

Prescribing and Clinical Effectiveness Bulletin

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NICE CLINICAL GUIDELINE 101, MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PRIMARY AND SECONDARY CARE (JUNE 2010)

Introduction

This special edition of the *PACE Bulletin* reviews the recommendations of the NICE Clinical Guideline on the management of Chronic Obstructive Pulmonary Disease (COPD) published earlier in the year. In conjunction with the Lincolnshire Respiratory Network, PACEF have developed some practical recommendations that will help to maximise both the effectiveness and cost-efficiency of prescribing within this disease area within the context of the NICE CG.

PACEF Recommendation

Prescribers should be mindful of the very different goals of inhaled treatment in asthma and COPD. In asthma, inhaled therapy can return lung function to normal, control symptoms and save lives. Inhaled therapy in COPD will at best only marginally improve lung function and there is very limited evidence for any beneficial effect on mortality. Patients should be advised of the goals of treatment in COPD. COPD treatment should be subject to regular review; where a medicine confers no additional benefit in terms of improved quality of life, dosage adjustment, discontinuation of the medicine or alternative therapies all need to be considered.

NICE Recommendations

Diagnosis of COPD

- All health professionals involved in the care of people with COPD should have access to spirometry and be competent in the interpretation of the results (see Respiratory Forum advice below).

PACEF Comment:

Appropriate prescribing in COPD depends on an accurate diagnosis of the condition and any co-morbidities. Diagnosis of COPD depends on history, the presence of a risk factor (usually smoking) and spirometry. The aim of prescribing for COPD is to alleviate symptoms and to reduce exacerbations. Medicines have little or no effect on the progression of COPD. Other interventions, particularly smoking cessation, and pulmonary rehabilitation have greater benefit.

Respiratory Forum Advice on Spirometry

- All GP practices should have health professional(s) with access to spirometry and be competent in the interpretation of the results.
- Spirometry can be performed by any healthcare worker who has undergone appropriate training and who keeps their skills up to date.
- Spirometry services should be supported by quality control processes.
- At the time of initial diagnostic evaluation, in addition to spirometry, other examinations and investigations should be considered as appropriate.
- COPD Classification should use the 'GOLD/NICE 2010' criteria (see Appendix 1).

NICE Recommendations (cont'd)

Stopping Smoking

- All COPD patients still smoking, regardless of age, should be encouraged to stop, and offered help to do so, at every opportunity.

Pulmonary Rehabilitation

- Pulmonary rehabilitation should be provided for all patients with COPD who need it, including those who have had a recent hospitalisation for an acute exacerbation.

Effective inhaled therapy: FEV1 greater than or equal to 50% of predicted

- **For people requiring regular maintenance inhaled therapy with an FEV1 greater than or equal to 50% of predicted, either a long acting beta agonist (LABA) or a long acting muscarinic antagonist (LAMA) should be prescribed.**

The cost difference between the various treatment options is illustrated below:

Drug	Daily dose	Cost (£)pa
LABAs		
Formoterol Easyhaler®	12mcg BD	£144
Formoterol Atimos Modulite®	12mcg BD	£219
Formoterol caps for inhalation (Foradil)	12mcg BD	£284
Formoterol Oxis Turbohaler®	12mcg BD	£302
Salmeterol Serevent Evohaler®	50mcg BD	£356
Indacaterol Onbez Breezhaler®	150 or 300mcg OD	£356
LAMAs		
Tiotropium Spiriva Handihaler®	18mcg OD	£424
Tiotropium Spiriva Respimat®	5mcg OD	£441

PACEF Recommendation: LABAs and LAMAs

The NICE Guideline Development Group (GDG) conclude that both LABAs and LAMAs are clinically effective within this context and that there is no strong evidence to favour one treatment over another. Where treatments are considered to be similarly effective and equally well tolerated, the treatment of the lowest acquisition cost is preferred. As a result of this, it is recommended that the formoterol Easyhaler dry powder device should be the first line maintenance therapy of choice within this context; formoterol Atimos Modulite presents a reasonable alternative for those requiring a metered dose inhaler

