Prescribing Bronchodilators Alone and with Inhaled Corticosteroids in COPD

Chronic obstructive pulmonary disease (COPD) is characterised by reduced airflow on expiration due to airway obstruction that is, at best, partially reversible, and usually worsens over time. Patients with COPD have reduced lung function and worsening of symptoms (exacerbations). The combined effects of dyspnoea, reduced exercise capacity, and repeated exacerbations cause impairment of the health-related quality of life of many patients with COPD. Both the GOLD and NICE guidelines recommend a stepwise approach to disease management, with bronchodilators being the mainstay of treatment.1,2

Bronchodilators and inhaled corticosteroids (ICS) in COPD

Short-acting bronchodilators. Short-acting bronchodilators are recommended initially, as needed, in patients with breathlessness and exercise limitation.1,2 There are two classes of short-acting bronchodilators: short-acting  β2-agonists (SABAs) and short-acting muscarinic antagonists (SAMAs). SABAs are the most commonly used short-acting bronchodilators in COPD.2 SABAs act directly on bronchial smooth muscle to cause bronchodilation; these have an onset of action within a few minutes of inhalation and last for up to 4 hours.2,4 SAMAs work by inhibiting resting broncho-motor tone, which is increased in patients with COPD. The onset of action for SAMAs is typically 30-45 minutes, with the bronchodilating effect generally lasting longer than that of SABAs, with some bronchodilator effects generally apparent up to 8 hours after administration.4,5

Side-effects of SABAs include tremor or tachycardia in high doses and/or in susceptible patients.1 The main side effect of SAMAs is dry mouth.1

Long-acting bronchodilators. In patients with persistent symptoms, regular maintenance treatment with long-acting bronchodilators is indicated. These long-acting bronchodilators give a prolonged reduction in breathlessness with an improvement in exercise ability. They also have the additional benefits of reducing exacerbation frequency, improving health status, and increasing measures of lung function.1,2 Both long-acting  β2-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs), previously known as long-acting anticholinergics, exhibit these benefits.1 In more severe disease, the use of multiple therapies becomes common and a trial of LABA/ICS combination is recommended. If symptoms persist, therapy can be stepped up with a LABA/ICS plus LAMA combination being offered.

Make a note: Inhaled bronchodilator therapy remains the cornerstone of management for stable COPD. By acting favourably on the functional work of breathing, and the reversible element of airway obstruction in COPD, bronchodilators reduce breathlessness and improve exercise capacity. These drugs can be ‘stepped up’ depending on need and response.

Guideline-based symptom control

Most guidelines recommend a step-wise approach to therapy which should be based on symptoms such as breathlessness and disability rather than on FEV1 alone.2,3 Indices of breathlessness such as the MRC Dyspnoea Score, measures outcomes of daily living, and exacerbation frequency, should all influence the type of therapy chosen for an individual patient.

The 2010 update to the NICE COPD guidelines suggest that in patients with intermittent symptoms (breathlessness and exercise limitation):3

Step 1: Patients needing short-term relief of symptoms

Start on either a SABA or a SAMA. These should be used as required to relieve breathlessness and exercise limitation.

Step 2: Patients with persistent symptoms or exacerbations despite the use of a short-acting bronchodilator

Offer a long-acting bronchodilator as maintenance therapy (the exact choice of drug depends on patient choice, cost, inhaler technique and the drug’s potential to reduce exacerbations).3 Combining long-acting bronchodilators and ICS also adds significant improvements to clinical outcomes over and above the benefits when either group of drug is used on its own. The recent update to the NICE COPD guidance suggests the following:3

- In people with stable COPD and an FEV1 ≥ 50% who remain breathless or have exacerbations despite maintenance therapy with a LAMA or a LABA:
  - Consider LABA+ICS in a combination inhaler or
  - Consider LAMA in addition to a LABA where ICS is declined or not tolerated.

- If FEV1 < 50%: Start therapy with LABA/ICS in a combination inhaler, or LAMA.

