



An update on the pharmacological management of stable COPD

New guidelines for the management of Chronic Obstructive Pulmonary Disease (COPD) were released by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and the Lung Foundation Australia in 2020. It is likely that these documents will inform the New Zealand guidelines to be published later in 2020. This article highlights the new management strategies recommended by these international guidelines.

KEY PRACTICE POINTS:

- Non-pharmacological interventions continue to underpin COPD management, including smoking cessation, regular exercise, pulmonary rehabilitation and annual influenza vaccination
- All patients with COPD should be prescribed a short-acting bronchodilator for relief of acute breathlessness, i.e. the short-acting muscarinic antagonist (SAMA) ipratropium or a short-acting beta₂-agonist (SABA) either salbutamol or terbutaline, or the combination SABA/SAMA salbutamol + ipratropium
- Long-acting muscarinic antagonists (LAMAs), e.g. tiotropium, glycopyrronium and umeclidinium, are now recommended internationally as the first-line long-acting bronchodilators for patients with persistent symptoms of COPD; long-acting beta₂-agonists (LABAs) are prescribed if LAMAs are contraindicated or not tolerated, whereas previously LABAs were first-line with LAMAs.
- Combination LABA/LAMAs are recommended for patients with persistent or troubling symptoms or whose lung function has declined significantly or who continue to experience exacerbations, despite LAMA or LABA monotherapy
- Triple therapy, i.e. a LABA/LAMA + an inhaled corticosteroid (ICS), may be appropriate for patients who have experienced two or more exacerbations in a year
- A blood eosinophil count may help to predict which patients with COPD are most likely to benefit from ICS treatment; levels $\geq 0.3 \times 10^9/L$ are associated with the greatest likelihood of benefit, levels $< 0.1 \times 10^9/L$ the least benefit. Spirometry is no longer recommended to guide the use of ICSs.
- It is now clearer when withdrawal of ICS treatment may be beneficial, i.e. where there is no evidence of benefit, the patient develops pneumonia or if they are clinically stable without a history of recent exacerbations

N.B. Information on aspects of care not covered in this article such as patient education, COPD action plans, nutritional guidance, exacerbation management, treatment of advanced symptoms and end-of-life care are available from: "The optimal management of patients with COPD – Part 2: Stepwise escalation of treatment" <https://bpac.org.nz/BPJ/2015/February/copd-part2.aspx>

An outline of COPD essentials in primary care

Chronic obstructive pulmonary disease (COPD) is characterised by persistent respiratory symptoms and an airflow limitation caused by noxious exposure to particles or gases.¹ It is estimated to be the fourth leading cause of death in New Zealand, following ischaemic heart disease, stroke and lung cancer.²

The exact prevalence of COPD in New Zealand is unknown. It has been conservatively estimated that one in every 15 people aged over 45 years has COPD, with a substantial number of additional people with undetected early-stage disease.³

COPD is associated with significant health disparities. Hospitalisation rates due to COPD are over five times higher for people living in the most deprived quintile, compared to people living in the least deprived quintile.⁴ Māori have COPD hospitalisation rates that are 3.5 times higher and COPD mortality rates 2.2 times higher, than people of non-Māori, Pacific or Asian ethnicity.⁴ Early investigation and diagnosis of COPD, combined with optimal management is critical in reducing these disparities in the most affected communities.

Diagnosis, assessment and non-pharmacological management


A diagnosis of COPD is typically based on the following factors, particularly in patients aged over 40 years:^{1,5}

- Breathlessness on exertion, cough and sputum production
- Long-term exposure to tobacco smoke or noxious exposure to respiratory irritants, e.g. pollution, occupational chemicals or unventilated cooking fires (more common in immigrants from less developed countries)
- Post-bronchodilator $FEV_1/FVC^* < 0.70$ on spirometry

* FEV_1 = Forced expiratory volume in 1 second, FVC = forced vital capacity

 Further information on COPD diagnosis is available from: <https://bpac.org.nz/BPJ/2015/February/copd-part1.aspx>


Assess COPD severity with spirometry and by the level of symptoms the patient is experiencing at diagnosis and review annually to measure progression. The COPD Assessment Test (CAT) is a short eight-item tool that provides a broad assessment of the patient's quality of life, e.g. sputum production, sleep quality and confidence in leaving their home, on a scale of zero to 40 (most severe). The Modified Medical Research Council (mMRC) dyspnoea scale is a brief assessment of functional disability that determines the impact of breathlessness on the patient's daily life.¹ The CAT and mMRC can both be useful when assessing COPD in primary care.¹

