Asthma-COPD Overlap Syndrome: An overview of the new GINA/GOLD guidelines

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Background
This article explores a new syndrome, ACOS – Asthma-COPD Overlap Syndrome and presents the new GINA/GOLD Guidelines. The diagnosis and management of ACOS will be addressed with recommendations for onward referral should the patient’s condition warrant it.

Asthma-COPD overlap Syndrome (ACOS) is “characterised by persistent airflow obstruction with several features usually associated with asthma and several features associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD”.

ACOS occurs in people that have asthma, are over 40 and who smoke or non-smokers with long standing asthma who progress to COPD. In 2014, GINA & GOLD published a joint guidance on the diagnosis and management of ACOS.

The prevalence of ACOS was demonstrated in a screening questionnaire carried out by Marco et al, which showed 1.6% in 20-44 age group, 2.1% in 45-64 age group and 4.5% in 65-84 age group. It has been documented that patients with ACOS experience more frequent and severe exacerbations and experience longer hospital stays than patients with either asthma or COPD alone.

GINA/GOLD GUIDELINES FOR ASTHMA, COPD AND ASTHMA-COPD OVERLAP SYNDROME (ACOS)

Step-wise approach to ACOS
GINA/GOLD (2014) recommend a step-wise approach to diagnosis, management, and onward referral of the patient presenting with ACOS. The Guidelines ask:

Step 1: Does the patient have chronic airways disease?
Step 2: The syndromic diagnosis of asthma, COPD and ACOS in an adult patient
Step 3: Spirometry
Step 4: Commence initial therapy
Step 5: Referral for specialised investigations (if necessary)

Diagnosis
Step 1: Does the patient have chronic airways disease?
A first step in diagnosing these conditions is to identify patients at risk of, or with significant likelihood of having chronic airways disease, and to exclude other potential causes of respiratory symptoms. This is based on a detailed medical history, physical examination, and other investigations.
Clinical history
Features that should prompt consideration of chronic airways disease include:

- History of chronic or recurrent cough, sputum production, dyspnoea, or wheezing; or repeated acute lower respiratory tract infections
- Report of a previous doctor diagnosis of asthma or COPD
- History of prior treatment with inhaled medications
- History of smoking tobacco and/or other substances
- Exposure to environmental hazards, e.g. occupational or domestic exposures to airborne pollutants.

Physical examination
- May be normal
- Evidence of hyperinflation and other features of chronic lung disease or respiratory insufficiency
- Abnormal auscultation (wheeze and/or crackles).

Radiology
- May be normal, particularly in early stages
- Abnormalities on chest X-ray or CT scan (performed for other reasons such as screening for lung cancer), including hyperinflation, airway wall thickening, air trapping, hyperlucency, bullae or other features of emphysema
- May identify an alternative diagnosis, including bronchiectasis, evidence of lung infections such as tuberculosis, interstitial lung diseases or cardiac failure.

Screening questionnaires
Many screening questionnaires have been proposed to help the clinician identifying subjects at risk of chronic airways disease, based on the above risk factors and clinical features. Examples are the Asthma Control Test and the COPD Assessment Test.

STEP 2. The syndromic diagnosis of asthma, COPD and ACOS in an adult patient
Given the extent of overlap between features of asthma and COPD, the approach proposed focuses on the features that are most helpful in distinguishing asthma and COPD (Table 1a).