(MDI) with or without a spacer*. The formoterol Oxis Turbohaler and the salmeterol Serevent Evohaler are prohibitively expensive (over twice the price of the formoterol Easyhaler) and should no longer be used first line within this context. PACEF reviewed the indacaterol Onbrez Breezhaler in September 2010 and it was designated RED-RED due to lack of long term safety and efficacy data and a prohibitive price (see *PACE Bulletin*, Vol 4, No 18 (October 2010)). Prescribers are reminded that either a LABA or a LAMA is recommended by NICE at this stage; combination LABA and LAMA therapy is not recommended due to lack of evidence of additional benefit over a single component at optimum dosage.

* *The SPC for Atimos Modulite states:* "The use of a spacer device with the inhaler is usually recommended for patients who have difficulty in coordinating inhalation with actuation, however, no clinical data are available for Atimos Modulite with spacers." PACEF supports the use Atimos Modulite with a spacer where appropriate. This is based on the fact that Fostair (formoterol / beclometasone) in the same inhaler device and in the same extra-fine particle formulation is licensed for use with the Aerochamber plus spacer device. Serevent inhaler is licensed for use with the Volumatic

Effective inhaled therapy: FEV1 less than 50% of predicted

- For people requiring regular maintenance inhaled therapy with an FEV1 less than 50% predicted and frequent exacerbations either a LABA/inhaled corticosteroid (ICS) combination inhaler or a LAMA should be prescribed.

PACEF Recommendation: ICS/LABA Combination Inhalers

Patients should be made aware of the risks of inhaled corticosteroids in the treatment of COPD, particularly non-fatal pneumonia. The *BNF* states that high doses of inhaled corticosteroids used for prolonged periods can induce adrenal suppression. Both of the LABA/ICS combination inhalers licensed for COPD (Symbicort 400/12 Turbohaler and Seretide 500 Accuhaler), deliver doses of ICS within the *BNF* definition of high-dose inhaled steroids. As a result of this, all COPD patients prescribed these LABA/ICS combination inhalers should be supplied with a steroid warning card.

NICE estimate that up to 70% of COPD patients in the UK are prescribed inhaled steroids. Based on the evidence, it is likely that many of these patients are gaining little or no benefit from the inhaled steroid; at the same time these patients are at considerable risk of unwanted local and systemic effects. The relatively low level of prescribing of single component LABA inhalers in Lincolnshire suggests that LABA/ICS combination inhalers are commonly prescribed even in the FEV1 greater than 50% group. A change in this prescribing pattern would improve both the safety and cost-effectiveness of prescribing for these patients without compromising quality of care.

Where a LABA/ICS combination inhaler is indicated, only licensed products at licensed doses for COPD should be prescribed (i.e. Symbicort 400/12 (1 puff twice daily) or Seretide 500 Accuhaler (1 puff twice daily)). Prescribers are reminded that LABA/ICS combination inhalers used in the treatment of COPD need to be prescribed at doses licensed for COPD. The two licensed products are comparably priced (as illustrated below), with Symbicort Turbohaler marginally lower in cost than Seretide 500 Accuhaler. Seretide 250 inhaler is not licensed for use in COPD and should not be prescribed for this indication.

A cost comparison of the two licensed LABA/ICS combination inhalers is provided below:

Recommended Treatment Choices	Dose	No. of doses	Price	Cost (£) pa
Budesonide (400mcg)/ formoterol (12mcg) dry powder inhaler (DPI) (Symbicort Turbohaler 400/12)	1 actuation twice daily	60	£38.00	£456
Fluticasone (500mcg)/ salmeterol (50mcg) DPI (Seretide 500 Accuhaler)	1 actuation twice daily	60	£40.92	£491

PACEF Recommendation: Long Acting Muscarinic Antagonists (LAMAs)
Prescribers are reminded that **either** a LABA/ICS combination inhaler **or** a LAMA is recommended by NICE at this stage. If a patient declines steroid therapy or does not benefit from a LABA/ICS combination inhaler, a long acting muscarinic antagonist (LAMA) inhaler should be prescribed. Tiotropium is the recommended LAMA of choice.

