



## Chronic Obstructive Pulmonary Disease (COPD): Diagnosis and Management

Effective Date: February 22, 2017 (Medication table revised July 2020)

### Scope

This guideline provides recommendations for the diagnosis and management of adults aged  $\geq 19$  years with chronic obstructive pulmonary disease (COPD).

### Key Recommendations

- Use spirometry to confirm airflow obstruction in all patients suspected of having COPD. **[Amended, 2017]**
- Promote smoking cessation or reduction (even in long-term smokers) to improve symptom control and slow the progression of COPD, among other benefits. **[2011]**
- Refer patients with moderate to severe COPD to pulmonary rehabilitation. **[2011]**
- Implement pharmacologic therapy in a stepwise approach and use the lowest step that achieves optimal control based on the patient's severity of COPD. **[New, 2017]**
- Develop an exacerbation action plan with the patient for pharmacologic therapies including short-acting bronchodilators, oral corticosteroids, and antibiotics. **[Amended, 2017]**
- Use routine follow-ups to evaluate the patient's inhaler technique and adherence regularly. Evaluating inhaler technique is particularly important in patients who are older, frail, or cognitively impaired. **[New, 2017]**

### Definition

COPD is characterized by persistent airflow limitation that is typically progressive, not fully reversible, and associated with an abnormal inflammatory response of the lungs to noxious particles or gases (e.g., exposure to cigarette smoke). The two most common conditions that contribute to COPD are emphysema (destruction of alveoli) and chronic bronchitis (inflammation of bronchioles). COPD may present with comorbidities and exacerbations which contribute to overall symptom severity affecting the patient's daily activities and quality of life. These features are most prominent in patients with moderate to severe COPD, but even patients with mild COPD can experience exacerbations.<sup>1</sup>

Acute exacerbation of COPD (AECOPD) is characterized by an increase in dyspnea, cough and/or sputum that is beyond normal day-to-day variation. It may be acute in onset, but can also have a more indolent onset and result in a change in regular medication.<sup>1</sup> Patients who experience an acute exacerbation have a significantly higher mortality rate than those with stable COPD.<sup>2</sup> This mortality risk increases as the number of exacerbations increases.

### Epidemiology

#### ► Prevalence

Approximately 138,500 individuals aged  $\geq 45$  years in BC have been diagnosed with COPD (approximately 6% of British Columbians aged  $\geq 45$  years).<sup>3</sup> Many individuals have unrecognized COPD and remain undiagnosed.<sup>4</sup>

#### ► COPD and Comorbidities

COPD patients commonly present with comorbidities which reduce quality of life. In patients with mild to moderate COPD, cardiovascular diseases are the leading cause of hospitalizations and the second leading cause of mortality after lung cancer. In severe and very severe COPD, respiratory failure and pneumonia are the leading causes of morbidity and mortality. However, even in these patients, cardiovascular diseases remain a major concern.<sup>5</sup>

## Diagnosis

While a diagnosis is based on a combination of medical history and physical examination, **it is the documentation of airflow limitation using spirometry that confirms the diagnosis.**

Consider a COPD diagnosis for a patient  $\geq 40$  years of age who has:

- 1) Respiratory symptoms, including:
  - dyspnea (progressive, persistent and worse with exercise);
  - chronic cough; and
  - increased sputum production.

**AND** 2) One of the following:

- history of exposure to cigarette smoke;
- history of environmental/occupational exposure to smoke, dust or gas/fumes;
- frequent respiratory infections; or
- family history of COPD.

Consider alternative diagnoses. Asthma and asthma-COPD overlap syndrome (ACOS) are the two primary differential diagnoses to rule out (see Table 1 for features). Other alternative diagnoses include:

- heart failure (e.g., older patients, when breathlessness is out of proportion to spirometry results; measuring B-type natriuretic peptide (BNP) levels may help in diagnosing heart failure); and
- tuberculosis (e.g., high risk populations – aboriginal, foreign born).

**Table 1. Typical features of asthma, COPD and ACOS**

Feature	Asthma	COPD	ACOS
<b>Age of onset</b>	Childhood	Age $\geq 40$ years	Age $\geq 40$ years but may have symptoms in childhood
<b>Pattern of respiratory symptoms</b>	Vary over time, limit activity, worse during night or early morning; triggered by exercise, laughter, exposure to allergens, respiratory illness	Chronic and continuous, particularly during exercise, with “better” or “worse” days	Symptoms (including exertional dyspnea) are persistent but variability may be prominent
<b>Lung function</b>	Record of variable airflow limitation (e.g., BD reversibility, AHR)	FEV <sub>1</sub> may improve with therapy but post-BD FEV <sub>1</sub> /FVC $< 0.7$ persists	Airflow limitation not fully reversible but often with current or historical variability
<b>Lung function between symptoms</b>	May be normal	Persistent airflow limitation	Persistent airflow limitation
<b>Past/family history</b>	Allergies and childhood asthma	Exposure to noxious particles and gases (e.g., tobacco)	Asthma diagnosis (current/previous), allergies and/or noxious exposures
<b>Time course</b>	Improves spontaneously or with treatment, but may result in fixed airflow limitation	Slowly progressive over years despite treatment	Symptoms typically persistent but significantly improved by treatment; progression is usual and treatment needs are high
<b>Chest x-ray</b>	Normal	Hyperinflation and other changes of COPD	Similar to COPD
<b>Exacerbations</b>	Occur but the risk can be considerably reduced by treatment	Reduced by treatment. Comorbidities contribute to impairment	More common than in COPD and are reduced by treatment; comorbidities can contribute to impairment

**Adapted from:** Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Updated 2016.

**Abbreviations:** ACOS = asthma-COPD overlap syndrome; AHR = airway hyperresponsiveness; BD = bronchodilatory; COPD = chronic obstructive pulmonary disease; FEV<sub>1</sub> = forced expiratory volume in 1 second; FVC = forced vital capacity.

## ► Investigations or Tests

### Spirometry

**Send ALL patients suspected of having COPD for confirmation of the diagnosis by spirometry.** A COPD diagnosis is confirmed when a post-bronchodilator spirometry measurement indicates that there is airflow limitation which is not fully reversible ( $FEV_1 / FVC$  ratio  $< 0.7$  or  $FEV_1 / FVC <$  lower limit of normal values). A  $FEV_1$  predicted measurement is not needed for diagnosis, but is useful in the assessment of severity.

Timely access to spirometry may be a challenge in rural and remote communities, but should remain a reasonable goal. Assuming access to spirometry can occur in a reasonable time frame, a referral to a specialist should not be done before objectively confirming the diagnosis of COPD.