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>ASTHMA</th>
<th>COPD</th>
<th>ACOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Usually childhood but can commence at any age</td>
<td>Usually &gt; 40 years of age</td>
<td>Usually age ≥40 years, but may have had symptoms in childhood or early adulthood</td>
</tr>
<tr>
<td>Pattern of respiratory symptoms</td>
<td>Symptoms may vary over time (day to day, or over longer periods), often limiting activity. Often triggered by exercise, emotions including laughter, dust or exposure to allergens.</td>
<td>Chronic usually continuous symptoms, particularly during exercise, with ‘better’ and ‘worse’ days</td>
<td>Respiratory symptoms including exertional dyspnoea are persistent but variability may be prominent</td>
</tr>
<tr>
<td>Lung function</td>
<td>Current and/or historical variable airflow limitation, e.g. BD reversibility, AHR</td>
<td>FEV1 may be improved by therapy, but post-BD FEV1/FVC &lt;0.7 persists</td>
<td>Airflow limitation not fully reversible, but often with current</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>May be normal between symptoms</td>
<td>Persistent airflow limitation</td>
<td>Persistent airflow limitation</td>
</tr>
<tr>
<td>Past history or family history</td>
<td>Many patients have allergies and a personal history of asthma in childhood, and/or family history of asthma</td>
<td>History of exposure to noxious particles and gases (mainly tobacco smoking and biomass fuels)</td>
<td>Frequently a history of doctor-diagnosed asthma (current or previous), allergies and a family history of asthma, and/or a history of noxious exposures</td>
</tr>
<tr>
<td>Time course</td>
<td>Often improves spontaneously or with treatment, but may result in fixed airflow limitation</td>
<td>Generally, slowly progressive over years despite treatment</td>
<td>Symptoms are partly but significantly reduced by treatment. Progression is usual and treatment needs are high</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Usually normal</td>
<td>Severe hyperinflation &amp; other changes of COPD</td>
<td>Similar to COPD</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>Exacerbations occur, but the risk of exacerbations can be considerably reduced by treatment</td>
<td>Exacerbations can be reduced by treatment. If present, comorbidities contribute to impairment</td>
<td>Exacerbations may be more common than in COPD but are reduced by treatment. Comorbidities can contribute to impairment</td>
</tr>
<tr>
<td>Typical airway inflammation</td>
<td>Eosinophils and/or neutrophils</td>
<td>Neutrophils in sputum, lymphocytes in airways, may have systemic inflammation</td>
<td>Eosinophils and/or neutrophils in sputum.</td>
</tr>
</tbody>
</table>
Flutiform is indicated for the regular treatment of asthma in adults and adolescents (12 years and over), where use of a combination product (inhaled corticosteroid [ICS] and long-acting β2-agonist [LABA]) is appropriate. Flutiform 250/10µg indicated in adults only.

Flutiform® is a registered trademark of Jagotec AG, and is used under licence.

Modern aerosol device with a patient-facing dose counter

** Open label study, significant increase in FEV1 5 mins after dosing (p<0.001) (Jalibers et al: Onset of Bronchodilatation with fluticasone/formoterol combination versus fluticasone/salmeterol in an open-label, randomised study; Adv Ther 2012)**

* 8-12 month open label study, significant improvement in spirometric secondary endpoints vs baseline (Mansur et al.)

** Long Term Safety and Efficacy of fluticasone/formoterol combination therapy in Asthma; JAMP - Vol 25, No0, 2012 p1-10**

** 6-12 month open label study, significant improvement in IPP in all patients of mild asthma. For patients with severe asthma the ICS therapy should be established before prescribing a fixed-dose combination product. Patients as their treatment is stepped down. ICSs alone are first line treatment for most patients.

** During an exacerbation, during significantly worsening asthma, and should not be stopped abruptly. Patients should use a spacer device may also cause an increased systemic exposure. Increased exposure can be expected in patients with severe hepatic impairment. Prolonged treatment with high doses of corticosteroids may result in adrenal suppression and acute adrenal crisis, particularly in adolescents and children or potentially as a result of trauma, surgery, infection or rapid dose reduction. Patients should be advised that Flutiform contains a small amount of alcohol, however this negligible amount does not pose a risk to patients. Flutiform is not recommended in children under 12 years of age. Interactions: Caution is advised in long-term co-administration with strong CYP3A4 inhibitors (e.g. rifampicin, dexamethasone, rimexolone, reboxetine, rifostericin, ketoconazole and telithromycin). co-administration should be avoided if possible. Flutiform is not recommended in patients with severe asthma. Individuals should be advised to report any of the active substances or excipients. Contra-indications: Hypersensitivity to any of the active substances or excipients. Adverse events should also be reported to Mundipharma Pharmaceuticals Limited on 01 206 3800/1800 991830 (outside of office hours).**

Innovation

Modern aerosol device with a patient-facing dose counter

Please read the Summary of Product Characteristics before prescribing.