 The CAT and mMRC are available from: www.catestonline.org/patient-site-test-page-english.html and <https://bpac.org.nz/copd-tool>

Non-pharmacological interventions are first-line in COPD management as they are the most effective way to improve symptom control and quality of life and modify disease progression, regardless of what pharmacological treatments are ultimately required. Non-pharmacological interventions include:^{1,5}

- Smoking cessation; the most important factor to improve symptoms and slow disease progression
- Regular exercise; aim for as much as fitness will allow
- Pulmonary rehabilitation; offered to all patients, where available as it improves breathlessness substantially more than inhaled medicines
- Creating a written COPD action plan indicating what to do if the patient's condition deteriorates
- Annual influenza immunisation and appropriate pneumococcal immunisation reduces the risk of serious respiratory infections and COPD exacerbations*

* People with COPD are eligible for a funded influenza vaccination but not a funded pneumococcal vaccine. If affordable to the patient, it is recommended they receive both PCV13 and Pneumovax23 (see **Immunisation Handbook** for further details)

 Further information on smoking cessation is available from: <https://bpac.org.nz/BPJ/2015/October/smoking.aspx>

 Further information on pulmonary rehabilitation is available from: <https://bpac.org.nz/2017/copd.aspx>

A stepwise approach guides the use of inhaled medicines in the management of patients with stable COPD, taking into account:^{1,5}

- Symptom severity
- Exacerbation frequency
- Patient preference for medicine and inhaler type, e.g. some patients may find manipulating certain inhaler types difficult
- Likelihood of experiencing adverse effects
- Regimen complexity

Check the patient's treatment adherence and inhaler technique at each consultation, and especially before making changes to their treatment regimen. This can also be done by community pharmacists; consider adding a note to the prescription asking the pharmacist to check the patient's technique.


Treatment of COPD with inhaled medicines

All patients with COPD require inhaled medicines. Alongside non-pharmaceutical interventions, medicines improve symptoms, exercise tolerance and quality of life and may reduce the frequency and severity of COPD exacerbations.¹ There is, however, no conclusive evidence that medicines can prevent the long-term decline in lung function associated with COPD.¹

Bronchodilator treatment regimens need to be individualised as the effect is often difficult to predict.¹ Inhaled medicines are initiated as therapeutic trials and the patient's response monitored; a different inhaler or class of bronchodilator can be prescribed if the treatment response is not sufficient, after checking adherence and inhaler technique. Table 1 provides updated recommendations on the use of inhaled medicines for patients with COPD including initiating LAMAs at Step 2, in preference to LABAs, and the use of blood eosinophil levels to guide the use of ICSs.

Table 1: The stepwise escalation of pharmacological treatment for COPD, based on disease severity, adapted from the Lung Foundation Australia (2018) to include GOLD guidance (2020)^{1,6}

Severity	MILD	MODERATE	SEVERE
	<ul style="list-style-type: none"> ■ Few symptoms ■ Breathless on moderate exertion ■ Little or no effect on daily activities ■ Cough and sputum production ■ FEV₁ typically ≈ 60–80% predicted 	<ul style="list-style-type: none"> ■ Breathless walking on level ground ■ Increasing limitation of daily activities ■ Recurrent chest infections ■ Exacerbations requiring oral corticosteroids and/or antibiotics ■ FEV₁ typically ≈ 40–59% predicted 	<ul style="list-style-type: none"> ■ Breathless on minimal exertion ■ Daily activities severely restricted ■ Exacerbations of increasing frequency and severity ■ FEV₁ typically < 40% predicted
Medicine management	<p>CHECK device technique and adherence at each visit and reiterate the importance of smoking cessation, regular exercise and pulmonary rehabilitation, as appropriate.</p> <p>Step 1: START with a short-acting inhaler for as needed use, e.g. salbutamol, terbutaline, ipratropium or the combination salbutamol + ipratropium.</p> <p>Step 2: ADD a LAMA e.g. tiotropium, glycopyrronium or umeclidinium, or a LABA, e.g. salmeterol, indacaterol or formoterol, as an alternative.</p> <p>Step 2a: CONSIDER the need for a combination LABA/LAMA, e.g. indacaterol/glycopyrronium, vilanterol/umeclidinium or olodaterol/tiotropium, depending on the patient's symptoms</p> <p>Step 3: CONSIDER adding an ICS, e.g. fluticasone* (furoate or propionate) or budesonide: triple therapy may be appropriate for patients with ≥ 1 exacerbation requiring hospitalisation or ≥ 2 moderate exacerbations in the previous 12 months, AND significant symptoms despite LABA/LAMA or ICS/LABA treatment. Patients with a blood eosinophil count ≥ 0.3 × 10⁹/L are most likely to benefit from ICS treatment; patients with a blood eosinophil count < 0.1 × 10⁹/L are least likely to benefit.</p>		

