Managing stable chronic obstructive pulmonary disease
Focusing on inhalers

Key messages

1. Check smoking status and offer smoking cessation counselling at every opportunity.
2. Use LAMA when response to short-acting bronchodilators is inadequate.
3. Offer LAMA+LABA in patients with persistent symptoms and exacerbations.
4. Use ICS with LAMA+LABA only when there are further exacerbations despite LAMA+LABA therapy.
5. Switch patients on ICS without exacerbations in the past year to LAMA or LAMA+LABA.

Appropriate COPD management reduces morbidity and mortality

In Singapore, COPD patients have disproportionately more doctor visits, emergency department admissions, and hospitalisations compared to patients with other conditions. Although not fully reversible, COPD is preventable and clinically manageable even within primary care.

Main treatment goals in managing stable COPD are reducing symptoms and future exacerbations. Managing it with appropriate inhalers, as well as non-drug measures, are important in reducing COPD-associated morbidity and mortality.
Smoking cessation reduces decline in lung function (Figure 1)\(^5\) and mortality at any stage of COPD. **Check smoking status in every COPD patient and encourage them to reduce or preferably quit smoking.** Studies have shown that even brief clinician advice—less than three minutes—produces long-term smoking abstinence rates of 13.4%.\(^6\)

**Smoking cessation is the most effective single intervention**

Pharmacotherapy can reduce symptoms, frequency and severity of exacerbations, and improve quality of life. They have not been shown to modify the long-term rate of decline in lung function.\(^2\)

Treatment is based on individualised **symptom** and **exacerbation risk** assessment (Figure 2). A stepwise intensification of drug therapy is recommended for patients with persistent symptoms or further exacerbations.

Inhalers registered for COPD in Singapore are listed in Figure 3. It includes inhaled bronchodilators and inhaled corticosteroids (ICS). **Inhaled bronchodilators are central in managing COPD.**

Patient resources on smoking cessation, including cessation programmes, can be found in the Health Promotion Board’s Quit Fix booklet at www.healthhub.sg.

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**Assess inhaler technique and compliance regularly**

Incorrect inhaler technique is common. Before stepping up therapy, assess whether patients are compliant with their inhalers and using them correctly.

Provide patients with sufficient information and demonstration on correct inhaler use for optimal benefits. For an inhaler technique checklist, please refer to www.nationalasthma.org.au.
Inhaled bronchodilators: SABA, SAMA, LABA, and LAMA

Inhaled bronchodilators relax bronchial smooth muscles, relieving bronchospasm and dyspnoea. They are central in preventing or reducing COPD symptoms. They comprise beta_2-agonists and antimuscarinics, and can be short- or long-acting.

Short-acting bronchodilators (SABA or SAMA) as relievers

SABA or SAMA can be used as needed to relieve intermittent dyspnoea in all COPD patients. Those with only occasional symptoms may be controlled with relievers alone. If symptoms worsen, or the need for short-acting bronchodilators increases, re-evaluate and switch patients to maintenance long-acting bronchodilators.

Long-acting bronchodilators: LAMAs as mainstay

Compared to ICS, long-acting bronchodilators are preferred as the initial maintenance therapy. Using long-acting bronchodilators regularly improves lung function, dyspnoea, health status, and reduces exacerbation rates. LAMAs are preferred as they have a greater effect on reducing exacerbations compared with LABAs.

If a patient has persistent symptoms or further exacerbations despite treatment with LAMA, offer LAMA+LABA therapy. LAMA+LABA therapy should also be used as initial treatment in patients with significant symptoms and increased exacerbation risk.

Refer to Figure 2’s treatment algorithm for COPD patients.

Inhaled corticosteroids (ICS)

ICS have a limited role in COPD management. However, they are often widely prescribed across all stages of COPD regardless of exacerbation risk. Of patients treated with ICS, it is estimated that only half are true ICS candidates.

Besides oral thrush, regular use of ICS increases the risk of pneumonia, especially in certain patient subgroups such as:

- Patients with severe disease
- Smokers
- Elderly
- Patients with low body mass index
- Patients with a previous history of exacerbation or pneumonia

Offer ICS combined with LAMA+LABA only in patients with further exacerbations despite LAMA+LABA therapy (Figure 2).

However, ICS may be the first choice for patients with findings suggestive of asthma-COPD overlap (ACO). Consider specialist referral for this group of patients.

Other drugs in COPD management

MethyIxanthines such as theophylline, mucolytics, and macrolides can also be used but should be reserved as adjuncts to inhaled therapy.
Figure 2. Stepwise intensification of pharmacotherapy for COPD patients

CAT, COPD Assessment Test (CAT™); ICS, inhaled corticosteroid; LABA, long-acting beta₂-agonist; LAMA, long-acting muscarinic antagonist; mMRC, Modified British Medical Research Council; SABA, short-acting beta₂-agonist; SAMA, short-acting muscarinic antagonist.

Non-drug measures are equally important

Prescribe influenza and pneumococcal vaccinations

Both influenza and pneumococcal vaccinations decrease lower respiratory tract infections. Offer yearly influenza vaccination to all COPD patients. To those 65 and older, offer pneumococcal vaccinations PCV13 and PPSV23. Offer PPSV23 to younger COPD patients. Refer to the National Adult Immunisation Schedule (NAIS) for guidance, including use of Medisave for the vaccinations.