**Prescribing Information Ireland. Please read the Summary of Product Characteristics before prescribing.**
Table 1b assists the clinician in determining if the patient has asthma or COPD. If three or more boxes are checked for either asthma or COPD, that diagnosis is suggested. It there are similar number of boxes checked in each column, the diagnosis of ACOS should be considered.

**Step 3: Spirometry**

Spirometry is essential for the assessment of patients with suspected chronic disease of the airways in order to confirm or exclude the diagnosis. It should be performed at either the initial or a subsequent visit in order to avoid unnecessary trials of various therapies. Spirometry confirms chronic airflow limitation but is of more limited value in distinguishing between asthma with fixed airflow obstruction, COPD and ACOS (GINA & GOLD, 2014).

Measurement of peak expiratory flow (PEF), although not an alternative to spirometry, if performed repeatedly on the same meter over a period of 1–2 weeks may help to confirm the diagnosis of asthma by demonstrating excessive variability, but a normal PEF does not rule out either asthma or COPD. A high level of variability in lung function may also be found in ACOS.

After the results of spirometry and other investigations are available, the provisional diagnosis from the syndrome-based assessment must be reviewed and, if necessary, revised. As shown in Table 2, spirometry at a single visit is not always confirmatory of a diagnosis, and results must be considered in the context of the clinical presentation, and whether treatment has been commenced. Inhaled corticosteroids and long-acting bronchodilators influence results, particularly if a long withhold period is not used prior to performing spirometry. Further tests might therefore be necessary either to confirm the diagnosis or to assess the response to initial and subsequent treatment.

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**Table 1b: Features that favour Asthma or COPD GINA and GOLD, 2014**

<table>
<thead>
<tr>
<th>FEATURES</th>
<th>ASTHMA</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Onset before age 20 years</td>
<td>Onset after age 40 years</td>
</tr>
<tr>
<td>Pattern of respiratory symptoms</td>
<td>Variation in symptoms over minutes, hours or days</td>
<td>Persistence of symptoms despite treatment</td>
</tr>
<tr>
<td></td>
<td>Symptoms worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnoea</td>
</tr>
<tr>
<td></td>
<td>Symptoms triggered by exercise, emotions</td>
<td>Chronic cough and sputum preceded onset of dyspnoea unrelated to triggers</td>
</tr>
<tr>
<td>Lung function</td>
<td>Record of variable airflow limitation (spirometry, peak flow)</td>
<td>Record of persistent airflow limitation (post-bronchodilator FEV1/FVC &lt; 0.7)</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>Lung function normal between symptoms</td>
<td>Lung function abnormal between symptoms</td>
</tr>
<tr>
<td>Past history or family history</td>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic condition</td>
<td>Heavy exposure to a risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td>Time course</td>
<td>No worsening of symptoms over time. Symptoms vary either seasonally, or from year to year May improve spontaneously or have an immediate response to BD or to ICS over weeks</td>
<td>Symptoms slowly worsening over time (progressive course over years) Rapid-acting bronchodilator treatment provides only limited relief.</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>
Improvement in early morning, daily and night-time COPD symptoms.¹*

*compared to placebo

Twice daily administration¹

Abbreviated Prescribing Information Please consult the Summary of Product Characteristics (SPC) for the full prescribing information. Presentation: Inhalation powder in a white inhaler with an integral dose indicator and a green dosage button. Each delivered dose contains 375 µg aclidinium bromide equivalent to 322 µg of aclidinium. Also, contains lactose. Use: Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Dosage: For inhalation use. Recommended dose is one inhalation of 322 µg aclidinium twice daily. Patients should be instructed on how to administer the product correctly. No dose adjustments are required for elderly patients, or those with renal or hepatic impairment. No relevant use in children and adolescents. Contraindications: Hypersensitivity to aclidinium bromide, atropine or its derivatives, including ipratropium, oxitropium or tiotropium, or to any of the excipients. Warnings and Precautions: Do not use in asthma. Stop use if paradoxical bronchospasm occurs and consider other treatments. Do not use for the relief of acute episodes of bronchospasm. Use with caution in patients with myocardial infarction in the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure functional classes III and IV. Dry mouth, observed with anticholinergic treatment, may be associated with dental caries in the long term. Use with caution in patients with symptomatic prostatic hyperplasia or bladder-neck obstruction or with narrow-angle glaucoma. Do not use in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption. Interactions: Do not administer with other anticholinergic-containing medicinal products. No other interactions expected. Please consult the SPC for more details. Fertility, pregnancy and lactation: No data on use in pregnancy. Consider risk-benefit before using during lactation. Side-effects: Common (1-10%): Sinusitis, nasopharyngitis, headache, cough, diarrhoea. Uncommon (0.1-1%): Blurred vision, tachycardia, palpitations, dysphonia, dry mouth, rash, pruritus, urinary retention. Rare (0.01-0.1%): Hypersensitivity. Not known: Angioedema. Pack sizes: Carton containing 1 inhaler with 60 unit doses. Legal category: POM Marketing Authorisation Number: EU/1/12/778/002 Marketing Authorisation holder: AstraZeneca AB, 16-151 95 Södertälje, Sweden. Marketed by: A. Menarini Pharmaceuticals Ireland Ltd, Castlecourt, Monkstown Farm, Monkstown, Glenageary Co. Dublin. Further information is available on request to A. Menarini Pharmaceuticals Ireland Ltd or may be found in the SPC. Last updated: March 2015