#### *Borderline Spirometry Results*

There is some controversy regarding the fixed cut-off of  $< 0.7$  for  $FEV_1 / FVC$  ratio versus using  $<$  lower limit of normal values. There is some evidence that a fixed ratio can lead to over diagnosis in older populations, under diagnosis in young people, and a gender difference.<sup>6</sup> Recent evidence also suggests that some current or former smokers may have symptoms of COPD without meeting spirometric criteria for a COPD diagnosis.<sup>7</sup> For borderline results, repeat spirometry after a few months.

Consider alternative diagnoses for all patients with borderline spirometry results or if breathlessness is out of proportion to spirometry results. If  $FEV_1$  response to bronchodilator is:

- $\geq 400$  mL, strongly consider asthma or ACOS.
- $< 400$  mL (but  $\geq 200$  mL and  $\geq 12\%$  of  $FEV_1$ ), consider asthma or ACOS depending on the history and pattern of symptoms (see Table 1 above).

### Chest X-ray

A chest x-ray is not helpful in diagnosing COPD. A chest x-ray that shows hyperinflation may suggest COPD, but the diagnosis requires objective confirmation with spirometry. A chest x-ray may be useful, and should be documented, if there are concerns about other significant comorbidities (e.g., heart failure, tuberculosis, pneumonia).

### Other Pulmonary Function Tests

Other pulmonary function tests (e.g., body plethysmography, diffusing capacity, arterial blood gas measurement) are not required for a COPD diagnosis, but may be helpful in assessing the severity of COPD or when considering alternative diagnoses. For example, a body plethysmography may help in the assessment of severity of COPD, but is not essential.

Peak flow meter readings may help rule out asthma, but their usefulness in assessing COPD remains unclear.

## ► Assessment of COPD Severity

Once the diagnosis is confirmed, determine the level of COPD severity (see Table 2) by using the patient's:

- current level of symptoms;
- $FEV_1$  predicted;
- risk of exacerbation; and
- presence of comorbidities.

#### *Assessment Tools*

To assist in determining the current level of a patient's symptoms, use a tool such as the COPD Assessment Test (CAT) (website: [www.catestonline.org](http://www.catestonline.org)). The MRC Breathlessness/Dyspnea Scale (website: [www.mrc.ac.uk/research/facilities-and-resources-for-researchers/mrc-scales](http://www.mrc.ac.uk/research/facilities-and-resources-for-researchers/mrc-scales)) may also be useful.

**Table 2. Levels of severity in COPD<sup>1,6</sup>**

COPD Severity	Symptoms	FEV <sub>1</sub> (% predicted)	History of exacerbations	Comorbidities
<b>Mild</b>	<ul style="list-style-type: none"> <li>Breathlessness on moderate exertion</li> <li>Recurrent chest infections</li> <li>Little or no effect on daily activities</li> </ul>	≥ 80	Frequency increases with severity	Exist across all severity levels (e.g., cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, anxiety or depression, lung cancer, peripheral vascular disease and sleep apnea)
<b>Moderate</b>	<ul style="list-style-type: none"> <li>Increasing dyspnea</li> <li>Breathlessness walking 100 m on level ground</li> <li>Increasing limitation of daily activities</li> <li>Cough and sputum production</li> <li>Exacerbations requiring corticosteroids and/or antibiotics</li> </ul>	50 – 79		
<b>Severe</b>	<ul style="list-style-type: none"> <li>Dyspnea on minimal exertion</li> <li>Daily activities severely curtailed</li> </ul>	30 – 49		
<b>Very severe</b>	<ul style="list-style-type: none"> <li>Expiring regular sputum production</li> <li>Chronic cough</li> </ul>	< 30		

## Management

The therapeutic goals of COPD management include:<sup>8</sup>

- to alleviate breathlessness and other respiratory symptoms that affect daily activities;
- to prevent and reduce the frequency and severity of acute exacerbations;
- to minimize disease progression and reduce the risk of morbidity/mortality; and
- to optimally manage comorbidities (if present) to reduce exacerbations and COPD symptoms related to comorbidities.

When developing the patient's therapeutic goals and a management plan, consider:

- using a shared decision-making approach with the patient, taking into account patient preferences and capabilities (e.g. cognitive ability, language barriers);
- including a chronic disease and self-management approach facilitated by health professionals, as it can significantly improve health status and reduce hospital admissions for exacerbations by 40%;<sup>9</sup>
- using non-pharmacological and pharmacological interventions based on the individual patient's level of severity,
- simplifying the medication regime in the context of other conditions and treatments, particularly in the elderly; and
- reviewing the treatment approach regularly to eliminate medications that are not improving symptoms or reducing exacerbations.

### 1. Lifestyle and Self-Management

The patient's understanding of, and participation in, optimal care may improve coping skills and quality of life and reduce the likelihood of hospitalization from COPD. Educate the patient and their family or caregiver about lifestyle and self-management strategies – refer to *Associated Documents: Resource Guide for Patients*.

Help the patient identify resources and a support team (e.g., educator, pharmacist, nurse, dietitian). Refer to *Associated Documents: COPD Management Services Referral Form* for Vancouver Coastal Health, Providence Health Care and Fraser Health. Refer to health authorities for referral services in other areas.

#### ► Smoking Cessation

Promote smoking cessation or reduction (even in long-term smokers) and avoidance of second-hand smoke. Smoking is the main cause of COPD and the main contributing factor for disease progression. Smoking cessation has immediate benefits including: 1) improving symptom control, 2) slowing progression of disease, 3) improving cardiovascular outcomes, and 4) reducing long-term risk of lung cancer.

- For assistance in quitting smoking, refer patients to QuitNow at HealthLinkBC by telephone at 8-1-1 or website: [www.quitnow.ca](http://www.quitnow.ca).
- For more information on effective pharmacological aids for smoking cessation, refer to the BC Smoking Cessation program website: [www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/what-we-cover/drug-coverage/bc-smoking-cessation-program](http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/what-we-cover/drug-coverage/bc-smoking-cessation-program).

### ► Physical Activity

Encourage exercise and a more active lifestyle. Remaining active despite symptoms of shortness of breath must remain a priority for all patients with COPD.

### ► Pulmonary Rehabilitation and Respiratory Services

Moderate to severe COPD patients should be referred to a pulmonary rehabilitation program (where available) and to community respiratory services. Home and Community Care programs offered by health authorities include home visits by a respiratory therapist for COPD patients, among other things.

- To find a program in BC, contact HealthLink BC at 8-1-1, refer to the Referral Resources section below, or contact health authorities regarding local services.
- A list of pulmonary rehabilitation programs in BC is available at [prrl.rehab.med.ubc.ca/bc-pulmonary-rehabilitation-programs-contacts/](http://prrl.rehab.med.ubc.ca/bc-pulmonary-rehabilitation-programs-contacts/).