 The updated bpac^{nz} COPD prescribing tool can be used to select medicines and inhaler types based on the patient's symptom severity and preference, available from: <https://bpac.org.nz/copd-tool>

Step 1: Prescribe short-acting bronchodilators to control occasional symptoms

Continue prescribing short-acting bronchodilators to all patients with COPD for the relief of acute breathlessness.¹ The following medicines all provide short-term improvements in breathlessness for patients with occasional symptoms of COPD:^{1,5}

- Short-acting muscarinic antagonist (SAMA), ipratropium
- Short-acting beta₂-agonists (SABAs), salbutamol or terbutaline
- Combination SABA/SAMA, salbutamol + ipratropium

Ipratropium produces greater improvements in lung function than SABA monotherapy and is generally better tolerated.⁵

The frequent use of short-acting bronchodilators, e.g. more than four times daily, is not recommended and if this is occurring, a long-acting bronchodilator should be initiated.¹

For easy reference, Table 2 provides the trade names for inhaled medicines funded for COPD treatment.

Step 2: Add a long-acting bronchodilator for persistent breathlessness

Long-acting muscarinic antagonists (LAMAs) are now first-line at Step 2 for patients with continuous COPD symptoms or frequent exacerbations, despite regular and correct use of a short-acting bronchodilator, if they meet the endorsement criteria for (see: "June, 2020: Temporary changes to funding criteria for some inhalers"):^{1,5}

- Glycopyrronium
- Tiotropium
- Umeclidinium

This is a change in guidance that has occurred in recent years as previously there was insufficient evidence to recommend one class of long-acting bronchodilator over another. LAMAs improve symptoms and quality of life and are associated with greater reductions in exacerbation rates and possibly fewer adverse effects, compared to LABAs.¹

If LAMAs are contraindicated, however, a LABA will help to reduce COPD symptoms and may also improve lung function and patient quality of life.⁵

N.B. Concurrent treatment with an ICS is not needed in patients with COPD (without features of asthma) who are taking a LABA. Combined ICS/LABA treatment is essential in patients with asthma due to the increased mortality risk associated with LABA monotherapy.

Ipratropium should be withdrawn before initiating a LABA and a SABA prescribed for as-needed symptom relief. Explain to patients that a SAMA and a LABA should not be taken concurrently. A SABA may be prescribed to patients taking a LABA, e.g. salmeterol, indacaterol or formoterol. Ipratropium may continue to be used for occasional symptom relief by patients taking a LABA.

It is not necessary to trial a short-acting bronchodilator before initiating a long-acting bronchodilator;^{1, 5} SABA-induced tachyphylaxis does not occur in people with COPD, therefore in contrast to asthma, trialling a short-acting inhaler is not predictive of the patient's tolerance to a long-acting medicine. If a patient has previously been taking a short-acting bronchodilator, the initiation of a long-acting inhaler aims to decrease the need for the short-acting inhaler.

June, 2020: Temporary changes to funding criteria for some inhalers

From 1 June, 2020, COPD diagnosis by spirometry will no longer be necessary for the following medicines to be funded: glycopyrronium (Seebri-Breezhaler), tiotropium bromide (Spiriva and Spiriva Respimat) and umeclidinium (Incruse Ellipta). Once the risk of exposure to COVID-19 is clinically negligible, the spirometry requirement will be reinstated, i.e. the COPD diagnosis must include spirometry and the prescription be endorsed accordingly.