Management of ACOS

**STEP 4: Commence initial therapy**

Faced with a differential diagnosis equally balanced between asthma and COPD (i.e. ACOS), it is recommended that treatment should be started accordingly for asthma. This recognizes the important role of inhaled corticosteroids (ICS) in preventing morbidity and even death in patients with uncontrolled asthma symptoms, for whom even seemingly ‘mild’ symptoms (compared to those of moderate or severe COPD) might indicate significant risk of a life-threatening attack.

- If the syndromic assessment suggests asthma or ACOS, or there is significant uncertainty about the diagnosis of COPD, it is prudent to start treatment as for asthma until further investigation has been performed to confirm or refute this initial position.
  - Treatments will include an ICS (in a low or moderate dose, depending on level of symptoms).
  - A long-acting beta2-agonist (LABA) should also be continued (if already prescribed), or added. However, it is important that patients should not be treated with a LABA without an ICS (often called LABA monotherapy) if there are features of asthma.
  - If the syndromic assessment suggests COPD, appropriate symptomatic treatment with bronchodilators or combination therapy should be commenced, but not ICS alone (as monotherapy).
  - Treatment of ACOS should also include advice about other therapeutic strategies including:
    - Inhaler technique
    - Education including self-management strategies
    - Smoking cessation
    - Pulmonary rehabilitation
    - Vaccinations
    - Treatment of comorbidities, as advised in the respective GINA (2015) and GOLD (2015) reports.

- In a majority of patients, the initial management of asthma and COPD can be satisfactorily carried out at primary care level. However, both the GINA (2015) and GOLD (2015) strategy reports make provision for referral for further diagnostic procedures at relevant points in patient management (see Step 5). This may be particularly important for patients with suspected ACOS, given that it is associated with worse outcomes and greater health care utilisation.

**STEP 5: Referral for specialised investigations (if necessary)**

Referral to a respiratory expert and further evaluation is necessary in the following situations:

- Patients with persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty, especially if an alternative diagnosis (e.g. bronchiectasis, post-tuberculosis scarring, bronchiolitis, pulmonary fibrosis, pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms) needs to be excluded.
- Patients with suspected asthma or COPD in whom atypical or additional symptoms or signs (e.g. haemoptysis, significant weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease) suggest an additional pulmonary diagnosis. This should prompt early referral, without necessarily waiting for a trial of treatment for asthma or COPD.

Table 2: Spirometric measures in asthma, COPD and ACOS (GINA/GOLD, 2014)