### ► Diet Considerations

Ensure adequate diet to maintain body mass index in the “normal” range (20 to 25 kg/m<sup>2</sup>), as it is essential in limiting disease progression and reducing morbidity and mortality related to COPD. Reduced body mass index (and in particular anorexia) is one of the most important risk factors for COPD progression.

### ► Air Quality

Encourage patients to stay indoors when air quality is poor, as air quality may have a significant effect on COPD symptoms and the risk of exacerbations.

### ► Oxygen Therapy

The goal of oxygen therapy is to maintain PaO<sub>2</sub> ≥ 60 mmHg or SpO<sub>2</sub> ≥ 90% at rest, on exertion and during sleep. (PaO<sub>2</sub> = partial pressure of oxygen in arterial blood, SpO<sub>2</sub> = % oxygen saturation). Oxygen therapy may be a useful addition to increase exercise capacity. Refer to *Appendix C: BC Home Oxygen Program Medical Eligibility*, or to health authorities for local criteria regarding coverage.

### ► Immunization

Individuals with COPD are at higher risk of complications of influenza and pneumococcal infection. While the polysaccharide pneumococcal vaccine may provide some protection against morbidity for patients with COPD, the evidence remains limited.<sup>10</sup>

Encourage an annual influenza vaccine, which is provided free of charge in BC to adults with COPD – refer to website: [www.healthlinkbc.ca/healthlinkbc-files/inactivated-influenza-vaccine](http://www.healthlinkbc.ca/healthlinkbc-files/inactivated-influenza-vaccine).

The pneumococcal polysaccharide vaccine is recommended, and provided free of charge in BC, for adults with COPD. Some patients with specific comorbidities or undergoing certain treatments (e.g., chemotherapy) may also benefit from the pneumococcal conjugate vaccine. Some international COPD guidelines also suggest a booster of the pneumococcal polysaccharide vaccine at 5-10 years. Refer to HealthLink BC (website: [www.healthlinkbc.ca/healthlinkbc-files/pneumococcal-polysaccharide-vaccine](http://www.healthlinkbc.ca/healthlinkbc-files/pneumococcal-polysaccharide-vaccine)) and Immunize Canada (website: [www.immunize.ca/en/diseases-vaccines/pneumococcal.aspx](http://www.immunize.ca/en/diseases-vaccines/pneumococcal.aspx)).

### ► Advance Care Planning

Initiate advance care planning discussions for all patients with a diagnosis of COPD. Advance care planning should be tailored to the needs of the patient along the disease trajectory, and should incorporate the patient’s values and goals, indicate potential outcomes, and identify health care professionals involved in care. The advanced care plan is also an opportunity to identify the patient’s alternate substitute decision maker or representative.

- For assistance, the Ministry of Health’s advance care planning guide *My Voice – Expressing My Wishes for Future Health Care Treatment* is available at website: [gov.bc.ca/advancecare](http://gov.bc.ca/advancecare).

## 2. Pharmacologic Management

When developing the patient's therapeutic goals and pharmacologic management plan, individualize the plan based on the patient's symptoms, exacerbation history, response to treatment and their risk of adverse effects. For more information on specific medications, refer to *Appendix A: Prescription Medication Table for COPD*.

### ► Inhaled Medications

Many new inhaled medications, including fixed dose combinations, have been introduced in recent years. It is recommended to:

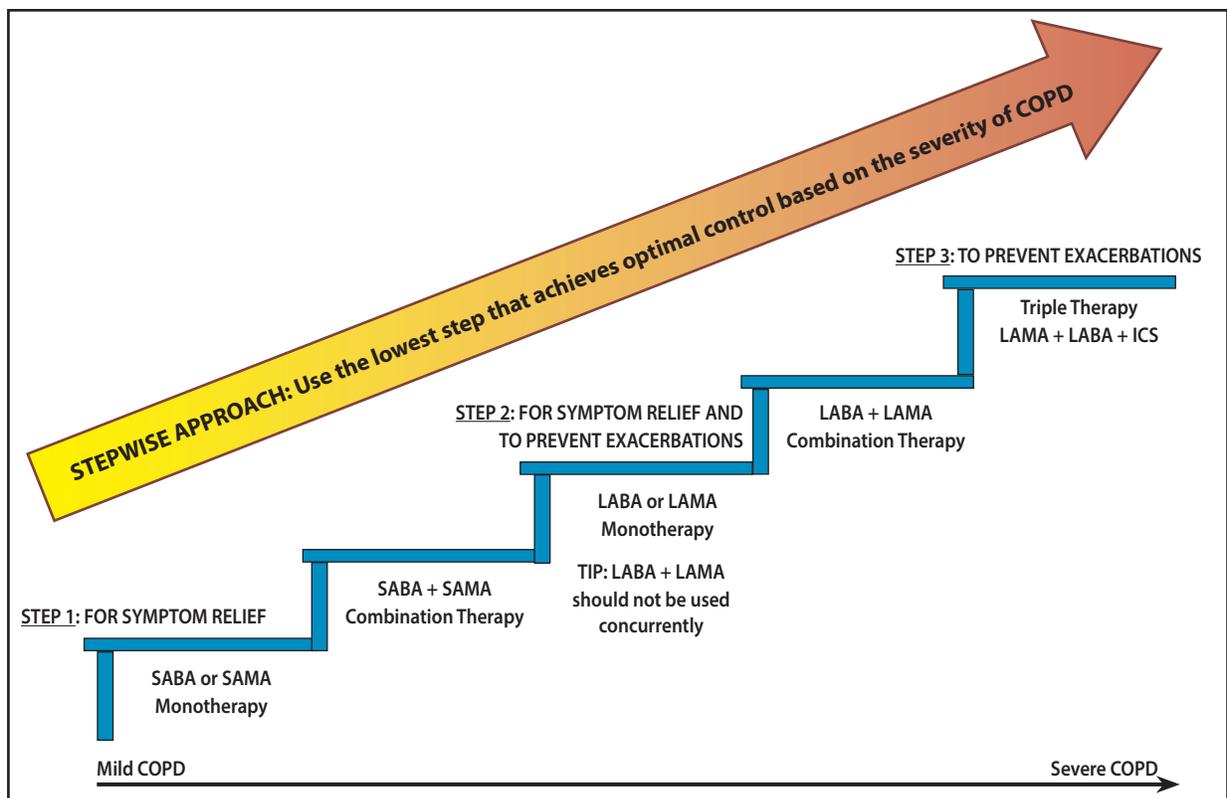
- Ensure that drug classes are not duplicated when initiating or modifying drug therapy.
- Evaluate the patient's inhaler technique and adherence regularly, as up to 90% of patients use their device incorrectly. Evaluating inhaler technique is particularly important in patients who are older, frail, or cognitively impaired. For information on how to use different inhalers, refer patients to website: [www.lung.ca/lung-health/get-help/how-use-your-inhaler](http://www.lung.ca/lung-health/get-help/how-use-your-inhaler).
- Consider prescribing a spacer for metered dose inhalers; however it should be noted that spacers require regular maintenance and cleaning to ensure optimal use.

