COPD, a common preventable and treatable disease, is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. COPD is a preventable and treatable disease.

It has two components:

- its pulmonary component is characterised by airflow limitation that is not fully reversible
  - FEV1:FVC ratio <70%, post-bronchodilator (measured via spirometry)
- its extrapulmonary effects (weight loss, nutritional abnormalities, skeletal muscle dysfunction, and increased risk for myocardial infarction, osteoporosis, etc.) contribute to the severity in individual patients.

Epidemiology

An estimated 210 million people worldwide have COPD of which an estimated 110,000 people are in Ireland. (Murtagh et al, 2005) The worldwide prevalence of COPD is >10%. More than 3 million people died of COPD in 2005, which is equal to 5% of all deaths globally that year. Worldwide COPD ranked as the fourth leading cause of death and is expected to become the third leading cause by 2030. Total deaths from COPD are projected to increase by >30% in the next 10 years without interventions to cut risks, particularly exposure to tobacco smoke.

There is an increasing prevalence of COPD in women (MMWR, 2008) with an increased risk of COPD in the economically deprived as socioeconomic status is inversely related to risk of COPD. In relation to other diseases, COPD is the fourth leading cause of morbidity and mortality, the leading cause of disability and the sixth in prevalence of major conditions (See Table One).

Risk factors

The risk factors for COPD include:

- Exposure to particles such as tobacco smoke, occupational dusts, indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings and outdoor air pollution
- Lung growth and development
- Gender – males more susceptible than females
- Age – risk increases with age
- Respiratory infections
- Socioeconomic status
- Asthma/bronchial hyper-reactivity
- Chronic bronchitis

Pathophysiology of COPD

COPD is characterised by airflow limitation, air trapping and decreased exercise tolerance. Frequently, by the time the patient presents with symptoms, many have progressed to moderate COPD. Many patients who have mild COPD on their spirometry will not have symptoms. When airflow is limited, air gets trapped in the lungs which is first recognised by the patient on exercising. Air trapping impacts on the patient by affecting their ability to inhale. It also affects their exercise tolerance and causes patients to limit their activities.

Diagnosis and assessment

The diagnosis and assessment of COPD involves assessing symptoms, airflow limitation, risk of exacerbations and co-morbidities.

Assessing symptoms

The characteristic symptoms of COPD are chronic and progressive dyspnea, cough and sputum production that can be variable from day-to-day. Dyspnea is usually progressive, persistent and characteristically worse with exercise. Patients may have an intermittent or unproductive cough, but many patients will commonly cough up white/clear non-purulent sputum. Symptoms can be assessed using the COPD Assessment Tool (CAT test) and the Medical Research Council Dyspnoea (MRC) scale. The CAT test is an 8-item measure of health status impairment in COPD. The MRC scale is illustrated in Table Two.

Table One: Prevalence of COPD in relation to other major conditions.
Source: Adapted from GOLD 2015.
Assessing airflow limitation
Airflow limitation is assessed by spirometry. An FEV₁/FVC ratio post bronchodilator of less than 70% indicates airflow limitation. The severity of airflow limitation is then assessed by the FEV₁. (See Table Three). The bronchodilator of choice used for reversibility testing is Salbutamol 200mcg – 400mcg via spacer device with the spirometry repeated 15 minutes post administration.

In patients with FEV₁/FVC < 70%:
- GOLD 1: Mild  FEV₁ ≥ 80% predicted
- GOLD 2: Moderate  50% ≤ FEV₁ < 80% predicted
- GOLD 3: Severe  30% ≤ FEV₁ < 50% predicted
- GOLD 4: Very Severe  FEV₁ < 30% predicted
*Based on Post-Bronchodilator FEV₁

Assessing risk of exacerbations
If the patient has had two exacerbations or more within the last year or an FEV₁ <50 % of predicted value, they are considered high risk for exacerbations in the future.

Assessing co-morbidities
Patients with COPD are at increased risk for:
- Cardiovascular diseases
- Osteoporosis
- Respiratory infections
- Anxiety and depression
- Diabetes
- Lung cancer
These comorbid conditions may influence mortality and hospitalizations and should be looked for routinely, and treated appropriately.3

Combining assessments and classification of COPD
GOLD recommend combining the assessments from airflow limitation, risk of exacerbations and symptoms (Table Four) to classify patients as A, B, C, or D (Table Five). This classification assists the health care professional with treatment options and it ensures that patients are prescribed the most appropriate medication for the degree of severity of their COPD.