<table>
<thead>
<tr>
<th>SPIROMETRIC VARIABLE</th>
<th>ASTHMA</th>
<th>COPD</th>
<th>ACOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV1/FVC pre – or post BD</td>
<td>Compatible with diagnosis</td>
<td>Not compatible with diagnosis</td>
<td>Not compatible unless other evidence of chronic airflow limitation</td>
</tr>
<tr>
<td>Post-BD FEV1/FVC &lt;0.7</td>
<td>Indicates airflow limitation but may improve spontaneously or on treatment</td>
<td>Required for diagnosis (GOLD)</td>
<td>Usually present</td>
</tr>
<tr>
<td>FEV1 ≥80% predicted</td>
<td>Compatible with diagnosis (good asthma control or interval between symptoms)</td>
<td>Compatible with GOLD classification of mild airflow limitation (categories A or B) if post – BD FEV1/FVC &lt;0.7</td>
<td>Compatible with diagnosis of mild ACOS</td>
</tr>
<tr>
<td>FEV1 &lt;80% predicted</td>
<td>Compatible with diagnosis. Risk factor for asthma exacerbations</td>
<td>An indicator of severity of airflow limitation and risk of future events (e.g. mortality and COPD exacerbations)</td>
<td>An indicator of severity of airflow limitation and risk of future events (e.g. mortality and exacerbations)</td>
</tr>
<tr>
<td>Post-BD increase in FEV1 &gt;12% and 200 ml from baseline (reversible airflow limitation)</td>
<td>Usual at some time in course of asthma, but may not be present when well controlled</td>
<td>Common and more likely when FEV1 is low, but ACOS should also be considered or on controllers</td>
<td>Common and more likely when FEV1 is low, but ACOS should also be considered</td>
</tr>
<tr>
<td>Post-BD increase in FEV1 &gt;12% and 400ml from baseline (marked reversibility)</td>
<td>High probability of asthma</td>
<td>Unusual in COPD</td>
<td>Consider ACOS Compatible with diagnosis of ACOS</td>
</tr>
</tbody>
</table>
Presentation

Symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of COPD

Treatment of asthma where the use of a combination (inhaled corticosteroid and long acting

Indication Asthma: Symbicort® Turbohaler® 100/6; 200/6; 400/12; Inhalation Powder

Symbicort® Turbohaler® 200/6: 200mcg budesonide/Inhalation and 6mcg formoterol fumarate dihydrate/Inhalation.

Symbicort® Turbohaler® 400/12: Each metered dose contains 400mcg budesonide/Inhalation and 12mcg formoterol fumarate dihydrate/Inhalation. Refer to the SmPC for information on the method of administration.

Symbicort Turbohaler 100/6: 100mcg budesonide/Inhalation and 6mcg formoterol fumarate dihydrate/Inhalation. Symbicort® Turbohaler® 200/6: 200mcg budesonide/Inhalation and 6mcg formoterol fumarate dihydrate/Inhalation. Symbicort® Turbohaler® 400/12: Each metered dose contains 400mcg budesonide/Inhalation and 12mcg formoterol fumarate dihydrate/Inhalation. Refer to the SmPC for information on the method of administration.

Systemic effects may occur, particularly at high doses prescribed for long periods e.g. Cushing’s syndrome, Cushingoid behavior changes (predominantly in children), angina pectoris, prolongation of QTc-interval, hyperglycaemia, taste perversion, sleep disorders.

Rare: hyperactivity, anxiety, taste perversion, sleep disorders.

Very Rare:

urticaria, pruritus, dermatitis, angioedema and anaphylactic reactions.

Adverse effects are common and are usually associated with inhalation therapy. An increase in the number of asthma exacerbations may occur. An exacerbation of asthma may be increased in patients on high doses of inhaled corticosteroids, particularly higher than recommended doses, may also result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress e.g. severe infections or elective surgery. Transfer from oral steroid therapy to Symbicort may result in the appearance of allergic or urticarial symptoms which will need treatment. In rare cases, breathlessness, headache, nausea and vomiting may occur due to insufficient glucocorticoid effect and temporary increase in the dose of oral glucocorticoids may be necessary. To minimise risk of oropharyngeal candida infection patients should rinse mouth with water. Observe caution in patients with thymosinophils, phaeoquistocytosis, diabetes mellitus, untreated hypothyroidism, or severe cardiovascular disorders.

Dose Interactions Concomitant treatment with potent CYP3A4 inhibitors should be avoided. If this is not possible the time interval between administration should be as long as possible. Symbicort maintenance and reliever therapy is not recommended in these patients. Not recommended with beta adrenergic blockers (including eye drops) unless compelling reasons. Concomitant administration with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine) and TCAs can prolong the QTc-interval and increase the risk of ventricular arrhythmias. L-Copa, L-thyroxine, oestrogen and alcohol can impair cardiac tolerances. Concomitant administration with MAOIs, including agents with similar properties such as furazadione and procarbazine, may precipitate hypertensive. Elevated risk of arrhythmias in patients receiving antiarrhythmics with halogenated hydrocarbons. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides.