**Bronchodilator medications** are central to symptom management in COPD, and should be prescribed on an as-needed or regular basis to prevent or reduce symptoms.<sup>1</sup>

### ► Stepwise Approach to Pharmacologic Therapy

Implement pharmacologic therapy in a stepwise approach and use the lowest step that achieves optimal control based on the patient's severity of COPD (see Figure 1). When assessing for the next step, consider exertional dyspnea, functional status, history of exacerbations, complexity of medicines or devices, patient preference (e.g., cost and ability to adhere to treatment plan) and occurrence of adverse effects. Refer to *Appendix A: Prescription Medication Table for COPD* for information on dosing, drug costs, Pharmacare coverage, and therapeutic considerations.

**Figure 1. Stepwise approach to pharmacologic management based on severity of COPD**



**Abbreviations:** COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LABA = long-acting beta<sub>2</sub>-agonist; LAMA = long-acting antimuscarinic antagonist; SABA = short-acting beta<sub>2</sub>-agonist; SAMA = short-acting muscarinic antagonist.

### **Step 1: SAMA or SABA Therapy – For symptom relief**

- For all symptomatic patients, prescribe a short-acting inhaled bronchodilator (short-acting beta<sub>2</sub>-agonist (SABA) or short-acting muscarinic antagonist (SAMA) for acute, short-term relief of shortness of breath.<sup>6</sup>
- For those with moderate to severe COPD, **SAMA** or **SABA** monotherapy is recommended. Limited evidence suggests that SAMA reduces the risk of AECOPD, improves quality of life and lung function, and may be better tolerated, as compared to SABA monotherapy.<sup>10,11</sup>
- If symptoms are not well controlled with monotherapy, consider combination therapy of SAMA + SABA.<sup>10</sup>

### **Step 2: Additional LAMA or LABA Therapy – For symptom relief and to prevent exacerbations**

- At the next step in symptom management, consider monotherapy with a long-acting beta<sub>2</sub>-agonist (LABA) or a long-acting antimuscarinic antagonist (LAMA). Limited evidence suggests **LAMA** may reduce the number of moderate and severe exacerbations compared to LABA therapy.<sup>12,13</sup> Given the limited evidence, consider a substantial trial of **LAMA**, followed by a **LABA** (or vice versa), then continue with the patient's preferred therapy.<sup>13</sup>
- If monotherapy does not provide adequate relief of symptoms, consider a combination of **LABA + LAMA**, which provides slightly better quality life and lung function over either therapy alone, and reduces exacerbations compared to LABA alone.<sup>14</sup> Fixed dose combination inhalers of LABA with a LAMA are available,<sup>8</sup> and have been shown to be superior to inhaled corticosteroid (ICS) + LABA combination in reducing symptoms and preventing exacerbations in COPD.<sup>15</sup>
- **Ipratropium bromide/Atrovent® (a SAMA) and a LAMA should not be used concurrently.**<sup>6,10</sup>

### **Step 3: Triple Therapy – To prevent exacerbations**

- For those with moderate to severe COPD and repeated exacerbations (e.g., FEV<sub>1</sub> < 50% predicted and ≥ 2 exacerbations in the past 12 months), a triple combination therapy of a LABA + ICS and LAMA is recommended.<sup>6</sup>
- Fixed dose combination inhalers of an ICS with a LABA are available; if a combination inhaler is initiated, discontinue the use of the single agent LABA inhaler.<sup>6</sup>
- The use of ICS with COPD remains controversial (see Controversies in Care section below). ICS monotherapy is not recommended, and if used in combination therapy, use the lowest possible dose.

### **► Treatment of Acute Exacerbations of COPD (AECOPD)**

Acute exacerbations are characterized by sustained (e.g., 48 hours or more) worsening of shortness of breath and coughing, usually with increasing sputum volume. The most common cause of AECOPD is a viral or bacterial infection; however, there are a number of non-infectious causes of exacerbations including: pleural effusion, heart failure, pulmonary embolism, and pneumothorax.

**Severe AECOPD complicated by acute respiratory failure is a medical emergency and the patient should seek immediate treatment.** However, more than 80% of exacerbations can be managed on an outpatient basis with pharmacologic therapies including short-acting bronchodilators, oral corticosteroids, and antibiotics.<sup>1</sup> Develop an exacerbation action plan with the patient (see *Associated Document: COPD Flare-up Action Plan*). Note that there are some populations for which a written action plan may not be appropriate, including patients with cognitive disabilities, patients who cannot adequately follow instructions, and patients with significant comorbidities that might increase the risk of steroid-adverse effects.<sup>16</sup>

Pharmacologic therapies may include:

- 1) **short-acting bronchodilator** for initial treatment of acute exacerbations
  - Adequate doses of bronchodilator (e.g., salbutamol 400 to 800 mcg [4 to 8 puffs]) delivered via metered dose inhaler with a spacer is equivalent to 2.5 mg by nebulizer and is as effective. Administer salbutamol frequently (up to every couple of hours) and titrate to response.<sup>6</sup>
- 2) **oral corticosteroids** in most moderate to severe COPD patients<sup>1</sup>
  - A dose of 40 mg of prednisone per day for 5 days is an appropriate dose.<sup>17</sup> However, a dose of 50 mg of prednisone per day is often used in Canada because of its availability in a single tablet. Lower doses may need to be used, especially in the presence of diabetes mellitus.
  - Evidence suggests that systemic corticosteroids in AECOPD shorten recovery time, improve lung function, improve arterial hypoxemia, and reduce the risk of early relapse, treatment failure, and duration of hospitalization.<sup>1</sup>

- There is a well-powered randomized controlled trial comparing 5 versus 14 days of oral corticosteroids showing similar efficacy.<sup>17</sup>
- For most patients, tapering of the corticosteroid dose should not be necessary.<sup>1,6</sup>
- Systemic corticosteroids have not been shown to reduce AECOPD beyond the initial 30 days of an exacerbation and the long-term use of systemic corticosteroids is not recommended as the risk of adverse events far outweighs any potential benefits.