Further information on the change for each product can be found on the PHARMAC website:

- Glycopyrronium-seebri-breezhaler (powder for inhalation 50 mcg per dose)
- Tiotropium-bromide-Spiriva (powder for inhalation, 18 mcg per dose) and Spiriva Respimat (soln for inhalation 2.5 mcg per dose)
- Umeclidinium- Incruse Ellipta (powder for inhalation 62.5 mcg per dose)

Step 2a: Prescribe a combination long-acting bronchodilator if monotherapy is not effective

For patients with persistent or troubling symptoms, e.g. CAT score ≥ 20, or whose lung function has declined significantly or who continue to experience exacerbations, despite LABA or LABA monotherapy, one of the following combination LABA/LAMAs is recommended for those meeting Special Authority criteria:^{1,5}

- Indacaterol/glycopyrronium
- Olodaterol/tiotropium
- Vilanterol/umeclidinium

Table 2: Inhaled medicines funded in New Zealand for the treatment of COPD, by class and trade name

Class	Medicine	Trade name
Short-acting bronchodilators		
Short-acting muscarinic antagonist (SAMA)	Ipratropium	Atrovent
Short-acting beta ₂ -agonists (SABAs)	Salbutamol	Respigen, SalAir, Ventolin*
	Terbutaline	Bricanyl
SABA/SAMA combination	Salbutamol + ipratropium	Duolin HFA
Long-acting bronchodilators		
Long-acting muscarinic antagonists (LAMA)	Glycopyrronium	Seebri†
	Tiotropium	Spiriva, Spiriva Respimat†
	Umeclidinium	Incruse Ellipta†
Long-acting beta ₂ -agonists (LABA)	Formoterol*	Fordail, Oxis
	Indacaterol	Onbrez
	Salmeterol	Serevent, Meterol
LABA/LAMA combinations	Indacaterol/glycopyrronium	Ultibro Breezhaler**
	Olodaterol/tiotropium	Spiolto Respimat**
	Vilanterol/umeclidinium	Anoro Ellipta†
Inhaled corticosteroids (ICS)		
ICS/LABA combinations	Budesonide + formoterol	Symbicort, Vannair
	Fluticasone (furoate) + vilanterol	Breo Ellipta
	Fluticasone (propionate) + salmeterol	RexAir, Seretide
ICS‡	Budesonide	Pulmicort
	Fluticasone	Flixotide, Floair

* Partially funded

† From 1 June, 2020, COPD diagnosis by spirometry will temporarily no longer be necessary for these medicines to be funded. Once the risk of exposure to COVID-19 is clinically negligible, the spirometry requirement will be reinstated, i.e. the COPD diagnosis must include spirometry and the prescription be endorsed accordingly.

** Special Authority funding for initiation requires patients be stabilised on a LAMA and that they are likely to receive additional benefit from a combination inhaler. Special Authority renewal requires that patients be adherent to treatment and the prescriber considers that they have improved symptom control.

‡ ICS Inhalers should only be prescribed alongside a LABA/LAMA in patients with COPD (unapproved indication)

Use an eosinophil count and exacerbation history to determine ICS benefit

A patient's blood eosinophil count may indicate the degree to which treatment with an ICS is likely to prevent future exacerbations.¹ The relationship between blood eosinophil counts and the protective effect of ICS treatment is continuous and increases from $< 0.1 \times 10^9/L$, where no or very little benefit is likely, to $> 0.3 \times 10^9/L$ where patients are likely to gain the greatest benefit.¹

Exacerbation history is, however, the strongest predictor of exacerbation risk and the decision to initiate an ICS requires the patient's exacerbation history to be known.¹ A blood eosinophil count therefore guides treatment, rather than being an absolute marker. A blood eosinophil count is unlikely to be helpful in a patient who has been recently diagnosed with COPD or in a patient without a history of exacerbations. Furthermore, the risk factors for exacerbations are not completely understood and other elements such as smoking history and genetics are also likely to contribute.¹

Blood eosinophil counts are relatively reproducible, but in patients with elevated levels fluctuations are more common and a single test may not be representative.¹ A second confirmatory eosinophil count in ten to 14 days is often performed in patients with high counts, prior to initiating an ICS; a single blood eosinophil count is sufficient in patients with low eosinophil levels. Patients taking oral corticosteroids should not undergo blood eosinophil counts to guide ICS treatment decisions as the results will not be representative of their underlying condition.

Funding changes for fluticasone and fluticasone with salmeterol inhalers

From 1 September, 2020, the Floair brand of fluticasone MDI and the RexAir brand of fluticasone with salmeterol MDI will no longer be funded.⁷ The Flixotide brand of fluticasone MDI and dry powder inhaler (DPI), and the Seretide brand of fluticasone with salmeterol MDI and DPI will be the only funded inhalers for these medicines until at least June, 2023.⁷

This decision does not affect the funding of fluticasone furoate with vilanterol.