<table>
<thead>
<tr>
<th>Risk</th>
<th>GOLD Classification of Airflow Limitation</th>
<th>Risk</th>
<th>Exacerbation history</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>GOLD 1: Mild  FEV₁ ≥ 80% predicted</td>
<td>1</td>
<td>≤ 1</td>
</tr>
<tr>
<td>1</td>
<td>GOLD 2: Moderate  50% ≤ FEV₁ &lt; 80% predicted</td>
<td>2</td>
<td>&gt; 1 ≥ 2</td>
</tr>
<tr>
<td>2</td>
<td>GOLD 3: Severe  30% ≤ FEV₁ &lt; 50% predicted</td>
<td>3</td>
<td>&gt; 2 ≥ 3</td>
</tr>
<tr>
<td>3</td>
<td>GOLD 4: Very Severe  FEV₁ &lt; 30% predicted</td>
<td>4</td>
<td>&gt; 3 ≥ 4</td>
</tr>
</tbody>
</table>

Table Four: Combined assessment of COPD
Source: Adapted from GOLD 2015.3

Other investigations
- Chest x-ray: Seldom diagnostic but valuable to exclude alternative diagnoses such as malignancy and to establish the presence of significant co-morbidities such as heart failure.
- Lung volumes and diffusing capacity: Help to characterise severity, but not essential to patient management. These tests are carried out in pulmonary function laboratories.
- Oximetry and arterial blood gases: Pulse oximetry can be used to evaluate a patient’s oxygen saturation and need for supplemental oxygen therapy.
- Alpha-1 antitrypsin deficiency screening: Should be performed when COPD develops in patients of caucasian descent under 45 years or with a strong family history of COPD.
- Exercise testing: Objectively measured exercise impairment, assessed by a reduction in self-paced walking distance (such as the 6 minute walking test) or during incremental exercise testing in a laboratory, is a powerful indicator of health status impairment.
and predictor of prognosis.

**Differential diagnosis**

Asthma is the primary differential diagnosis (See Table Six). Other differential diagnoses include congestive cardiac failure, lung cancer, TB, alpha one antitrypsin deficiency and cor pulmonale.

<table>
<thead>
<tr>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset in mid-life</td>
<td>Onset early in life (often childhood)</td>
</tr>
<tr>
<td>Symptoms slowly progressive</td>
<td>Symptoms vary from day to day</td>
</tr>
<tr>
<td>Long smoking history</td>
<td>Symptoms worse at night/early morning</td>
</tr>
<tr>
<td>Family history of asthma</td>
<td>Allergy, rhinitis, eczema present</td>
</tr>
</tbody>
</table>

Table Six: COPD versus Asthma

Source: Adapted from GOLD 2015.

**Key points for diagnosis and assessment of COPD**

- A clinical diagnosis of COPD should be considered in any patient who has dyspnoea, chronic cough or sputum production, and a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC <0.70 confirms the presence of persistent airflow limitation and thus of COPD.
- The goals of COPD assessment are to determine the severity of the disease, including the severity of airflow limitation, the impact on the patient’s health status, and the risk of future events.
- Comorbidities occur frequently in COPD patients, and should be actively looked for and treated appropriately if present.

Patients may have both asthma and COPD which is now termed as Asthma-COPD overlap syndrome (ACOS) and should be managed in accordance with GOLD.

**Management**

The main aim of treatment is to optimise bronchodilation by targeting the beta and muscarinic receptors in the airways. Dual bronchodilation, ie LABA plus LAMA is recommended at all stages of the disease. However, it is imperative that patients in the early stages of COPD, ie A and B, are commenced on bronchodilator therapy at earliest opportunity.

**Key points for therapeutic options for COPD**

- Smoking cessation has the greatest capacity to influence the natural history of COPD. Healthcare providers should encourage all patients who smoke to quit.
- Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
- All COPD patients benefit from regular physical activity and should repeatedly be encouraged to remain active.
- Appropriate pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- None of the existing medications for COPD have been shown conclusively to modify the long-term decline in lung function.
- Influenza and pneumococcal vaccination should be offered depending on local guidelines.
- Counselling delivered by physicians and other healthcare professionals significantly increases quit rates over self-initiated strategies.
- Nicotine replacement therapy as well as pharmacotherapy with varenicline, bupropion, and nortriptiline reliably increases long-term abstinence rates and are significantly more effective than placebo.