Bronchodilators and corticosteroids may be administered by nebulizer, metered-dose inhaler, or dry powder inhaler. While all of these devices are appropriate for treating COPD exacerbations, each has advantages and disadvantages. In choosing a drug/device combination, take into account the patient's cognitive and physical ability, ease of use, convenience, cost, and patient preferences.<sup>18</sup>

### 3) **antibiotic treatment**

- Patients presenting with symptoms and risk factors for bacterial infection may benefit from antibiotic treatment. While studies have shown large and consistent benefit from antibiotic use among COPD patients admitted to the ICU, the evidence for their use in patients with mild to moderate exacerbations is less clear.<sup>19</sup> However, the totality of data suggests that for patients with moderate to severe exacerbations, antibiotics are effective in reducing relapse rates in COPD.<sup>20</sup>
- Refer to *Appendix B: Antibiotic Treatment Recommendations for Acute Exacerbations of COPD*.

## ► **Controversies in Care**

### *Cardiovascular Risk and Ipratropium*

A small increase in cardiovascular events has been reported with the regular use of ipratropium in COPD patients.<sup>1</sup> However, this result has not been validated by a large randomized controlled trial (RCT) and further study is required.<sup>21</sup>

### *Cardiovascular Risk and Tiotropium*

One large, long-term clinical trial showed no evidence of cardiovascular risk when tiotropium was added to other standard therapies.<sup>21</sup>

### *Mortality Risk and Tiotropium*

A meta-analysis suggested that tiotropium delivered via the Respimat® inhaler was associated with a significantly increased risk of mortality when compared to placebo. However, in a large RCT comparing tiotropium via Respimat® to tiotropium via HandiHaler (dry powder inhaler), no differences in mortality or exacerbation rates were shown.<sup>22</sup>

### *Use of Inhaled Corticosteroid*

The effects of ICS on pulmonary and systemic inflammation in COPD remain controversial,<sup>1</sup> and the use of ICS in COPD management is limited to specific indications:

- ICS monotherapy has very modest effects on symptoms and exacerbations and its limited benefits are outweighed by potential adverse effects, including increased risk of pneumonia. As such, ICS monotherapy is not recommended.
- Triple therapy of a LABA, ICS and a LAMA has limited evidence to suggest it improves lung function and quality of life.<sup>1</sup> However, triple combination may be useful for the management of patients with moderate to severe COPD who continue to experience repeated exacerbations despite use of LABA/LAMA combination therapy or who have been recently hospitalized with severe COPD exacerbation.<sup>23</sup> As such, triple therapy is recommended for this indication.

### *Use of Methylxanthines*

The exact physiologic benefits of methylxanthines (xanthine derivatives, such as theophylline) remain unknown. There is limited data on the duration of action for both conventional release and extended release xanthine preparations. In the studies that have shown efficacy of theophylline in COPD, extended release formulations were used.<sup>1</sup> The use of theophylline in select patients with persistent symptoms was recommended in the previous version of this guideline (2011), and continues to be recommended by a number of international guidelines.<sup>1,6</sup> However, a Cochrane Review recommended against the use of methylxanthines for COPD exacerbations given that the evidence of potential benefit was modest and inconsistent, while potential adverse effects were significant.<sup>24</sup>

### *Use of Oral N-acetylcysteine (NAC)*

The routine use of NAC in the management of COPD remains controversial due to conflicting evidence and methodological issues in the trials.<sup>25</sup>

#### ► **Indications for Referral**

Refer patient to a specialist in cases where:

- the diagnosis is uncertain;
- a patient is < 40 years with COPD and limited smoking history, or has severe symptoms and disability which is disproportionate to their lung function;
- there is evidence of an alpha-1 antitrypsin (A1AT) deficiency (e.g. early onset of emphysema or COPD, unexplained liver disease, family history);
- there are signs and symptoms of hypoxemic or hypercarbic respiratory failure;
- there are severe or recurrent exacerbations and treatment failure;
- the patient has severe COPD and disability requiring more intensive interventions;
- a more intensive comorbidity assessment and management is required;
- a patient is frail and may benefit from multidisciplinary or comprehensive geriatric assessment, and/or
- there is difficulty in assessing home oxygen or sleep disorders.

Family physicians and nurse practitioners in participating areas may consider contacting the **Rapid Access to Consultative Expertise (RACE)** phone line to speak directly with a specialist, including respirologists, or accessing referral services through [PathwaysBC.ca](http://PathwaysBC.ca). Refer to the Referral Resources section below.

## Ongoing Management

---

#### ► **Follow-up Care**

Modify therapeutic goals and management plans as appropriate. Use routine follow-ups to ask about and monitor the patient's key clinical indicators, including:

- lung function;
- changes in symptoms (e.g. any improvement since starting/changing treatment; changes in level of breathlessness, activity level, sleep quality, etc.);
- exacerbation history (frequency, severity) and review of the Flare-Up Action Plan (website: [www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/copd\\_action\\_plan.pdf](http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/copd_action_plan.pdf));
- management of comorbidities (if present); and
- pharmacologic therapy adherence and inhaler technique.

#### ► **Palliative Care**

Making decisions about the intensity of palliative care is a highly individualized process and requires continuous review as COPD progresses. Once the decision to initiate palliative care is made, the goal of therapy is to manage symptoms, reduce treatment burden, and maximize comfort and quality of life. This may include providing support for the patient's family and caregivers. Consider referral to palliative care/hospice teams, if available.

Assess the need for home oxygen, non-pharmacologic therapies, and pharmacologic options for severe dyspnea (e.g., systemic opioids, anxiolytics).

For more information, refer to [BCGuidelines.ca](http://BCGuidelines.ca) – *Palliative Care for the Patient with Incurable Cancer or Advanced Disease* and BC Pharmacare's Palliative Care Benefits Program (website: [www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program](http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program)).