Fertility, Pregnancy and Lactation No data available on the potential effect on fertility. During pregnancy, use only when the benefits outweigh the potential risks. Budesonide is excluded in breast milk, however at therapeutic doses no effects on the child are anticipated.

Unwanted effects Common: headache, palpitations, tremor, candida infections in the oropharynx, coughing, mild irritation in the throat, hoarseness. Uncommon: tachycardia, nausea, dizziness, bruising, aspergillosis hyperactivity, anxiety, sleep disorders. Rare: hypoamylasemia, cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles, bronchospasm and immediate and delayed hypersensitivity reactions including exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction. Very Rare: psychiatric disorders including depression, behavioural changes (predominantly in children), engra phaeopete, prolongation of QTc-interval, hyperglycaemia, taste disturbances, Cushing’s syndrome, adrenal suppression, growth retardation, decrease in bone mineral density, oesophagus and gastric acid secretion in blood pressure. As with other inhalation therapy, paradoxical bronchospasm may occur in very rare cases.

Package Quantities Each Symbicort Turbohaler 100/6 or 200/6 contains 120 inhalations. Each Symbicort Turbohaler 400/12 contains 80 inhalations.

Further product information is available on request from: The MAH (address above), Freephone -1800 800 899.

Abridged Prescribing Information prepared 10/14.

AstraZeneca Respiratory

Abridged prescribing information prepared February 2015.
Clinical Review

Step 1: Diagnose Chronic Airways Disease
Do symptoms suggest chronic airways disease?

- Yes
- No → Consider other diseases first

Step 2: Syndromic Diagnosis in Adults
1. Assemble the features for asthma and COPD that best describe the patient.
2. Compare number of features in favour of each diagnosis and select a diagnosis

<table>
<thead>
<tr>
<th>Feature: if present suggests -</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td>Pattern of symptoms</td>
<td>Variation over minutes, hours or days</td>
<td>Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>Worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnoea</td>
</tr>
<tr>
<td></td>
<td>Triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic cough &amp; sputum preceded onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td>Lung function</td>
<td>Record of variable airflow limitation (spirometry or peak flow)</td>
<td>Record of persistent airflow limitation (FEV₁/FVC &lt; 0.7 post BD)</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Past history or family history</td>
<td>Previous doctor diagnosis of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>Heavy exposure to risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td>Time course</td>
<td>No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year</td>
<td>Symptoms slowly worsening over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>

Note: These features best distinguish between asthma and COPD. Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. If there are a similar number for both asthma and COPD, consider diagnosis of ACOS.

Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Asthma</th>
<th>Some features of asthma</th>
<th>Features of both</th>
<th>Could be ACOS</th>
<th>Possibly COPD</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidece in diagnosis</td>
<td>中标性哮喘</td>
<td>Possible asthma</td>
<td>Asthma</td>
<td>Some features of COPD</td>
<td>Possibly COPD</td>
<td>COPD</td>
</tr>
</tbody>
</table>

Step 3: Perform Spirometry
Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation

FEV₁/FVC < 0.7 post BD

Step 4: Initial Treatment

- Asthma drugs
  - No LABA monotherapy
  - LABA monotherapy
- COPD drugs
  - COPD drugs

*Consult GINA and GOLD documents for recommended treatment.

Step 5: Specialised Investigations or Refer If:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g., suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g., haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

Source: GINA/GOLD Guidelines for Asthma, COPD and Asthma-COPD Overlap Syndrome (ACOS).
Once-daily ULTIBRO BREEZHALER is indicated as maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD). ¹

¹ Ulitbro Breezhaler

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

**ADDITIONAL PRESCRIBING INFORMATION**

Please refer to Summary of Product Characteristics (SmPC) before prescribing. Presentation: Ulitbro Breezhaler 85mcg / 43mcg inhalation powder hard capsules containing indacaterol maleate and glycopyrronium bromide respectively and separate Ulitbro Breezhaler inhaler.

