COPD is a very common condition, which causes shortness of breath. COPD is an umbrella term for conditions including emphysema, chronic bronchitis and chronic asthma which is irreversible. The main risk factor is smoking or a history of past smoking cigarettes. At least one in 10 (10%) adults over the age of 40 years have COPD.

Guidelines

Australian guidelines for the management of COPD are called the COPD-X Guidelines. The key recommendations are summarised in the COPDX Plan:

- Case finding and confirm diagnosis
- Optimise function
- Prevent deterioration
- Develop a plan of care
- Manage exacerbations

Research on COPD medications usually measures the change in FEV1 (forced expiratory volume in one second), as well as patient-related clinical outcomes such as:

- St George’s Respiratory Questionnaire (SGRQ)
- Transition Dyspnoea Index (TDI)

The St George’s Respiratory Questionnaire is a 50-item questionnaire developed to measure health status (quality of life) across symptoms (frequency and severity), activity and impacts (psychosocial). TDI focal score measures impact of dyspnoea on three domains: functional impairment, magnitude of task and magnitude of effort.

Treatment

Current therapies target airflow limitation and pulmonary inflammation. The mainstay of treatment involves:

- Inhaled corticosteroids
- Long-acting beta₂-agonists (LABAs)
- Long-acting muscarinic antagonists (LAMAs)

Other treatments include short-acting bronchodilators (‘relievers’), oral bronchodilators (theophylline) and phosphodiesterase type-4 inhibitors (cilomilast, roflumilast).

Short-acting beta₂-agonists (SABAs) (salbutamol, terbutaline) improve lung function and daily breathlessness scores. They are usually prescribed for use as “rescue” medication, i.e. for relief of breathlessness, rather than for regular use.

Short-acting muscarinic antagonists (SAMAs) such as ipratropium bromide (Atrovent) have a longer duration of action than short-acting beta₂-agonists. They improve lung function and quality of life. Ipratropium bromide has a significantly greater effect on lung function compared to beta₂-agonists alone; in addition to improving quality of life and decreasing need for oral corticosteroid treatment. However, some studies have found that ipratropium bromide is associated with an increased risk of adverse cardiovascular effects.

Inhaled bronchodilators (LAMAs and LABAs) provide symptom relief, improve quality of life and may increase exercise capacity. In some patients, a response to bronchodilator therapy may require treatment for up to two months.

Inhaled corticosteroids (ICS) should be considered in people with moderate to severe COPD and frequent exacerbations. ICS include fluticasone, beclomethasone, budesonide and ciclesonide. They all may increase the risk of local oropharyngeal adverse effects and pneumonia; although risk of any pneumonia event has been found to be higher with fluticasone than budesonide. Long term use of systemic corticosteroids (prednisone, prednisolone) is not recommended.

LAMAs

Tiotropium improves quality of life, increases the number of patients with a clinically significant improvement, and reduces the number of patients with a clinically significant deterioration in quality of life. The newer LAMAs (umeclidinium, aclidinium and glycopyrronium) have been shown to be non-inferior to tiotropium, that is, they are just as effective as tiotropium.
LAMAs include:
- Tiotropium (*Spiriva Handihaler* and *Respimat*)
- Umeclidinium (*Incruse Ellipta*)
- Aclidinium (*Bretaris Genuair*)
- Glycopyrronium (*Seebri Breezhaler*)

Aclidinium is administered as one inhalation twice daily. Twice daily dosing improves early-morning symptoms (early morning cough, wheeze, shortness of breath, phlegm) and night-time symptoms (reduced frequency of breathlessness, cough, sputum production, wheezing).

Other LAMAs are administered once daily. There is no rationale to combine different LAMAs, either alone or in combination with LABAs.

LABAs
Long-acting beta₂-agonists cause prolonged bronchodilatation and can be administered once (indacaterol, Olodaterol, vilanterol) or twice daily (salmeterol, eformoterol). LABAs used for at least four weeks produce statistically significant benefits in lung function, quality of life, use of ‘reliever’ short-acting bronchodilators and acute exacerbations. LABAs do not significantly reduce mortality or serious adverse events.

LABAs include:
- Salmeterol (*Serevent Inhaler and Accuhaler*)
- Indacaterol (*Onbrez Breezhaler*)
- Eformoterol (*Oxis Turbuhaler*)
- Olodaterol (*Striverdi Respimat*)
- Vilanterol

Vilanterol is currently only available in combination products with a LAMA umeclidinium (*Anoro Ellipta*) and ICS fluticasone furoate (*Breo Ellipta*).

Combination therapy
When residents are not adequately controlled with a single long-acting bronchodilator, combining a LAMA and LABA may be beneficial.

A 2012 Cochrane systematic review of five studies found that the combination of tiotropium and a long-acting beta₂-agonist provided small improvements in health-related quality of life and bronchodilation, compared to tiotropium alone. A recent systematic review of currently available randomised trials of LAMA/LABA combinations for stable COPD demonstrated that LAMA/LABA combinations yield a greater improvement in trough FEV₁, and SGRQ and TDI scores than monotherapies. The review concluded that combination therapy is the most effective strategy in improving lung function, quality of life, symptom scores and moderate-to-severe exacerbation rates. Safety outcomes and severe exacerbations are similar with combination therapy when compared with monotherapies.

Current COPD treatment guidelines recommend a combination of a LAMA/LABA as an option for patients with significant symptoms and a low risk of exacerbations, patients with few symptoms and a high risk of exacerbations, and patients with many symptoms and high risk of exacerbations.

From 1 December 2015, four LAMA/LABA fixed-dose combination bronchodilators are PBS listed for adults with COPD:
- Eformoterol /aclidinium (*Brimica Genuair*)
- Indacaterol/glycopyrronium (*Ultibro Breezhaler*)
- Olodaterol/tiotropium (*Spiolto Respimat*)
- Vilanterol/umeclidium (*Anoro Ellipta*)

Eformoterol /aclidinium (*Brimica Genuair*) must be administered twice daily; whereas the other combination products are once daily. Olodaterol/tiotropium (*Spiolto Respimat*) requires two inhalations once daily. The Respimat device should be loaded and primed by the dispensing pharmacist. Indacaterol/glycopyrronium (*Ultibro Breezhaler*) consists of a capsule containing dry powder inhaled via a Breezhaler once daily at same time each day, which may require sufficient dexterity to load the capsule in the device. Genuair and Ellipta devices are likely to be easiest to use in older people with limited dexterity as they are pre-loaded with the active ingredient.

Device technique
It is critical that the inhaler device is used correctly during every administration. Metered dose inhalers or puffers should always be used with a spacer in older people.

A fixed-dose combination inhaler may be more convenient for residents rather than separate single-drug inhalers. Evidence suggests the drugs within each class of LAMAs and LABAs are broadly similar, so the choice of treatment may be tailored to ease of use of the different devices.

References
Cochrane Database Syst Rev 2012;4:CD008989
COPD-X Guidelines – Version 2.43 (September 2015)