### ► References

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: <http://goldcopd.org/>.
2. Soler-Cataluna JJ. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax*. 2005 Nov 1;60(11):925–31.
3. BC Ministry of Health. BC Chronic Disease Estimates: Chronic Obstructive Pulmonary Disease, Prevalence, BC, 1992/1993 to 2013/2014. Released March 1, 2015.
4. Tan WC, Bourbeau J, FitzGerald JM, Cowie R, Chapman K, Hernandez P, et al. Can age and sex explain the variation in COPD rates across large urban cities? A population study in Canada. *Int J Tuberc Lung Dis*. 2011 Dec 1;15(12):1691–8.
5. Sin DD. Is COPD Really a Cardiovascular Disease? *Chest*. 2009 Aug;136(2):329–30.
6. The COPD-X Plan: Australian and New Zealand Guidelines for the Management of Chronic Obstructive Pulmonary Disease (Concise Version). 2015. Available at: [copdx.org.au/](http://copdx.org.au/).
7. Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, et al. Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function. *N Engl J Med*. 2016 May 12;374(19):1811–21.
8. O'Donnell DE, Hernandez P, Kaplan A, Aaron S, Bourbeau J, Marciniuk D, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2008 update - highlights for primary care. *Can Respir J*. 2008 Feb;15 Suppl A:1A–8A.
9. Bourbeau J, Julien M, Maltais F, Rouleau M, Beupré A, Bégin R, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med*. 2003 Mar 10;163(5):585–91.
10. Criner GJ, Bourbeau J, Diekemper RL, Ouellette DR, Goodridge D, Hernandez P, et al. Prevention of Acute Exacerbations of COPD. *Chest*. 2015 Apr;147(4):894–942.
11. Appleton S, Jones T, Poole P, Pilotto L, Adams R, Lasserson TJ, et al. Ipratropium bromide versus short acting beta-2 agonists for stable chronic obstructive pulmonary disease. In: The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews* [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2006 [cited 2016 Dec 17]. Available from: <http://doi.wiley.com/10.1002/14651858.CD001387.pub2>
12. Vogelmeier C, Hederer B, Glaab T, Schmidt H, Rutten-van Mölken MPMH, Beeh KM, et al. Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD. *N Engl J Med*. 2011 Mar 24;364(12):1093–103.
13. Chong J, Karner C, Poole P. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. In: The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews* [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2012 [cited 2016 Dec 17]. Available from: <http://doi.wiley.com/10.1002/14651858.CD009157.pub2>
14. Farne HA, Cates CJ. Long-acting beta 2 -agonist in addition to tiotropium versus either tiotropium or long-acting beta 2 -agonist alone for chronic obstructive pulmonary disease. In: The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews* [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2015 [cited 2016 Dec 17]. Available from: <http://doi.wiley.com/10.1002/14651858.CD008989.pub3>
15. Wedzicha JA, Banerji D, Chapman KR, Vestbo J, Roche N, Ayers RT, et al. Indacaterol–Glycopyrronium versus Salmeterol–Fluticasone for COPD. *N Engl J Med*. 2016 Jun 9;374(23):2222–34.
16. Fan VS, Gaziano JM, Lew R, Bourbeau J, Adams SG, Leatherman S, et al. A comprehensive care management program to prevent chronic obstructive pulmonary disease hospitalizations: a randomized, controlled trial. *Ann Intern Med*. 2012 May 15;156(10):673–83.
17. Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA*. 2013 Jun 5;309(21):2223–31.
18. Geller DE. Comparing clinical features of the nebulizer, metered-dose inhaler, and dry powder inhaler. *Respir Care*. 2005 Oct;50(10):1313–1321–1322.
19. Vollenweider DJ, Jarrett H, Steurer-Stey CA, Garcia-Aymerich J, Puhan MA. Antibiotics for exacerbations of chronic obstructive pulmonary disease. In: The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews* [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2012 [cited 2016 Dec 17]. Available from: <http://doi.wiley.com/10.1002/14651858.CD010257>
20. Quon BS, Gan WQ, Sin DD. Contemporary Management of Acute Exacerbations of COPD. *Chest*. 2008 Mar;133(3):756–66.
21. Tashkin DP, Celli B, Senn S, Burkhart D, Kesten S, Menjoge S, et al. A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2008 Oct 9;359(15):1543–54.
22. Wise RA, Anzueto A, Cotton D, Dahl R, Devins T, Disse B, et al. Tiotropium Respimat Inhaler and the Risk of Death in COPD. *N Engl J Med*. 2013 Oct 17;369(16):1491–501.
23. Singh D, Papi A, Corradi M, Pavlišová I, Montagna I, Francisco C, et al. Single inhaler triple therapy versus inhaled corticosteroid plus long-acting  $\beta$ 2-agonist therapy for chronic obstructive pulmonary disease (TRILOGY): a double-blind, parallel group, randomised controlled trial. *Lancet Lond Engl*. 2016 Sep 3;388(10048):963–73.
24. Barr RG, Rowe BH, Camargo CA. Methylxanthines for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2003;(2):CD002168.
25. Aboussouan LS. UpdatetoDate®: Role of mucoactive agents in treatment of COPD. Last Updated May 6, 2014.

### ► Referral Resources

#### • RACE – Rapid Access to Consultative Expertise Program

A telephone advice line from a selection of specialty services for general practitioners.

- For Vancouver Coastal Health Region: [www.raceconnect.ca](http://www.raceconnect.ca) or by telephone at 604-696-2131 (Vancouver area) or 1-877-696-2131 (toll free); Monday to Friday, 8 am to 5 pm.
- For Northern Health: [www.northernpartnersincare.ca/northernrace](http://www.northernpartnersincare.ca/northernrace) or by telephone at 1-877-605-7223
- Kootenay Boundary RACE: [www.divisionsbc.ca/kb/race](http://www.divisionsbc.ca/kb/race) or by telephone at 1-844-365-7223 (toll free)
- Fraser Valley RACE and South Island RACE: RACEapp+ (download for free at Apple and Android stores) [www.raceapp.ca](http://www.raceapp.ca)

#### • BC Pulmonary Rehabilitation Programs, [prrr.rehab.med.ubc.ca/bc-pulmonary-rehabilitation-programs-contacts](http://prrr.rehab.med.ubc.ca/bc-pulmonary-rehabilitation-programs-contacts)

The Pulmonary Rehabilitation Research Laboratory at UBC has compiled a list of pulmonary rehab program and contact information across BC.

- **Pathways**, [pathwaysbc.ca](http://pathwaysbc.ca)

An online resource that allows GPs and nurse practitioners and their office staff to quickly access current and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. In addition, Pathways makes available hundreds of patient and physician resources that are categorized and searchable.

#### ► **Additional Resources**

- **BC Ministry of Health – Advance Care Planning**, [www.health.bc.ca](http://www.health.bc.ca)  
In addition, each health authority also has an Advance Care Planning website.
- **Practice Support Program**, [www.gpsc.bc.ca/what-we-do/professional-development/psp](http://www.gpsc.bc.ca/what-we-do/professional-development/psp)  
Includes learning modules on COPD and end-of-life care.
- **Living Well with COPD: A Plan of Action for Life**, [www.livingwellwithcopd.com](http://www.livingwellwithcopd.com)
- **BC Lung Association**, [bc.lung.ca](http://bc.lung.ca)

► **Diagnostic code:** 496 (chronic airways obstruction, not elsewhere classified)

#### ► **Appendices**

- Appendix A: Prescription Medication Table for COPD
- Appendix B: Antibiotic Treatment Recommendations for Acute Exacerbation of COPD
- Appendix C: BC Home Oxygen Program Medical Eligibility

#### ► **Associated Documents**

- Patient Care Flow Sheet
- COPD Flare-up Action Plan
- Resource Guide for Patients
- COPD Management Services Referral Form (for Vancouver Coastal Health, Providence Health Care and Fraser)

This guideline is based on scientific evidence current as of the effective date.