Encourage exercise and pulmonary rehabilitation

Reduced physical activity is common in COPD patients and results in poorer outcomes. Encourage patients to exercise regularly. Simple aerobic exercises such as walking three to four times a week for 20 to 30 minutes is beneficial. Coupling this with strengthening exercises such as repeated movements with weights has additional benefits.

Pulmonary rehabilitation programmes are available in restructured hospitals. They improve symptoms, quality of life, and exercise tolerance. A key component of the programmes is structured exercise training, recommended twice a week for 6 to 8 weeks. Education and self-management strategies are also incorporated to target behavioural change, with the aim of improving patient well-being and long-term adherence to health-enhancing behaviours.
### RELIEVERS — SHORT-ACTING BRONCHODILATORS

<table>
<thead>
<tr>
<th>Short-acting beta(_2)-agonist (SABA)</th>
<th>Short-acting muscarinic antagonist (SAMA)</th>
<th>SAMA+SABA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol, MDI, DPI*</td>
<td>Ipratropium, MDI, DPI*</td>
<td>Ipratropium + fenoterol, Berodual N, MDI</td>
</tr>
</tbody>
</table>

### MAINTENANCE — LONG-ACTING BRONCHODILATORS

**Long-acting muscarinic antagonist (LAMA)**

<table>
<thead>
<tr>
<th>Umeclidinium, Incruse Ellipta</th>
<th>Glycopyrronium, Seebri Breezhaler</th>
<th>Tiotropium, Spiriva Respimat</th>
</tr>
</thead>
</table>

**LAMA+ long-acting beta\(_2\)-agonist (LABA)**

<table>
<thead>
<tr>
<th>Umeclidinium + vilanterol, Anoro Ellipta</th>
<th>Glycopyrronium + indacaterol, Ultibro Breezhaler</th>
<th>Tiotropium + olodaterol, Spiolto Respimat</th>
</tr>
</thead>
</table>

### MAINTENANCE — INHALED CORTICOSTEROID (ICS)† COMBINATIONS

**LABA+ICS**

<table>
<thead>
<tr>
<th>Formoterol + budesonide, Symbicort Turbuhaler and Rapihaler</th>
<th>Salmeterol + fluticasone, Seretide Accuhaler</th>
<th>Vilanterol + fluticasone, Relvar Ellipta</th>
</tr>
</thead>
</table>

Note: Only the 9/320 mcg and 4.5/160 mcg formulations are registered for COPD.

Note: Only the 50/500 mcg formulation is registered for COPD. Seretide Evohaler (below) is registered for asthma, not COPD.

Note: Only the 25/100 mcg formulation is registered for COPD.

List of inhalers registered and available for COPD in Singapore. Active ingredients in bold denote availability on government subsidy list. List updated as of 25 Sep 2018. Please refer to product inserts for detailed information on the inhalers.

* Available as generics.
† ICS (beclomethasone, budesonide, fluticasone) should only be used in combination with LAMA+LABA.

DPI, dry-powder inhaler; MDI, metered-dose inhaler.

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**Check if your patient is doubling up on inhalers**

**Do not double up** on inhalers from the same class of drugs.

For example, if a patient is already on one LAMA such as umeclidinium, do not prescribe another, such as glycopyrronium or tiotropium.

**Do not double up** on inhalers containing an antimuscarinic (SAMA, LAMA, or LAMA+LABA).

This includes a SAMA with LAMA, because of potential antimuscarinic/anticholinergic side effects such as dry mouth and urinary retention.

**Do not double up** on inhalers containing a LABA (LAMA+LABA, LABA+ICS).

Common side effects include tremors, palpitations, and headaches.
About the Agency

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health (MOH). ACE develops evidence-based “Appropriate Care Guides” or ACGs to guide a specific area of clinical practice. ACGs are aimed at complementing MOH Clinical Practice Guidelines when these are available, by providing additions and updates as reflected in the evidence at the time of development, and incorporating cost-effectiveness considerations where relevant. The ACGs are not exhaustive of the subject matter. When using the ACGs, the responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional. This ACG will be reviewed 3 years after publication, or earlier, if new evidence emerges that requires substantive changes to the recommendations.

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Principal Head (Evaluation)
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg

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Driving better decision-making in healthcare

References

1. Ng TP. Unit 1. Epidemiology of COPD. SFP. 2013.

Expert group

Lead discussants
Dr Valerie Teo (NHGP)
A/Prof John Abisheganaden (TTSH)

Chairperson
Prof Lim Tow Keang (NUH)

Group members
Ms Choo Yee Mun (NTFGH)
A/Prof Gerald Chua (NTFGH)
Dr Eng Soo Kiang (ICCK - 24 Hour Family Clinic)
Mr Lee Tingfeng (TTSH)
A/Prof Loo Chian Min (SGH)
Dr Tan Hsien Yung David (NUP)
Adj Asst Prof Tan Tze Lee (The Edinburgh Clinic)
Adj A/Prof Augustine Tee (CGH)

This ACG has been adapted with permission from the Global Initiative for Chronic Obstructive Lung Disease (GOLD), Global Strategy for the Diagnosis, Management, and Prevention of COPD (2018) and the Global Initiative for Asthma (GINA), Global Strategy for Asthma Management and Prevention (2018).