

### Strategies to optimise inhaled therapy

**C**hronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction, which is usually progressive, not fully reversible and will not change markedly over several months (National Clinical Guideline Centre (NCGC), 2010).

#### Aims of inhaled therapy

The early use of inhaled corticosteroids is advised in asthma management to reverse inflammatory changes and achieve normal or near normal lung function. In COPD, however, the focus is on bronchodilation with inhaled corticosteroids being introduced much later in the disease process, usually if the patient is having two or more exacerbations per year.

#### Measuring severity

The severity of COPD can be measured in objective and subjective ways, which may not always correlate. Objectively, FEV<sub>1</sub> as a percentage of the predicted value can be used to measure severity, as

#### Key Points

- ▶  $\beta_2$ -agonist and anticholinergic bronchodilators work in different ways and may need to be used together to achieve optimal symptom relief in COPD
- ▶ Both short- and long-acting  $\beta_2$ -agonists and anticholinergics have a role to play in treatment
- ▶ The decision about which to use should be based on suitability and patient preference
- ▶ Corticosteroids are not licensed for use as monotherapy in COPD and may be introduced in combination with bronchodilators later in the disease process

recommended by the National Institute for Health and Clinical Excellence (NICE) (NCGC, 2010). However, a patient's perception of the severity of his/her symptoms is also important; if the treatment

aim is to reduce symptoms, it is important to understand how symptomatic the patient is (*Table 1*).

The MRC dyspnoea scale can be used to determine not only how symptomatic a patient is initially, but also to measure improvement in symptoms after initiating a therapy (*Table 2*). From 2009, the Quality and Outcomes Framework (QOF) included measurement and recording of the MRC dyspnoea scale score for all patients on the practice COPD register (British Medical Association and NHS Employers, 2009).

## Using bronchodilator therapy

The aim of treating COPD should be symptom control and reducing exacerbations, which are both associated with improved quality of life. NICE recommends the use of bronchodilators in symptomatic patients, with different approaches used to achieve optimal symptom relief in individual patients (*Figure 1*).

Two types of bronchodilator can be used in COPD:  $\beta_2$ -agonists and muscarinic

**Table 1. Definition of severity of COPD**

Severity	Definition
	FEV <sub>1</sub> /FVC ratio <0.7 with:
<b>Stage 1: Mild</b>	FEV <sub>1</sub> 80% predicted or more but with symptoms of COPD
<b>Stage 2: Moderate</b>	FEV <sub>1</sub> 50–79% predicted
<b>Stage 3: Severe</b>	FEV <sub>1</sub> 30–49% predicted
<b>Stage 4: Very severe</b>	FEV <sub>1</sub> less than 30% predicted

From: National Clinical Guideline Centre, 2010

antagonists (anticholinergics). Both are available in short-acting and long-acting versions. NICE no longer advocates the use of regular short-acting bronchodilators, stating that in most cases of mild COPD as-required use is as effective as regular use (NCGC, 2010). If regular use is necessary to treat persistent symptoms, a long-acting reliever inhaler should be used. The guidance does not recommend one type over another and also moves away from recommending the use of both types of bronchodilator together as standard practice, unless this has been shown to be effective in a specific patient (NCGC, 2010). The decision about which to use should be based on suitability and patient preference (*Table 3*).

Bronchodilators reverse airway obstruction and reduce microvascular leakage and the inflammatory mediators of bronchoconstriction. There are several options when choosing bronchodilator therapies in COPD.  $\beta_2$ -agonists stimulate  $\beta$ -adrenoreceptors, increasing concentrations of cyclic adenosine monophosphate (cAMP), leading to relaxation of the smooth muscles. Muscarinic antagonists block the effect of acetylcholine (ACh), a powerful bronchoconstrictor.