The guideline was developed by the Guidelines and Protocols Advisory Committee, approved by Doctors of BC and adopted by the Medical Services Commission.

## THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

### **The principles of the Guidelines and Protocols Advisory Committee are to:**

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

### **Contact Information:**

Guidelines and Protocols Advisory Committee  
PO Box 9642 STN PROV GOVT  
Victoria BC V8W 9P1

Email: [hlth.guidelines@gov.bc.ca](mailto:hlth.guidelines@gov.bc.ca)

Website: [www.BCGuidelines.ca](http://www.BCGuidelines.ca)

### **Disclaimer**

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**



## Appendix A: Prescription Medication Table for COPD<sup>1-4</sup>

Generic Name Trade Name Dosage Forms and Strengths	Usual Adult Daily Dose	Cost per Device <i>Approx. cost per usual daily dose</i>	PharmaCare Coverage	Therapeutic Considerations
<b>SHORT-ACTING RELIEVER MEDICATIONS</b>				
<b>Short-Acting Beta<sub>2</sub> Agonists (SABA)</b>				
<b>Salbutamol</b> Ventolin®, Airomir™, generics pMDI: 100 mcg/puff 200 doses 	<b>Acute relief:</b> 1 to 2 puffs prn <b>Prevention:</b> 1 to 2 puffs QID	\$10 \$0.20 to \$0.40 (1 to 2 puffs QID)	Regular Benefit	<ul style="list-style-type: none"> <li>Improves symptoms; does not reduce exacerbations.</li> <li>Potential adverse effects: tremor (particularly in the hands, usually disappears as treatment continues), cardiac arrhythmias (more likely in susceptible patients), tachycardia, restlessness, headache, muscle cramps, and nervousness.</li> <li>Use cautiously in patients with cardiovascular disorders (e.g., coronary insufficiency, arrhythmias, hypertension).</li> <li>Paradoxical bronchospasm is unusual and may be related to the propellant and in which case a dry powder formulation may be effective. An alternative therapy, such as a SAMA, may also be considered.</li> </ul>
Ventolin® Diskus® Diskus: 200 mcg/inhalation 60 doses 	<b>Acute relief:</b> 1 inhalation prn <b>Prevention:</b> 1 inhalation q4-6 hour (maximum 3-4 inhalations daily)	\$15 \$0.75 to \$1 (3 to 4 inhalations/day)	Non-benefit	
<b>Terbutaline</b> Bricanyl® Turbuhaler® Turbuhaler: 0.5 mg/inhalation 100 doses 	<b>Acute relief:</b> 1 to 2 inhalations prn (maximum 6 inhalations daily)	\$10 \$0.60 (6 inhalations/day)	Regular Benefit	
<b>Short-Acting Muscarinic Antagonist (SAMA) or Short Acting Anticholinergic</b>				
<b>Ipratropium bromide</b> Atrovent® pMDI: 20 mcg/puff 200 doses 	40 mcg (2 actuations) TID to QID <b>Maximum:</b> 240 mcg (12 actuations) daily, (minimum 4 hours between doses)	\$25 \$0.75 to \$1 (2 actuations TID to QID)	Regular Benefit	<ul style="list-style-type: none"> <li>Improves symptoms; does not reduce exacerbations.</li> <li>Potential adverse effects: headache, throat irritation, cough, dry mouth, GI motility disorders, dizziness, bitter/metallic taste.</li> <li>Use cautiously and monitor for worsening urinary retention in patients with pre-existing urinary tract obstruction.</li> <li>Use cautiously in patients with narrow-angle glaucoma.</li> <li>Avoid spraying the mist into the eyes (ocular complications have been reported).</li> <li>A SAMA and a LAMA should not be used concurrently.</li> </ul>
<b>Combination product: SABA and SAMA</b>				
<b>Ipratropium bromide salbutamol sulfate</b> Combivent® Respimat® Respimat inhaler: 20 mcg ipratropium bromide and 100 mcg salbutamol/actuation 120 doses 	1 inhalation QID <b>Maximum:</b> 6 inhalations/ 24 hours	\$35 \$1.17 (1 inhalation QID)	Regular Benefit	<ul style="list-style-type: none"> <li>Similar therapeutic considerations as SABAs and SAMAs (see above).</li> </ul>

Generic Name Trade Name Dosage Forms and Strengths	Usual Adult Daily Dose	Cost per Device <i>Approx. cost per usual daily dose</i>	PharmaCare Coverage	Therapeutic Considerations
<b>LONG-ACTING MEDICATIONS</b>				
<b>Long-Acting Muscarinic Antagonists (LAMA) or Long-Acting Anticholinergics</b>				
<b>Acclidinium bromide</b> Tudorza® Genuair®  DPI: 400 mcg 60 doses 	400 mcg BID	\$60 \$2 (1 inhalation BID)	Limited Coverage (after failed trial of Regular Benefit LAMAs)	<ul style="list-style-type: none"> <li>When initiating treatment with a LAMA, discontinue the use of any previous regularly scheduled short acting bronchodilator(s).</li> <li>Use SABA as a rescue medication PRN to treat acute bronchospasm.</li> <li>No convincing evidence to support one LAMA product is superior to another, consideration should be given to usability and adherence.</li> <li>Use cautiously and monitor for worsening urinary retention in patients with pre-existing urinary tract obstruction (e.g., prostatic hyperplasia).</li> <li>Use cautiously in patients with narrow-angle glaucoma.</li> <li>Potential adverse effects: headache, dry mouth, urinary retention, metallic taste, nasopharyngitis.</li> <li>Rinse mouth after inhalation to decrease dry mouth adverse event.</li> <li>Avoid spraying the mist into the eyes (ocular complications have been reported).</li> </ul>
<b>Glycopyrronium bromide</b> Seebri® Breezhaler®  Inhalation powder capsules via Breezhaler: 50 mcg Boxes of 30 capsules 	50 mcg once daily by oral inhalation	\$60 \$2 (1 inhalation daily)	Limited Coverage (after failed trial of Regular Benefit LAMAs)	
<b>Tiotropium bromide</b> Spiriva® HandiHaler®  Inhalation powder capsule via HandiHaler: 18 mcg Boxes of 30 capsules 	18 mcg once daily by oral inhalation	\$60 \$2 (1 inhalation daily)	Limited Coverage (after failed trial of Regular Benefit LAMAs)	
<b>Spiriva® RespiMat®</b>  Inhalation solution via RespiMat: 2.5 mcg per actuation 60 actuations 	5 mcg (2 actuations) once daily	\$60 \$2 (2 actuations daily)	Regular Benefit	
<b>Umeclidinium bromide</b> Incruse™ Ellipta®  DPI: 62.5 mcg 7 or 30 doses 	62.5 mcg once daily	\$55 \$1.83 (1 inhalation daily)	Regular Benefit	
<b>Long-Acting Beta<sub>2</sub> Agonists (LABA)</b>				
<b>Formoterol</b> Foradil®  Inhalation powder capsules via inhaler: 12 mcg Boxes of 60 capsules 	12 mcg BID via oral inhalation May increase to 24 mcg BID via oral inhalation, if required  <b>Maximum:</b> 48 mcg/day	Foradil®: \$60/60 capsules \$2 (1 inhalation BID)	Non-benefit	<ul style="list-style-type: none"> <li>Potential adverse effects: cough, headache, palpitations, tachycardia, tremor, muscle spasms, upper respiratory tract infection.</li> <li>Use cautiously in patients with cardiovascular disorders (e.g., coronary insufficiency, arrhythmias, hypertension).</li> <li>Monitor for hyperglycemia in diabetic patients when initiating therapy.</li> <li>LABAs are not typically used to treat acute bronchospasm (rapid onset, short acting bronchodilator should be used to treat acute symptoms).</li> <li>When initiating treatment with LABA, discontinue the use of any regularly scheduled SABA and transition to PRN use of the SABA.</li> <li>Do not use more often or at higher doses than recommended.</li> </ul>
<b>Indacaterol maleate</b> Onbrez® Breezhaler®  Inhalation powder capsules via Breezhaler: 75 mcg Boxes of 30 capsules 	75 mcg once daily by oral inhalation	\$55 \$1.83 (1 inhalation daily)	Limited Coverage	
<b>Salmeterol</b> SereVent® Diskus®  Diskus: 50 mcg/inhalation 60 doses 	50 mcg BID	\$70 \$2.33 (1 inhalation BID)	Limited Coverage	