**Non-pharmacological therapeutic management of COPD.**

1. **Smoking cessation**

Smoking cessation is of paramount importance in the management of COPD regardless of disease severity. Support given by health professionals significantly increases quit rates over self-initiated strategies. Even a brief (three minute) period of counselling to urge a smoker to quit results in smoking quit rates of 5-10%. Smoking cessation should be encouraged at all severities of the condition.

Nicotine replacement therapy (nicotine gum, nasal spray, transdermal patch, sublingual tablet, or lozenge) as well as treatment with Varenicline reliably increases long-term smoking abstinence rates and are significantly more effective than placebo.

2. **Pulmonary rehabilitation**

Pulmonary rehabilitation has been proven to have significant benefits in reducing dyspnoea, fatigue and exacerbations and improving quality of life in people with COPD. Although an effective pulmonary rehabilitation programme is six weeks, the longer the program continues, the more effective the results. If exercise training is maintained at home, the patient’s health status remains above pre-rehabilitation levels.

3. **Exercise**

Patients should be encouraged to carry out breathing exercises on a daily basis. These will assist in the expectoration of sputum. Exercises such as chest and shoulder exercises, shoulder raises, step ups and sit to stand exercises should be encouraged as this will assist in maintain upper body strength with the ultimate prevention of muscle wasting.

**Pharmacological management of stable COPD.**

Maintaining and maximising bronchodilation is key in COPD. This is done by the use of long-acting bronchodilators (LABAs), long-acting muscarinic agents (LAMAs), short-acting bronchodilator (SABAs) and sort-acting muscarinic agents (SAMAs). Other bronchodilator treatments include theophyllines which require regular patient monitoring as these agents interact with other commonly used drugs.

The use of inhaled corticosteroids in patients with COPD has been debated at length in recent years and should be reserved for patients who experience more than two exacerbations per year as combined therapy is associated with an increased risk of pneumonia.

Phosphodiesterases 4 (PDE4s) are the new kids on the block in COPD and are now available in Ireland. Rolflumilast is currently available and is used in secondary care as maintenance treatment in severe COPD. PDE4 is expressed in airway smooth muscle and, in vitro, PDE4 inhibitors relax lung smooth muscle. They also address the inflammatory process which is associated with COPD which is quite different to the inflammatory process in asthma. Selective PDE4 inhibitors are being developed for treating COPD.

All patients with COPD should be encouraged to have the seasonal Influenza vaccine. Pneumococcal polysaccharide vaccine is also recommended for COPD patients 65 years and older and for COPD patients younger than age 65 with an FEV1 <40% predicted.

The use of antibiotics, other than for treating infectious exacerbations of COPD and other bacterial infections, is currently not indicated. Patients with viscous sputum may benefit from mucolytics but the overall benefits are very small. Antitussives are not recommended.

Other therapeutic options for COPD include Long Term Oxygen
Once-daily ULTIBRO BREEZHALER is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).¹

# ULTIBRO BREEZHALER

## Start a New Chapter in COPD

**Once-Daily Dual Bronchodilator**

The first once-daily dual bronchodilator treatment for COPD.

**Marketing Authorisation Numbers:** EU/1/13/862/001 & 003.

**Legal Category:** POM Pack sizes. Cartons containing 6 capsules (1x6 capsule blister strips) and one Ultibro Breezhaler inhaler or 30 capsules (5x6 capsule blister strips) and one Ultibro Breezhaler inhaler.

**Marketing Authorisation Holder:** Novartis Europharm Limited, Frimley Business Park, Camberley, Surrey GU16 7JJ, UK.

**Presentation:** Ul tro Breezhaler ( 85mcg indacaterol maleate/43mcg glycopyrronium bromide) inhalation powder hard capsules containing indacaterol maleate and glycopyrronium bromide respectively and separate Ultibro Breezhaler inhaler.