Indications: A maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD). Dosage and administration: Recommended dose is the inhalation of one capsule once daily, administered at the same time of day each day, using the Ulitbro 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 end-stage renal disease requiring dialysis if the expected benefit outweighs the potential risk. No relevant use in the paediatric population. Contraindications: Hypersensitivity to the active substances or to any of the excipients. POM with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac failure, recent myocardial infarction, atrial fibrillation, angina pectoris, known or suspected prolongation of the QT interval or patients treated with medicinal products affecting the QT interval such as anti-arrhythmics, beta-blockers, SSRIs, selective adrenergic blockers, anticholinergics or sympathomimetic agents. Cardiovascular effects: In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. In patients with narrow-angle glaucoma, patients with urinary retention, treatment should be discontinued immediately and alternative therapy instituted. Anti-cholinergic effects related to glycopyrronium: Anticholinergic effects may occur. May cause a paradoxical bronchoconstriction or dry mouth. In patients who are unusually responsive to LABA’s. Asthma: ULTIBRO BREEZHALER SHOULD NOT BE USED FOR TREATMENT OF ASTHMA. Acute use: Please refer to Summary of Product Characteristics (SmPC) before prescribing.

**Presentation**: Ulitbro Breezhaler inhalation powder hard capsules containing indacaterol maleate and glycopyrronium bromide respectively and separate Ulitbro Breezhaler inhaler.

**Dosage and administration**: Once-daily ULTIBRO BREEZHALER is indicated as maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD). ¹

**Excipients**: For full list of excipients see SmPC.

**Interactions**: For full list of interactions see SmPC.

**References**: For full list of references see SmPC.
• When chronic airways disease is suspected but syndromic features of both asthma and COPD are few.
• Patients with comorbidities that may interfere with the assessment and management of their airways disease.
• Referral may also be appropriate for issues arising during ongoing management of asthma, COPD or ACOS, as outlined in the GINA\(^a\) and GOLD\(^b\) strategy reports.\(^1\)

**Conclusion**

This article has explored the new syndrome, ACOS, its diagnosis and management and has presented the GINA/GOLD Guidelines for same. ACOS can be managed in primary care with the practice nurse being an integral part of supporting and educating these patients. These patients require on-going education in relation to inhaler technique, adherence to medication regimes, non-pharmacological interventions such as vaccinations, breathing exercises and self-management. As these patients tend to have poorer outcomes than patients with either asthma or COPD alone, it is imperative, that they are adequately assessed and treated using the new guidance from GINA & GOLD\(^1\). As with any chronic condition, nurses are in a privileged position to assist patients attain and obtain an optimal quality of life.

**References**

4. GINA, 2015, Global Initiative for Management and Prevention of Asthma
5. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD), 2015, Global Strategy for Diagnosis, Management and Prevention of COPD.

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**MCQ ANSWERS:**

Q1  ACOS can be diagnosed in:
   a) adults under 20 who have asthma
   b) adults over 40 who have asthma and smoke
   c) adults with long-standing asthma who go on to develop COPD
   d) adults with emphysema
   **Answer:** b, c

Q2  There are 6 steps recommended by GINA/GOLD (2014) in the diagnosis and management of ACOS
   True or false
   **Answer:** True

Q3  In ACOS, on spirometry testing, the FEV1/FVC ratio will be:
   a) >80%
   b) 100%
   c) <70% pre bronchodilator
   d) <70% post bronchodilator
   **Answer:** c

Q4  Patients with a diagnosis of ACOS should be treated with:
   a) inhaled bronchodilator therapy (SABA) alone
   b) combined inhaled LABA and ICS
   c) inhaled LAMA alone
   d) oral steroids
   **Answer:** a, b, c

Q5  Patients should be referred to a respiratory specialist:
   a) when there is no improvement in condition with treatment
   b) when the patient has multiple co-morbidities
   c) patient has haemoptysis
   d) all of the above
   **Answer:** d

Q6  Patients who have ACOS are more likely to have:
   a) more prolonged hospital stays than patients who have asthma or COPD alone
   b) shorter hospital stays than patients who have asthma or COPD alone
   c) the same length of stay as patients who have asthma or COPD alone
   d) more attendances to the emergency department
   **Answer:** a