A cost comparison of the two licensed formulations of tiotropium reveals the Spiriva Handihaler to be preferable in terms of cost:

Long-acting muscarinic antagonists (LAMA)

Recommended Treatment Choices	Dose	No. of doses	Basic NHS Price	Cost (£) pa
Tiotropium Spiriva Handihaler (DPI) 18mcg	1 dose (contents of capsule) daily	30 capsules	£34.87 / £31.89	£383 to £418
Tiotropium Spiriva Respimat (MDI) 2.5mcg	2 actuations daily	60 actuations	£36.27	£435

PACEF Recommendation: Safety of Spiriva Respimat
A recent safety study covered by the MHRA in the *Drug Safety Update* for November 2010 reported that Spiriva Respimat was associated with a non-significant increase in all-cause mortality compared with placebo. By contrast, Spiriva Handihaler was associated with a decrease in all-cause mortality compared with placebo. This may be a chance finding of little significance, but pending further study, safety concerns tend to support Spiriva Handihaler as the preferred LAMA of choice as advocated above.

Effective inhaled therapy: Combination therapy

- Offer a LAMA in addition to a LABA/ICS combination inhaler to people with COPD who remain breathless or have exacerbations despite taking a LABA/ICS, irrespective of their FEV1.

PACEF Recommendation: Triple Therapy
Triple therapy (LABA plus ICS plus LAMA) is unproven and of questionable cost-effectiveness. Before initiating triple therapy, a full review of the patient should be carried out, including diagnosis, co-morbidities, smoking status, concordance and response to current therapies. Alternative management strategies should also be considered, Such a review could be carried out by a GP with an interest in COPD in conjunction with a specialist nurse. Where uncertainty remains, the patient could be referred to a specialist COPD Clinic for review. Referral to a specialist COPD clinic may be appropriate at any stage of treatment, particularly where there are difficulties around diagnosis.

Managing exacerbations

- Reduce frequency of exacerbations by appropriate use of inhaled corticosteroids, bronchodilators and vaccinations.
- The impact of exacerbations can be minimised by: self-management advice, prompt response to exacerbation, appropriate treatment (e.g. oral steroids and/or antibiotics), non-invasive ventilation when indicated and hospital-at-home or assisted-discharge schemes.

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Dr Mike Ward's treatment algorithms and summary tables entitled *Medicines Management of COPD at a Glance* have been amended to reflect local guidance and are provided as Appendices 2-6 to this *Bulletin*

November 2010

Appendix 1: COPD Classification

GOLD/NICE 2010		NICE 2004	
Patient classification	FEV1	Patient classification	FEV1
I Mild	>80%		
II Moderate	<80%	Mild	50-80%
III Severe	<50%	Moderate	30-49%
IV Very Severe	>30%	Severe	<30%