Combination LABA/LAMAs may improve lung function and reduce symptoms and exacerbations more than LAMA or LABA monotherapy.^{1,5} LABA/LAMA combinations are generally preferred to ICS/LABA combinations due to the increased risk of pneumonia associated with ICS treatment (see: "ICS use and pneumonia risk in patients with COPD").^{1,5}

Step 3: Reserve ICS treatment for patients with exacerbations and eosinophilic COPD

An eosinophilic pattern of COPD may help to predict which patients may receive more benefit from an ICS/LABA, e.g. fluticasone (furoate) + vilanterol, budesonide + formoterol or fluticasone (propionate) + salmeterol (see: "Funding changes for fluticasone and fluticasone with salmeterol inhalers") compared with a LABA/LAMA.¹ Those most likely to benefit include patients with:¹

- A history of exacerbations, i.e. ≥ 2 a year or one exacerbation requiring hospitalisation
- A blood eosinophil count $\geq 0.3 \times 10^9/L$
- Asthma-COPD Overlap Syndrome (ACOS [see: "Asthma COPD overlap is managed with an ICS/LABA"])

Patients with a blood eosinophil count $< 0.1 \times 10^9/L$ are least likely to benefit from an ICS/LABA (see: "Using an eosinophil count and exacerbation history to determine ICS benefit").¹ Previously, exacerbation history and spirometry to assess reversibility were used to determine which patients were likely to benefit from an ICS.

Weigh the potential benefits of long-term ICS treatment against the risks of adverse effects,

including oral candidiasis and hoarseness, skin bruising and pneumonia.¹

⁵ There is less robust evidence that ICS treatment is also associated with decreased bone density and increased fracture risk, an increased risk of diabetes and reduced glycaemic control in patients with diabetes, cataracts and mycobacterial infection, including tuberculosis, although, the risk is substantially lower than that associated with oral corticosteroids.¹ Localised adverse effects such as oral candidiasis and hoarseness may be prevented by using a spacer with metered dose inhalers (MDIs) and by oral rinsing following actuation.

Triple therapy may be appropriate for patients with severe COPD

Patients who have experienced two or more exacerbations in a year or one exacerbation requiring hospitalisation or those who are severely symptomatic, while taking a LABA/LAMA may benefit from triple therapy, i.e. LABA/LAMA + ICS.¹ A beneficial response to an ICS may be expected to occur in patients with a blood eosinophil count $> 0.1 \times 10^9/L$ and greater improvements are more likely as eosinophil

numbers increase.¹ The potential benefit of triple therapy, however, needs to be balanced against the increased risk of pneumonia associated with long-term ICS use.¹

When to consider withdrawal of ICS treatment

In recent years it has become clearer when withdrawal of ICS should be considered, i.e. if the patient:¹

- Shows no evidence of benefit after eight to 12 weeks and does not have a history of exacerbations
- Develops pneumonia or another ICS-related adverse effect
- Is clinically stable and does not have a history of frequent exacerbations, i.e. less than two moderate exacerbations or one exacerbation requiring hospitalisation per year


Closely monitor symptom severity and exacerbation frequency following ICS withdrawal.⁵ There is an increased risk of exacerbations following ICS withdrawal in patients with a blood eosinophil count $> 0.3 \times 10^9/L$,¹ and ICS withdrawal may not be appropriate for these patients.

In summary: regular assessment is crucial to optimise treatment

Non-pharmacological interventions (especially smoking cessation and pulmonary rehabilitation) remain the most effective tools in the management of stable COPD. Inhaled medicines, however, provide an important additional level of symptom control; assess the patient's adherence and inhaler technique at every consultation. The key recent changes concerning the use of inhaled medicines for patients with COPD include:

- LAMAs are recommended as the first-line long-acting bronchodilators, whereas previously LABAs were first-line with LAMAs
- Blood eosinophil levels are recommended to help predict which patients are most likely to benefit from ICS treatment
- Clearer guidance is now available for when withdrawal of ICS treatment may be beneficial

Any changes to the patient's treatment should be accompanied by meaningful assessment, e.g. what is the effect on the patient's COPD assessment test (CAT) score? Any improvements in symptoms should be expected within six weeks. Positive effects on exacerbation frequency require longer to become apparent, i.e. six to 12 months.

