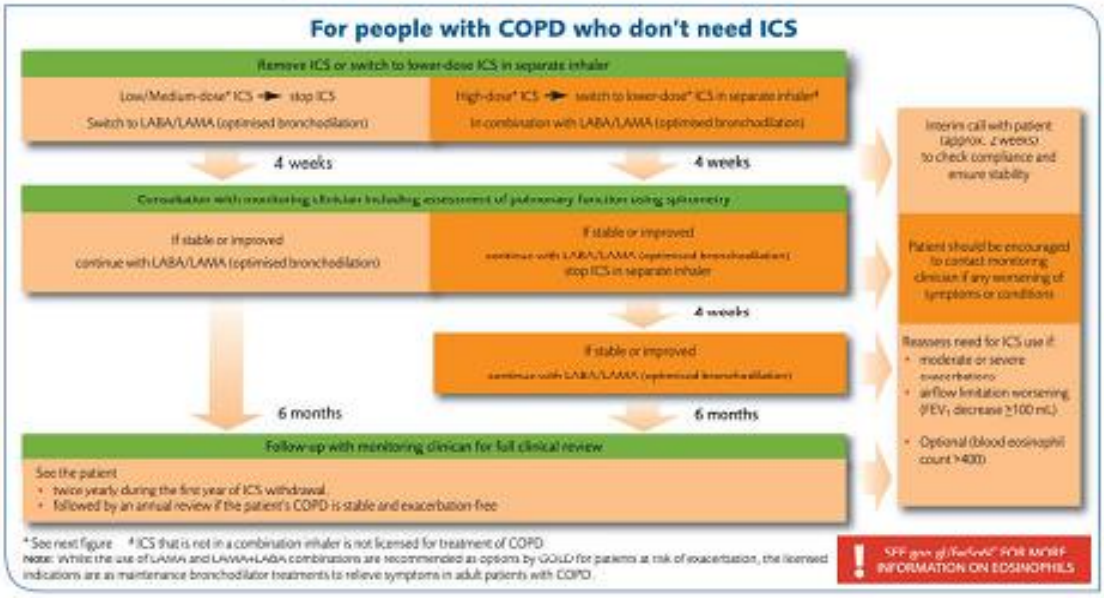

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the recommended first-line treatment is a LAMA (stepping up to LABA+LAMA if necessary) or a LABA+LAMA. In more symptomatic high risk patients, combination LABA+ LAMA is the preferred first-line treatment, with LAMA or ICS+ LABA given as alternative options [GOLD 2017]. If exacerbations persist on LABA+ LAMA, patients can be stepped up to LABA+ LAMA+ICS (triple therapy).

- Long-term ICS use is associated with a significant risk of pneumonia [Yawn 2013; Suissa 2013; Kew & Seniukovich 2014], and systemic effects [Price 2012]; therefore ICS-containing regimens are not recommended in low-risk patients, and should only be considered for high-risk patients with features of asthma, or as triple therapy if exacerbations persist despite treatment with a LABA+LAMA [GOLD 2017].
- Discontinuing ICS rapidly decreases the risk of serious pneumonia [Suissa 2015].
- Despite years of guidance on the limited role of ICS in COPD [GOLD 2001], there is evidence of inappropriate use of ICS in COPD patients who are at low risk of exacerbation [Vestbo 2014; Price 2014].
- Recent studies have indicated that ICS can be withdrawn in both low- and high-risk patients, provided adequate bronchodilator therapy is in place [Rossi 2014a; Rossi 2014b; Magnussen 2014]. Withdrawal of ICS only increased exacerbation rates in patients with both raised eosinophils and a history of frequent exacerbations [Calverley 2016].

ICS dose switch guidance

Commonly prescribed ICS treatments for COPD and recommended ICS in separate inhaler for change in treatment

Current treatment	Switch to
• Fluticasone/salmeterol - 250/50µg 1 puff twice daily	• LABA/LAMA
• Beclomethasone/formoterol - 100/6µg 2 puffs twice daily	• LABA/LAMA
• Fluticasone/vilanterol - 92/22µg 1 puff once daily	• LABA/LAMA
• Budesonide/formoterol - 400/12µg 1 puff twice daily - 200/6µg 2 puffs twice daily	• LABA/LAMA
• Budesonide/formoterol - 400/12µg 2 puffs twice daily	• LABA/LAMA plus - budesonide 200µg 2 puffs twice daily
• Fluticasone/salmeterol - 500/50µg 1 puff twice daily	• LABA/LAMA plus - fluticasone 250µg 1 puff twice daily

