19.1 Drugs for asthma and chronic obstructive pulmonary disease

Table 19–1 Inhalers used for asthma or COPD

See also Inhalers p 887

Brand® (device)	Corticosteroid	Beta$_2$ agonist	Anticholinergic	Cromone
Airomir Autohaler (MDI)		salbutamol[1]		
Alvesco (MDI)	ciclesonide			
Asmol (MDI)		salbutamol[1]		
Atrovent (MDI)			ipratropium[1]	
Bretaris Genuair (DPI)			aclidinium[2]	
Bricanyl Turbuhaler (DPI)		terbutaline[1]		
Flixotide (MDI)[3]	fluticasone propionate			
Flixotide Accuhaler (DPI)	fluticasone propionate			
Foradile Aerolizer (DPI)		formoterol (eformoterol)[4]		
Incruse Ellipta (DPI)			umeclidinium[2]	
Intal Spincaps (DPI)				cromoglycate
Intal, Intal Forte (MDI)				cromoglycate
Onbrez Breezhaler (DPI)		indacaterol[4]		
Oxis Turbuhaler (DPI)		formoterol[4]		
Pulmicort Turbuhaler (DPI)	budesonide			
Qvar Autohaler (MDI)	beclometasone			
Seebri Breezhaler (DPI)			glycopyrronium (glycopyrrolate)[2]	
Serevent Accuhaler (DPI)		salmeterol[4]		
Spiriva Handihaler (DPI)			tiotropium[2]	
Spiriva Respimat (mist MDI)			tiotropium[2]	
Tilade (MDI)				nedocromil
Ventolin (MDI)		salbutamol[1]		
Ventolin Rotacaps (DPI)		salbutamol[1]		
Fixed-dose combination inhalers				
Anoro Ellipta (DPI)		vilanterol[4]	umeclidinium[2]	
Breo Ellipta (DPI)	fluticasone furoate[5]	vilanterol[4]		
Brimica Genuair (DPI)		formoterol[4]	aclidinium[2]	
Flutiform (MDI)	fluticasone propionate	formoterol[4]		
SalplusF (MDI)	fluticasone propionate	salmeterol[4]		
Seretide (MDI)[3]	fluticasone propionate	salmeterol[4]		
Seretide Accuhaler (DPI)	fluticasone propionate	salmeterol[4]		
Spiolto Respimat (mist MDI)		olodaterol[4]	tiotropium[2]	
Symbicort Rapihaler (MDI)	budesonide	formoterol[4]		
Symbicort Turbuhaler (DPI)	budesonide	formoterol[4]		
Ultibro Breezhaler (DPI)		indacaterol[4]	glycopyrronium[2]	

1 short-acting
2 long-acting anticholinergic (also known as long-acting antimuscarinic or LAMA)
3 generic brands that name the drugs in the brand may also be available
4 long-acting beta$_2$ agonist (LABA)
5 not interchangeable with fluticasone propionate

Chronic obstructive pulmonary disease

See also Inhalers p 887, lungfoundation.com.au/health-professionals/copd

COPD is usually caused by smoking. Airflow limitation in COPD is persistent, progressive and not fully reversible.

Rationale for drug use

Symptom relief.

Improvement of exercise tolerance and quality of life.

Prevention or treatment of exacerbations and complications of COPD.

General measures

Identify and reduce risk factors such as smoking, dust, fumes, indoor and outdoor pollutants. Smoking cessation decreases the rate of lung function decline by 50% and prolongs survival; it is the most effective intervention for COPD. Encourage and support patients to stop smoking at every opportunity, see also Nicotine dependence p 872.

Check immunisation status: pneumococcal (p 922) and influenza (p 918) vaccines are recommended in COPD. Influenza vaccination decreases the risk of exacerbations, hospitalisation and death, but the value of pneumococcal vaccination has not been unequivocally established.

Pulmonary rehabilitation improves exercise capacity, dyspnoea and quality of life, and reduces hospitalisation. It should be offered to all COPD patients with functional impairment.

Long-term oxygen therapy (ideally >18 hours daily) improves quality of life and survival in COPD patients with hypoxaemia.

Surgery may be considered in selected patients for symptom relief (eg bullectomy, lung volume reduction).

Drug treatment of stable COPD

See also Table 19–2 Management of stable COPD p 883, Table 19–1 Inhalers used for asthma or COPD p 882

Inhaled drugs are the mainstay of treatment and are used in a step-up manner. Review 1–2 months after starting new therapy: if no improvement in symptoms despite good inhaler technique and compliance, consider alternative treatment. A longer trial may be required to assess effect of inhaled corticosteroids on exacerbations.

Short-acting bronchodilators

Inhaled short-acting beta$_2$ agonists (SABAs) or ipratropium, a short-acting anticholinergic, are used on an as-needed basis to relieve symptoms and improve exercise tolerance in the initial management of mild COPD. Individualise choice based on response, adverse effects and patient preference.