Step 3: Patients with ongoing symptoms and/or exacerbations

Offer a LAMA in addition to LABA+ICS to people with COPD who remain breathless or have exacerbations despite taking LABA+ICS, irrespective of their FEV1.1

Consider LABA+ICS in a combination inhaler in addition to LAMA for people with stable COPD who remain breathless or have exacerbations despite maintenance therapy with LAMA irrespective of their FEV1.1

Remember, do not rely solely on the results of lung function tests to evaluate how effective bronchodilator therapy is for your patient. Consider also subjective symptom improvement, how quickly symptom relief occurs, and effects on exercise capacity and activities of daily living. It is also important to check inhaler technique and adherence to therapy.
Use of inhaled therapies

**Breathlessness and exercise limitation**

<table>
<thead>
<tr>
<th>SABA or SAMA as required*</th>
<th>FEV$_1$ &lt; 50%</th>
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<tbody>
<tr>
<td><strong>LabA</strong></td>
<td>Exacerbations or persistent breathlessness</td>
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<tr>
<td><strong>LabA + ICS</strong> in a combination inhaler</td>
<td>Consent LabA + ICS declined or not tolerated</td>
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<tr>
<td><strong>LAMA</strong> in a combination inhaler</td>
<td>Consent LabA + ICS declined or not tolerated</td>
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<tr>
<td><strong>LAMA</strong></td>
<td>Consider therapy (less strong evidence)</td>
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**NICE use of inhaled therapies algorithm**

Please note: This algorithm should be used within the wider context of the management of COPD, including NICE algorithms 1, 2 and 3


**What you need to know**

Inhaled short-acting bronchodilator therapy is usually the initial therapy for symptom relief in COPD:

- SABAs are the most commonly used short-acting bronchodilators in COPD, with a quick onset of action and a duration of action of 4 hrs
- SAMAs generally last longer than SABAs (up to 8 hrs)

Long-acting bronchodilators are reserved for those patients who remain symptomatic (e.g. breathlessness or exacerbations) despite treatment with short-acting bronchodilators. In severe COPD additional treatment with ICS is often required:

- If FEV$_1$ ≥ 50% then start with LABA or LAMA
- If FEV$_1$ < 50% then offer LABA plus ICS in a combination inhaler or LAMA.

**Offer LAMA in addition to LABA+ICS to people with COPD who remain breathless or have exacerbations despite taking LABA+ICS, irrespective of their FEV$_1$.**

Consider LABA+ICS in a combination inhaler in addition to LAMA for people with stable COPD who remain breathless or have exacerbations despite maintenance therapy with LAMA irrespective of their FEV$_1$.

**Think about...**

- When should long-acting bronchodilator therapy be commenced and what should be the initial therapy?
- When would you introduce ICS to your patient?
- What measures would you use to assess treatment response?

**NICE 2010 update recommendations:**

In people with stable COPD who remain breathless or have exacerbations despite use of short-acting bronchodilators as required, offer the following as maintenance therapy:

- If FEV$_1$ ≥ 50% predicted: either LABA or LAMA
- If FEV$_1$ < 50% predicted: either LABA with an ICS in a combination inhaler, or LAMA.

Offer LAMA in addition to LABA+ICS to people with COPD who remain breathless or have exacerbations despite taking LABA+ICS, irrespective of their FEV$_1$.

Consider LABA+ICS in a combination inhaler in addition to LAMA for people with stable COPD who remain breathless or have exacerbations despite maintenance therapy with LAMA irrespective of their FEV$_1$.

**References**


**GLOSSARY**

$\beta_2$-agonist: a fast-acting bronchodilator drug that works by activating $\beta_2$ receptors in the airway; bronchodilator: a drug that relaxes and dilates the small airways and improves the passage of air into the lungs; corticosteroid: a type of drug related to a natural hormone and having anti-inflammatory properties; FEV$_1$: forced expiratory volume in 1 second, the volume of air breathed out in the first time from full lungs (a measure of lung function); muscarinic antagonist: a bronchodilator drug that works by blocking airway acetylcholine receptors