The following fixed ICS/LABA combination brands are licensed in COPD: Seretide Accuhaler, Airflusal Forspiro, Relvar Ellipta, Symbicort, Duoflo Spiromax, FostairMDI and Foster NEXThaler, Fobumix Easyhaler

References

Calverley PM, Tetzlaff K, Vogelmeier C, Fabbri LM, Magnussen H, Wouters E, Disse B, Finnigan H, Anjee GM, Watz H. Abstract: Evaluating blood eosinophils and exacerbation history to predict ICS response in COPD. *European Respiratory Journal* 2016 48:OA1973; DOI: 10.1183/13993003.congress-2016.OA1973

Global Initiative for Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease NHLBI/WHO Workshop Report 2001

Global Initiative for Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. 2017. http://www.goldcopd.com

Kew KM, Seniukovich A. Inhaled steroids and risk of pneumonia for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2014; 3(3)

Magnussen H, Disse B, Rodriguez-Roisin R, Kirsten A, Watz H, *et al*; WISDOM Investigators. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. *N Engl J Med* 2014; **371**(14): 1785–96

Price D, West D, Brusselle G, Gruffydd-Jones K, Jones R, Miravitlles M, Rossi A, Hutton C, Ashton VL, Stewart R, Bichel K. Management of COPD in the UK primary-care setting: an analysis of real-life prescribing patterns. *Int J Chron Obstruct Pulmon Dis* 2014

Price D, Yawn B, Brusselle G, Rossi A. Risk-to-benefit ratio of inhaled corticosteroids in patients with COPD. *Prim Care Respir J* 2012; **22**: 1: 92–100

Ross A, Cuerrero M, Conrado A. Withdrawal of inhaled corticosteroids can be safe in COPD patients at low risk of exacerbation: a real-life study on the appropriateness of treatment in moderate COPD patients (OPTIMO). *Respir Res* 2014b; 15:77

Rossi A, van der Molen T, del Olmo R, Papi A, Vehbe L, *et al*. INSTEAD: a randomised switch trial of indacaterol versus salmeterol/fluticasone in moderate COPD. *Eur Respir J* 2014a; **44**(6): 1548–56

Suissa S, Coulombe J, Ernst P. Discontinuation of Inhaled Corticosteroids in COPD and the Risk Reduction of Pneumonia. *Chest* 2015; **148**(5): 1177–83

Suissa S, Patenaude V, Lapi F, Ernst P. Inhaled corticosteroids in COPD and the risk of serious pneumonia. *Thorax* 2013; **68**: 1029–36

Vestbo J, Vogelmeier C, Small M, Higgins V. Understanding the GOLD 2011 Strategy as applied to a real-world COPD population. *Respir Med* 2014; **108**: 729–36

Yawn BP, Li Y, Tian H, Zhang J, Arcona S, *et al*. Inhaled corticosteroid use in patients with chronic obstructive pulmonary disease and the risk of pneumonia: a retrospective claims data analysis. *Int J Chron Obstruct Pulmon Dis* 2013; **8**: 295–304

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The original IPCRG version of the desktop helper was written by Dr Alan G Kaplan, Dr Miguel Román Rodríguez, Professor David B Price and Dr Ioanna Tsiligianni and can be obtained from http://goo.gl/ABT15K

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Appendix 4: NICE Inhaled Therapies Evidence Review

NICE in collaboration with the Cochrane Airways Group reviewed the evidence for inhaled therapies in COPD.

The information below is an excerpt from the NICE COPD guideline (NG 115)

Inhaled combination therapy

Dual therapy

The evidence showed that, compared with other dual therapy combinations and with monotherapy, the combination of long-acting muscarinic antagonists and long-acting beta2 agonists (LAMA + LABA):

- provides the greatest benefit to overall quality of life
- is better than other inhaled treatments for many individual outcomes (such as reducing the risk of moderate to severe exacerbations)
- is the most cost-effective option

The committee did not recommend a particular LAMA because they were not convinced that the evidence showed any meaningful differences in effectiveness between the drugs in this class. Instead, they updated the existing recommendation on drug and inhaler choice, based on their experience of what factors should be taken into account. In particular, minimising the number and types of inhalers prescribed will make it easier for people to use their inhalers correctly.

Most of the trials specifically excluded people with COPD and Asthma, so there was no direct evidence for this group. The committee recommended LABA + ICS (inhaled corticosteroids) based on their clinical experience and knowledge of the likely benefit of ICSs in certain specific COPD phenotype.

Although the combination therapies recommended in this guideline are the most effective options, some people are currently using different therapies, such as LAMA or LABA monotherapy, and may have their symptoms under control with these. The committee did not want to make people change treatments unnecessarily, so they made a recommendation highlighting that people did not need to switch treatments until their clinical needs changed.