Appendix 2: Medicines Management of Stable COPD at a Glance

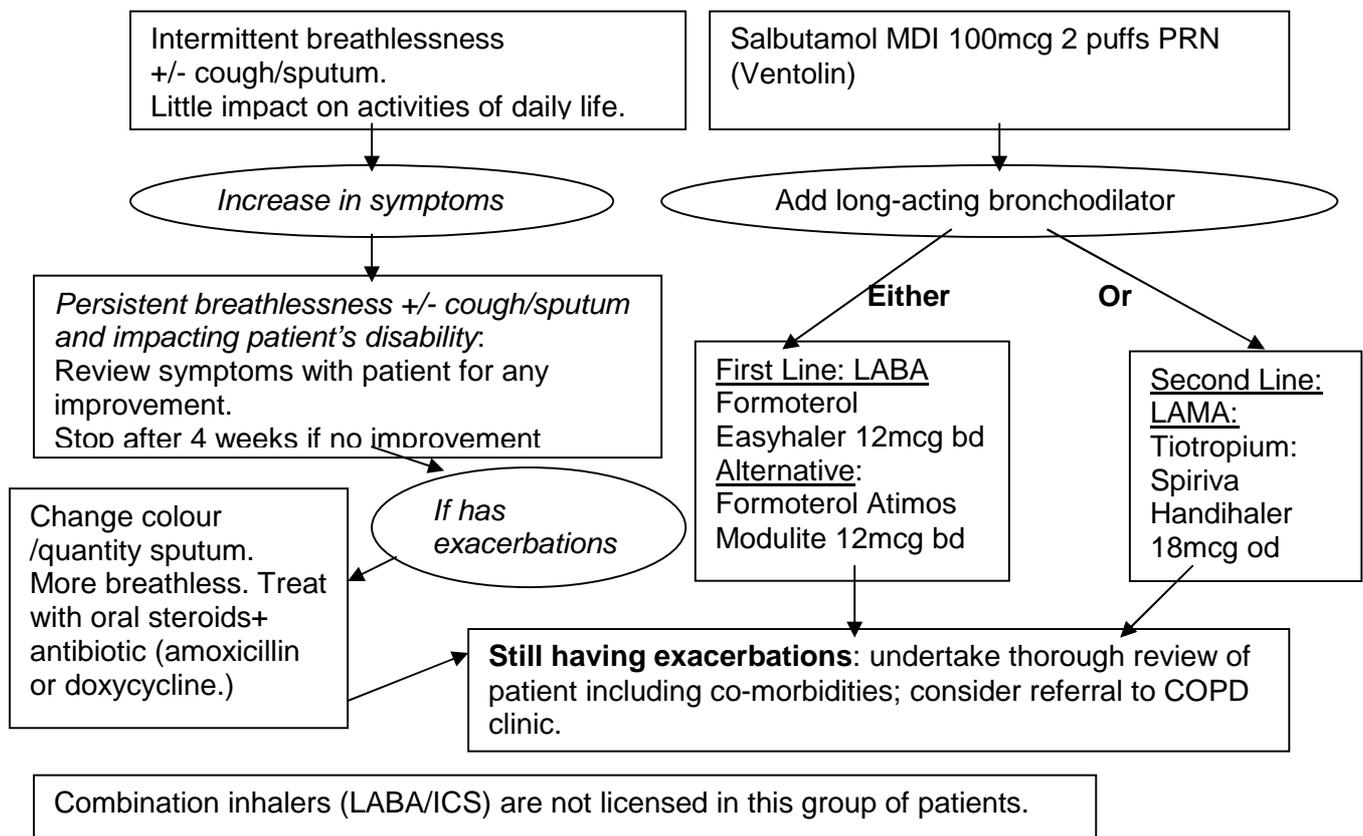
COPD affects patients in different ways. Some patients may be more troubled by breathlessness, others may develop ankle swelling and/or experience frequent hospital admissions.

Management should be guided by the **symptoms** and **disability**.

Remember that 25% **will have, cardiac disease**, as a cause of their disability.