**Indications:** A maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

**Dosage and administration:** Recommended dose is the inhalation of the content of one capsule once daily, administered at the same time of the day each day using the Ultibro Breezhaler inhaler. Capsules must not be swallowed. No dose adjustment required in elderly patients. For patients with mild and moderate hepatic impairment or for patients with mild to moderate renal impairment, no data available for use in patients with severe hepatic impairment and should only be used in patients with severe renal impairment or on- or off-label renal dosing requiring dialysis if the expected benefit outweighs the potential risk. Nephropathic patients, post transplant patients, and those undergoing renal dialysis should be carefully monitored. Patients who are on dialysis should be on a stable dose for at least 14 days prior to starting Ultibro Breezhaler.

**Contraindications:**
- Hypersensitivity to the active substances or to any of the excipients.
- Concomitant use of anticholinergic drugs, antihistamines, or 
- sympathomimetic agents.
Therapy (LTOT). The long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe and resting hypoxemia. Patients require assessment for LTOT and should be referred to a respiratory physician for assessment and suitability for LTOT. The combination of noninvasive ventilation (NIV) with long-term oxygen therapy may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia.

Management of acute exacerbations of COPD
An exacerbation is “an acute event characterised by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.” The most common causes of COPD exacerbations are viral upper respiratory tract infections and infection of the tracheobronchial tree. Diagnosis relies on the clinical presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation. The aim of treatment is to minimise the impact of the current exacerbation and to prevent the development of subsequent exacerbations. For every exacerbation the patient has, he/she will have a further decline in their FEV1.

The treatment of exacerbations involves maximizing short-acting bronchodilator therapy with or without short-acting anti-cholinergic therapy. Systemic corticosteroids and antibiotics can shorten recovery time and improve lung function and hypoxemia.

Managing co-morbidities
Many patients with COPD will have other co-morbidities. The presence of co-morbidities should not alter COPD treatment and co-morbidities should be managed as if the patient does not have COPD. Co-morbidities include ischaemic heart disease, atrial fibrillation, heart failure, hypertension, osteoporosis, anxiety, depression, lung cancer, metabolic syndrome and diabetes mellitus. Many patients will have more than one co-morbidity and consideration should be given to length of appointment when reviewing these patients.

Conclusion
COPD is a complex multiple system condition whereby patients can experience severe limitations to their quality of life. Patients require a skilled practice nurse to assist them in optimising their full potential. Education, empowerment and self-management are key to the success of preventing exacerbations and avoiding hospital admission. Practice nurses are well placed to provide these supports to patients by ensuring optimal inhaler technique, educating the patient in recognition of acute exacerbations and management of these, encouraging regular exercise and assisting with smoking cessation. With the development of a number of new therapies in recent times, people with COPD now have much more therapeutic options available to them and health professionals have much more to offer.

References available on request

Table Seven: Pharmacological therapeutic options for stable COPD

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA prn or SABA prn</td>
<td>LAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or LABA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>or SABA and SAMA</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA and LABA</td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or</td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LAMA and PDE4-inh.</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or LABA and PDE4-inh.</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and LAMA</td>
<td>Carbocysteine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or ICS+LABA and PDE4-inh.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>or LAMA and LABA</td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or LAMA and PDE4-inh.</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or SABA and SAMA</td>
<td></td>
</tr>
</tbody>
</table>

MCQs
Select the correct answer(s) to these questions.

Q1 The worldwide prevalence of COPD is
   a. <5%
   b. 10%
   c. >10%
   d. 15%

Q2 COPD is characterised by
   a. airflow restriction
   b. increased wheezing
   c. dyspnoea at rest
   d. airflow limitation, air trapping and decreased exercise tolerance

Q3 When assessing the patient with COPD, GOLD (2015) recommend
   a. carrying out spirometry
   b. carrying out Medical Research Council Scale for Dyspnoea
   c. assessing risk of exacerbations
   d. all of the above

Q4 When classifying COPD it is recommended to classify as
   a. 1,2,3,4
   b. A,B,C,D
   c. Mild, moderate, severe
   d. Early or late onset

Q5 The key to the management of stable COPD is
   a. Maximising and maintaining bronchodilation
   b. Maintaining blood pressure control
   c. Commencing patients on inhaled corticosteroids
   d. Long-term oxygen therapy

MCQ answers available on request.