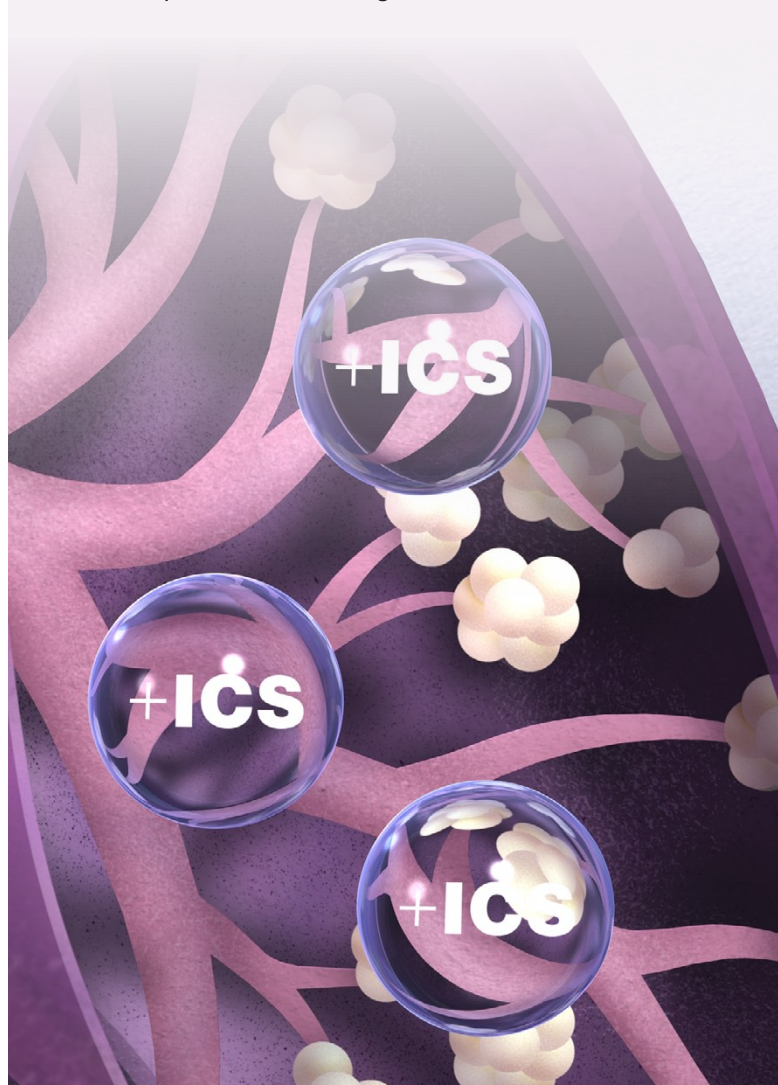
 Further information on the selection and use of inhaler devices in COPD is available from the Goodfellow webinar: www.goodfellowunit.org/events/asthma-and-copd-inhalers-%E2%80%93-every-breath-counts

ICS use and pneumonia risk in patients with COPD

Inhaled corticosteroids (ICS) are potent anti-inflammatory medicines that may reduce the duration, frequency and severity of COPD exacerbations.⁵ As they have a non-specific mechanism of action, ICSs also have the potential to compromise immunity, increasing the risk of respiratory infection and other adverse effects.

The use of ICS in patients with COPD is consistently associated with an approximate 1.5- to two-fold increased risk of developing pneumonia, depending on the dose.^{5,8} This increased risk of pneumonia is, however, not associated with an increased risk of pneumonia-related mortality or overall mortality, i.e. patients are more likely to develop pneumonia but there is no increased risk of death.⁵

Discontinuation of ICS treatment in patients with COPD rapidly attenuates the elevated risk of pneumonia. A large nested cohort study of more than 100,000 people with COPD treated with an ICS found a 37% decrease in the rate of serious pneumonia following ICS discontinuation.⁹



Asthma COPD overlap is managed with an ICS/LABA

COPD and asthma are both obstructive pulmonary diseases, but they differ in many ways, i.e. aetiology, inflammatory mediators and patterns of inflammation, treatment response and disease progression. Despite these differences, most people with COPD will display some degree of airflow limitation reversibility and some also have an inflammatory pattern of disease similar to asthma.⁵ Furthermore, some people with asthma develop an airflow obstruction similar to COPD.⁵ These mixed features can make it difficult to distinguish between COPD and adult onset asthma in people with a history of smoking. Approximately 27% of people with COPD also have features of asthma and this is referred to as Asthma-COPD Overlap Syndrome (ACOS).¹⁰ People with ACOS have a higher exacerbation rate than people with COPD alone.⁵

ACOS should be suspected in patients where FEV₁ increases by more than 400 mL on spirometry following bronchodilation,⁵ particularly if they have been diagnosed with asthma before age 40 years and they have a history of smoking.