Combining the two classes may provide additional benefit without increasing adverse effects. However, if regular use is required, it is preferable to step up to a long-acting bronchodilator. SABAs (used when required) may be continued throughout disease progression; ipratropium should be stopped when starting a long-acting anticholinergic.

Long-acting bronchodilators

Inhaled long-acting beta$_2$ agonists (LABAs) and long-acting anticholinergics (also known as long-acting antimuscarinics or LAMAs) are useful in patients who, despite the use of short-acting bronchodilators, remain symptomatic or have exacerbations. They reduce symptoms, frequency of exacerbations, hospitalisation, and improve exercise tolerance and quality of life.

Although there is no clear evidence to guide initial drug choice, long-acting anticholinergics are often used first as they may be slightly more effective than LABAs in preventing exacerbations in stable COPD. However, there appears to be little difference in mortality or overall quality of life.

Individualise choice based on response, adverse effects and patient preference. For example, if response is inadequate to a trial of a drug from one class, swap to a drug from the other class. For persistent symptoms, consider using both a LABA and a long-acting anticholinergic. In moderate or severe COPD, limited data show small improvements in quality of life measures and lung function with combination treatment compared with either a LABA or an anticholinergic alone. The many fixed-dose combination inhalers appear to have similar safety and efficacy, although there are no direct head-to-head comparisons.

COPD patients with coexisting asthma should also be treated with an inhaled corticosteroid if using a LABA (p 884).

Table 19–2 Management of stable COPD

See also Table 19–1 Inhalers used for asthma or COPD p 882

Steps	Comments
start with a SABA or ipratropium when required for symptom relief	• using a SABA with ipratropium may be more effective, but it is preferable to move to the next step
add or switch to a LABA **or** long-acting anticholinergic[1] for persistent symptoms	• try a drug from one class, then swap to the other if needed • continue SABA when required
use a LABA with a long-acting anticholinergic if still symptomatic	• don't double-up: when starting fixed-dose combination inhalers, stop all previous inhalers containing drugs from the same class • continue SABA when required
add an ICS if still symptomatic[2] (LABA + long-acting anticholinergic + ICS)	

ICS = inhaled corticosteroid; LABA = long-acting beta$_2$ agonist; SABA = short-acting beta$_2$ agonist

[1] stop ipratropium when starting a long-acting anticholinergic (also known as long-acting antimuscarinic or LAMA)

[2] FEV_1<50% and >2 exacerbations annually

Corticosteroids

Inhaled corticosteroids reduce frequency of exacerbations and improve quality of life in severe disease (eg FEV_1<50%). Guidelines recommend adding inhaled corticosteroids to long-acting bronchodilators in patients with persistent breathlessness and frequent exacerbations (eg >2 annually). However, inhaled corticosteroid use has been associated with an increased risk of pneumonia in COPD patients.

If there is no symptomatic benefit, some studies suggest it may be safe to withdraw inhaled corticosteroid treatment, provided long-acting bronchodilators (a LABA, long-acting anticholinergic or both) are maintained. However, close follow-up is recommended.

There is no role for inhaled corticosteroid monotherapy or long-term oral corticosteroids in the treatment of COPD.

Other treatment

Controlled release theophylline is effective in COPD compared to placebo, but not as effective or as well tolerated as inhaled long-acting bronchodilators. It has a narrow therapeutic range, potential for drug interactions, and requires concentration monitoring. In Australia, low doses are sometimes used in patients who still remain symptomatic despite optimal inhaled therapy. There is little published evidence to support dosing in this context; seek specialist advice.

Drug treatment of COPD exacerbations

Short-acting bronchodilators: increase dose and/or frequency of use during exacerbations. Inhaled SABAs and ipratropium may be used together until symptoms improve, although ipratropium is not recommended in the long term if the patient is already on a long-acting anticholinergic (additive anticholinergic adverse effects).

Short courses of oral corticosteroids shorten recovery time and reduce exacerbation severity and risk of early relapse. Although the optimum treatment duration has not yet been established, 5-day regimens may suffice; courses >14 days provide no further benefit and increase the risk of adverse effects. Consider osteoporosis (p 452) prevention in patients who require frequent courses.

Antibacterials are beneficial in exacerbations with clinical signs of infection (see Acute exacerbation of COPD p 102). Although there is some evidence that antibacterial prophylaxis may reduce exacerbation frequency in some patients, it is not recommended because it has no effect on hospitalisations or mortality, and there are concerns regarding adverse effects and antibacterial resistance.

Practice points

- check inhaler technique and compliance regularly
- minimise use of different devices by using fixed-dose combination inhalers (p 882) where possible, according to patient preference; when starting combination inhalers, stop all inhalers containing drugs from the same class
- in stable disease, administering bronchodilators via an MDI or DPI is preferred to nebulisation; consider use of a spacer with MDIs, particularly for patients with poor inspiratory effort, or impaired coordination and/or dexterity
- during an exacerbation, nebulisers or inhalers with spacers may be used to administer bronchodilators
- consider developing a written action plan for management of exacerbations, see *www.lungfoundation.com.au/health-professionals/clinical-resources/copd/copd-action-plan/*