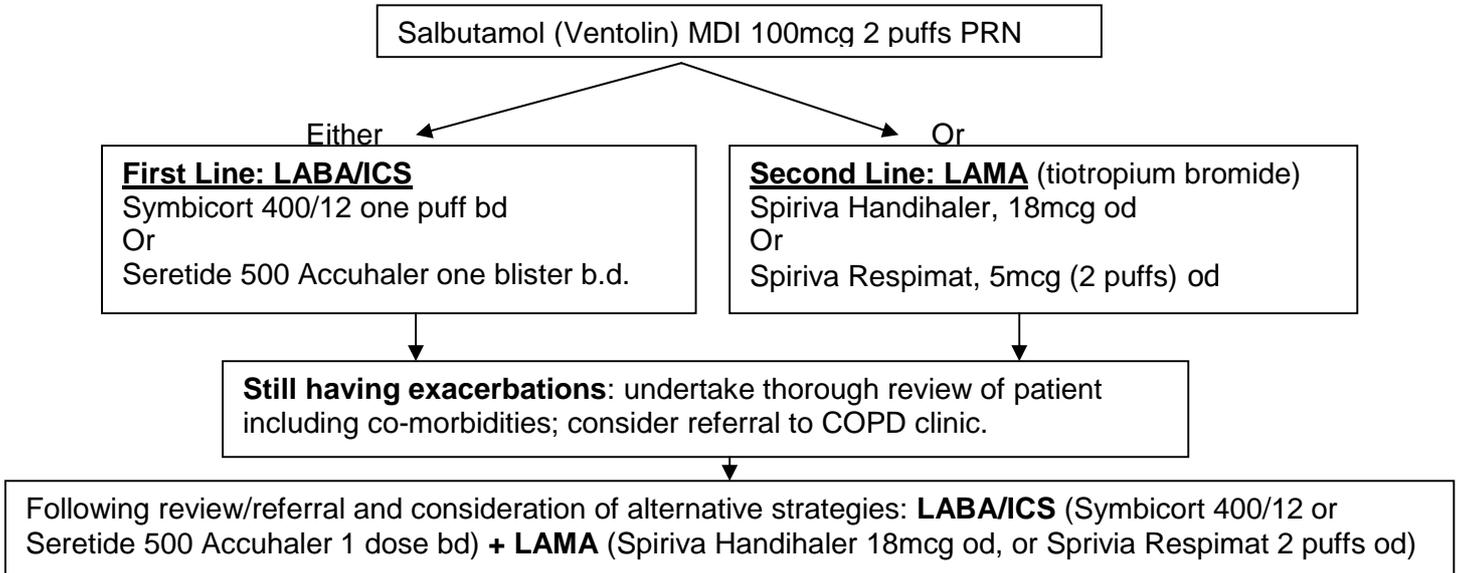
<p>All COPD patients still smoking, regardless of age, should be encouraged to stop, and offered help.</p> <p><i>For All patients with confirmed diagnosis of COPD:</i></p> <ul style="list-style-type: none"> ◆ Offer vaccinations: flu vaccination (annual) / pneumococcal (once only) ◆ Offer lifestyle advice e.g. exercise, nutrition ◆ Screen for anxiety and depression ◆ Record MRC dyspnoea score (QOF, Scores of 3-5 refer Pul Rehab) ◆ Screen for hypoxia (O₂ saturations < 92% refer for oxygen assessment) ◆ Give Self Management and Action Plans 	<p>Review Medicines</p> <ul style="list-style-type: none"> • Check adherence (compliance) with all prescribed medicines • Check inhaler technique • Review nebuliser therapy (use MDIs + spacer if possible) • Review symptom control, number of COPD exacerbations in last 12/12
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Appendix 3: Breathlessness and exercise limitation FEV₁ >50%



Offer pulmonary rehab if MRC score 3-5

Appendix 4: FEV1 < 50% & Frequent Exacerbations (2 or more per year)



Appendix 5: Chronic cough / sputum production

Consider a *trial of*:

- Carbocysteine capsules 750mg TDS for 6-8 weeks then 750mg BD if improvement in sputum production and reduction in viscosity.

Stop if no improvement. **There is no role for mucolytics in the prevention of exacerbations. Routine use is not recommended**

Appendix 6

Measurements / basic data

FEV1 absolute & % predicted

- Usual loss 40ml /yr

BMI

- <20 increased mortality –nutrition
- >35 ?also sleep apnoea

O2 sat

- <92% refer O2 assessment

Exacerbation Frequency

- frequent exacerbators need a treatment and diagnostic review

MRC dyspnoea score

- 3,4,5 refer to pulmonary rehabilitation

Smoking? – advice to stop

Frequent exacerbators

Check for co-morbidities

- Cardiac failure / IHD

Use Beta Blockers as they reduce death rates by 30% in COPD

Unusual organism

- Check for AFB, Pseudomonas

Wrong diagnosis?

- FEV1/FVC < 70% or >
- Bronchiectasis
- Cardiac failure

Is the treatment working?

1. Has your treatment made a difference to you?
2. Is your breathing easier?

If there is no benefit from a new treatment – you should consider stopping it

If the treatment is not working ? review diagnosis

FEV1/FVC ratio

- <70% Obstructive
- >80% Restrictive