**Table 2. MRC Dyspnoea Scale**

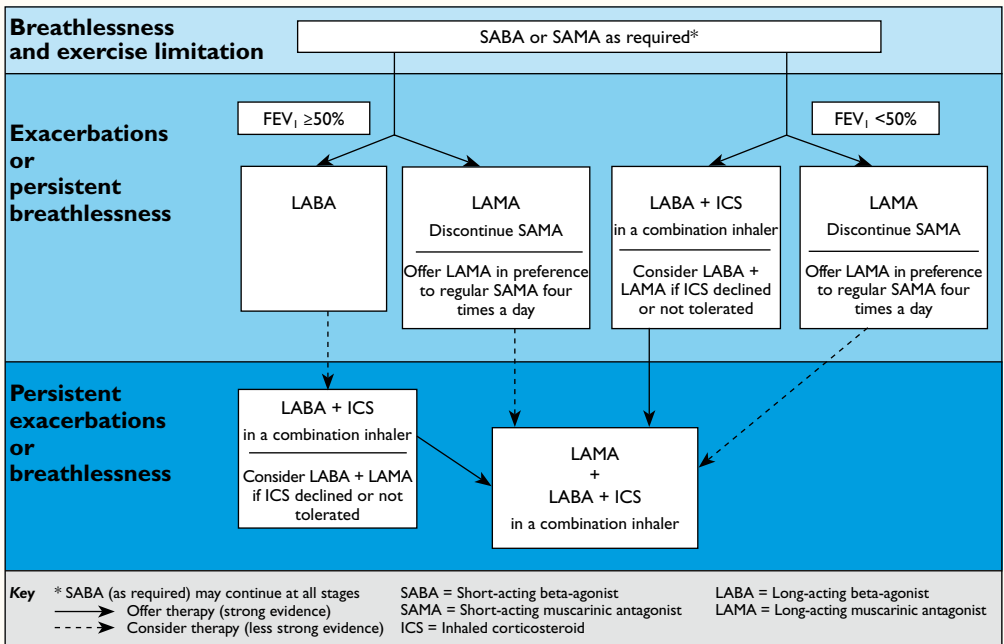
Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on walking up a slight hill
3	Walks slower than contemporaries on the level because of breathlessness, or has to stop for breath when walking at own pace
4	Stops for breath after walking about 100 m, or after a few minutes on the level
5	Too breathless to leave the house, or breathless when dressing or undressing

**Table 3. Inhaled bronchodilators for COPD**

Class	Dose
<b>SABA</b> Short-acting $\beta_2$ -agonist	Salbutamol 200 $\mu\text{g}$ as needed or 4 times daily Terbutaline 500 $\mu\text{g}$ as needed or 4 times daily
<b>LABA</b> Long-acting $\beta_2$ -agonist	Formoterol 12–24 $\mu\text{g}$ twice daily Salmeterol 50 $\mu\text{g}$ twice daily Indacaterol 150 $\mu\text{g}$ once daily
<b>SAMA</b> Short-acting muscarinic antagonist (anticholinergic)	Ipratropium 20–40 $\mu\text{g}$ 3 or 4 times daily via aerosol inhaler Ipratropium 40–80 $\mu\text{g}$ 3 or 4 times daily via dry-powder inhaler Ipratropium 250–500 $\mu\text{g}$ 3 or 4 times a day via nebulas
<b>LAMA</b> Long-acting muscarinic antagonist	Tiotropium 5 $\mu\text{g}$ once daily via Respimat Tiotropium 18 $\mu\text{g}$ once daily via Handihaler

From: Joint Formulary Committee, 2010.

Figure 1. Algorithm for the use of inhaled therapies in COPD (National Institute for Health and Clinical Excellence, 2010) (reproduced with permission).



**Table 4. Combined therapies for COPD**

Corticosteroid and long-acting $\beta_2$ -agonist	Device
Seretide 500 mg (fluticasone propionate and salmeterol)	Accuhaler
Symbicort 400 mg/12 mg (budesonide and formoterol)	Turbohaler

## Introducing inhaled corticosteroids

Inhaled corticosteroids have been shown to be effective in patients with recurrent exacerbations. The evidence for their use is strongest in reducing exacerbations and improving health status but there is no effect on mortality and there is evidence of an increased risk of pneumonia (Cazzola, 2009).

Inhaled corticosteroids are not licensed for use as monotherapy in COPD. The Medicines and Healthcare products Regulatory Agency (MHRA) (2009) has cited evidence of an increased risk of pneumonia in the use of corticosteroids for COPD. The MHRA (2009) reiterated the advice that inhaled steroids 'should be introduced only when COPD progresses to severe disease' and must not be used alone in COPD.

This is an important point. According to the recommendations of NICE (NCGC, 2010), the use of inhaled steroids usually follows the use of long-acting bronchodilators so that by the time the patient starts on an inhaled steroid it is given in a combination inhaler as the next step. There are only two licensed

combinations and devices for COPD (Table 4). All other inhaled steroids and/or combination therapies and/or devices are not licensed for use in COPD.

It can be seen, then, that inhalers combining a corticosteroid and a LABA may be used for symptom relief as well as for prevention of exacerbations, according to the updated NICE guidance (NCGC, 2010).

## References

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