An ICS/LABA is generally prescribed as the first-line long-term inhaled treatment for patients with ACOS. A LAMA is often added, i.e. triple therapy, for patients who experience persistent breathlessness or exacerbations. LABA monotherapy should be avoided in patients with ACOS because it is associated with a small but significantly increased risk of mortality in people with asthma.¹¹ ICS monotherapy is also not recommended for patients with ACOS.

Treatment recommendations for patients with ACOS are largely derived from expert opinion as patients with ACOS are often excluded from clinical trials involving COPD or asthma.

Acknowledgement: Article supported by PHARMAC

N.B. Expert reviewers do not write the articles and are not responsible for the final content. bpac^{nz} retains editorial oversight of all content.

References

1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease: 2020 Report. 2020. Available from: <https://goldcopd.org/wp-content/uploads/2019/11/GOLD-2020-REPORT-ver1.0wms.pdf> (Accessed Mar, 2020)
2. Asthma and Respiratory Foundation NZ. Key statistics: Respiratory disease in New Zealand. 2020. Available from: www.asthmafoundation.org.nz/our-work/research/key-statistics (Accessed May, 2020)
3. National Health Committee. Strategic overview: Respiratory disease in New Zealand (working draft). 2013. Available from: [www.moh.govt.nz/notebook/nbbooks.nsf/0/D8C3D421D082BC17CC257F7F006B67F4/\\$file/strategic-overview-respiratory-disease-nz.pdf](http://www.moh.govt.nz/notebook/nbbooks.nsf/0/D8C3D421D082BC17CC257F7F006B67F4/$file/strategic-overview-respiratory-disease-nz.pdf) (Accessed May, 2020)
4. Barnard L, Zhang J. The impact of respiratory disease in New Zealand: 2018 update. 2019. Available from: https://s3-ap-southeast-2.amazonaws.com/assets.asthmafoundation.org.nz/images/NZ-Impact-Report-2018_FINAL.pdf (Accessed May, 2020)
5. Yang I, Brown J, George J, et al. The COPD-X Plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease. 2020. Available from: <https://copdx.org.au/copd-x-plan/> (Accessed Apr, 2020)
6. Lung Foundation Australia. Stepwise management of stable chronic obstructive pulmonary disease (COPD). 2018; [Epub ahead of print]. Available from: <https://lungfoundation.com.au/wp-content/uploads/2018/09/Information-Paper-Stepwise-management-of-stable-COPD-Feb2019.pdf> (Accessed May, 2020)
7. PHARMAC. Decision to award sole supply for fluticasone and fluticasone with salmeterol metered dose inhalers. 2019. Available from: www.pharmac.govt.nz/news/notification-2019-12-12-fluticasone (Accessed Apr, 2020)
8. Yang M, Du Y, Chen H, et al. Inhaled corticosteroids and risk of pneumonia in patients with chronic obstructive pulmonary disease: A meta-analysis of randomized controlled trials. *Int Immunopharmacol* 2019;77:105950. doi:10.1016/j.intimp.2019.105950
9. Suissa S, Coulombe J, Ernst P. Discontinuation of Inhaled Corticosteroids in COPD and the Risk Reduction of Pneumonia. *Chest* 2015;148:1177–83. doi:10.1378/chest.15-0627
10. Alshabanat A, Zafari Z, Albanyan O, et al. Asthma and COPD Overlap Syndrome (ACOS): A Systematic Review and Meta Analysis. *PLoS ONE* 2015;10:e0136065. doi:10.1371/journal.pone.0136065
11. Weatherall M, Wijesinghe M, Perrin K, et al. Meta-analysis of the risk of mortality with salmeterol and the effect of concomitant inhaled corticosteroid therapy. *Thorax* 2010;65:39–43. doi:10.1136/thx.2009.116608



This article is available online at:
www.bpac.org.nz/2020/copd.aspx