Triple therapy

Not everyone with COPD will benefit from triple therapy. In addition, for some people the symptoms that give them the most problems are caused by other conditions (such as heart failure or anxiety) rather than their COPD. Because of this, a clinical review is needed first, to ensure that people only receive triple therapy if they will benefit from it. The committee envisaged that this review would take the form of a conversation with the person with COPD about their symptoms, rather than relying on tools such as the CAT score or MRC breathlessness score in isolation.

The committee decided that there should be separate recommendations on triple therapy for people who are currently taking LABA+ICS and for people taking LAMA+LABA. They agreed that there was stronger evidence from a greater number of studies that triple therapy benefits people taking LABA+ICS, compared with people taking LAMA+LABA.

For people currently taking LABA+ICS, the evidence showed that LAMA+LABA+ICS reduced the rate of severe exacerbations, improved FEV1, and did not increase the risk of pneumonia or other serious adverse events.

For people currently taking LAMA+LABA, the evidence showed that LAMA+LABA+ICS reduced the rate of serious exacerbations and provides some quality of life improvement. However, these improvements were smaller than the ones for people who were taking LABA+ICS before they started triple therapy. In addition, people who switched from LAMA+LABA to triple therapy were more likely to get pneumonia.

The criteria for starting triple therapy are based on the inclusion criteria for the studies the committee reviewed and their clinical judgement. For people who are currently taking LAMA+LABA, the committee made separate recommendations for:

- people who are having severe or frequent exacerbations, for whom the benefit of fewer exacerbations outweighs the increased risk of pneumonia

- people with less severe symptoms, for whom it is less clear if triple therapy provides enough benefits to outweigh the risk of pneumonia.

The 3-month trial is recommended to help identify people in the group with less severe symptoms who will benefit from triple therapy, while ensuring that people who do not benefit can easily switch back to LAMA+LABA. This is to avoid the situation where people continue on triple therapy, with the accompanying risks, without seeing any benefit. As part of the review at the end of the trial, the committee agreed that it was important to explicitly ask the person with COPD if taking the drug had improved their COPD symptoms.

The committee also recommended documenting the reason for continuing ICS, to encourage treatment review so that people are not exposed to the risks of this treatment if they do not benefit from it.

The committee looked at making recommendations for people with asthmatic features. However, the evidence excluded people with asthma and did not provide much information on asthmatic features (such as eosinophil count). Because of this, and because people with asthmatic features are likely to be covered by the recommendation for people taking LABA+ICS, the committee agreed not to make a specific recommendation for this group.

The committee did not make a recommendation in favour of single or multiple inhaler devices as the included evidence did not show a meaningful difference in clinical effectiveness between triple therapy compared to dual therapy based on the number of devices. From the economic evidence, using a single inhaler device was more cost effective, but the committee agreed that there were circumstances where using more than one inhaler to deliver triple therapy may be more appropriate for a particular person with COPD. Finally, the committee had already made a recommendation about the factors to be taken into account when choosing an inhaler device and these included minimising the numbers and types of inhalers where possible and cost so an additional recommendation on this issue was unnecessary

How the recommendations might affect practice

The recommendation on LAMA+LABA dual therapy is likely to increase the number of people with COPD who are having this treatment. The higher cost of dual therapy compared with monotherapy may result in a significant resource impact, but cost savings are also likely from a reduction in treatments needed for exacerbations (including hospitalisation).

Using LABA+ICS for people with features of asthma/features suggesting steroid responsiveness is in line with current practice.

The recommendations may result in an increase in the number of people who are prescribed triple therapy and an increase in the number of people who need treatment for pneumonia, although this may be mitigated by the relatively widespread current use of triple therapy. However, the criteria for who should be offered triple therapy and the recommendation for a trial period should limit the impact of both of these changes.

Triple therapy regimens have a higher cost than dual long-acting bronchodilator regimens. However, this cost is likely to be at least partially offset by savings from reduced numbers of exacerbations and better management of symptoms for people switching to triple therapy.

It is already routine in practice to have a clinical review before starting triple therapy. The recommendation on clinical review may increase the scope of this review. However, any costs incurred from this should be offset by savings from more optimal management of symptoms in people with COPD, which should be associated with fewer primary care and/ or hospital visits.

The recommendation on how to choose drugs and inhalers covers factors that prescribers routinely consider, so is not a change in practice. However, minimising the number and type of inhaler devices and avoiding unnecessary within-class switching may produce cost savings through lower upfront spending and better symptom control.
Full details of the evidence and the committee's discussion are in evidence review F: inhaled therapies.