Generic Name Trade Name Dosage Forms and Strengths	Usual Adult Daily Dose	Cost per Device Approx. cost per usual daily dose	PharmaCare Coverage	Therapeutic Considerations
<b>Combination: LAMA and LABA</b>				
<b>Acclidinium/formoterol fumarate</b> Duaklir™ Genuair® DPI: 400/12 mcg 60 doses 	400/12 mcg BID	\$65 \$2.17 (1 inhalation BID)	Limited Coverage	<ul style="list-style-type: none"> <li>Potential adverse effects: throat irritation, cough, influenza, upper respiratory tract infection, tooth abscess, headache, tremor, dry mouth.</li> <li>Do not administer a combination LAMA and LABA product concurrently with other products containing LABA or LAMA.</li> <li>Similar therapeutic considerations as LABAs and LAMAs (see above).</li> </ul>
<b>Indacaterol/glycopyrronium</b> Ultibro® Breezhaler® Inhalation powder capsules via Breezhaler: 100 mcg/50 mcg Boxes of 30 capsules 	100 mcg/50 mcg once daily by oral inhalation	\$85 \$2.83 (1 inhalation daily)	Limited Coverage	
<b>Tiotropium/olodaterol</b> Inspiro™ RespiMat® Inhalation solution via RespiMat: 2.5/2.5 mcg 60 actuations 	5 mcg/5 mcg (2 inhalations) once daily	\$70 \$2.33 (2 inhalations daily)	Limited Coverage	
<b>Umeclidinium/vilanterol</b> Anoro™ Ellipta® DPI: 62.5/25 mcg 30 doses 	62.5 mcg/25 mcg once daily	\$95 \$3.17 (1 inhalation daily)	Limited Coverage	
<b>Combination: Inhaled Corticosteroid (ICS) and LABA</b>				
<b>Budesonide/ formoterol fumarate</b> Symbicort® Turbuhaler® DPI: 200 mcg/6 mcg 120 doses 	400 mcg / 12 mcg BID	\$100 \$3.33 (400 mcg/ 12 mcg BID)	Non-benefit for COPD (Limited Coverage benefit for asthma)	<ul style="list-style-type: none"> <li>Potential adverse effects: palpitations, oropharyngeal candidiasis, headache, tremor, throat irritation, coughing, hoarseness.</li> <li>Risk of oropharyngeal candidiasis and hoarseness can be reduced by using a spacer with pMDI AND by rinsing mouth and throat after each use (and cleansing dentures if applicable).</li> <li>ICS is associated with an increased risk of pneumonia, particularly at higher doses.</li> </ul>
<b>Fluticasone furoate/vilanterol</b> Breo® Ellipta® DPI: 100 mcg/25 mcg 30 doses <b>NOTE: 200/25 mcg DPI is not indicated for use in COPD</b> 	100 mcg/25 mcg once daily	\$95 \$3.17 (100 mcg/ 25 mcg daily)	Limited Coverage	
<b>Fluticasone propionate/ salmeterol</b> Advair® Diskus®, generics DPI via Diskus: 250/50 mcg and 500/50 mcg 60 inhalations <b>NOTE: 100/50 mcg DPI is not indicated for use in COPD</b> 	250/50 mcg: 1 inhalation BID 500/50 mcg: 1 inhalation BID	Diskus: 250/50 mcg: \$55 \$1.83 (1 inhalation BID) 500/50 mcg: \$80 \$2.67 (1 inhalation BID)	Limited Coverage	
Advair® MDI: 125/25 mcg and 250/25 mcg 120 inhalations <b>NOTE: MDI is not indicated for use in COPD</b> 	125/25 mcg or 250/25 mcg: 2 inhalations BID	MDI: 125/25 mcg: \$115 \$3.83 (2 inhalations BID) 250/25 mcg: \$165 \$5.50 (2 inhalations BID)	Limited Coverage	

Generic Name Trade Name Dosage Forms and Strengths	Usual Adult Daily Dose	Cost per Device <i>Approx. cost per usual daily dose</i>	PharmaCare Coverage	Therapeutic Considerations
<b>Combination: LAMA, LABA and ICS</b>				
<b>Umeclidinium/vilanterol/fluticasone furoate</b> Trelegy™ Ellipta® DPI: 62.5/25/100 mcg 30 doses 	62.5 mcg/ 25 mcg/ 100 mcg once daily	\$145 \$4.83 (1 inhalation daily)	Limited Coverage	<ul style="list-style-type: none"> <li>For patients with frequent exacerbations who have been taking LAMA-LABA therapy.</li> <li>IMPACT trial: yearly rate of moderate/severe exacerbations lower with triple therapy: 0.91 (ICS-LABA-LAMA) compared to 1.07 (ICS-LABA) and 1.21 (LAMA-LABA).</li> <li>Asthmatics discontinued ICS prior to study entry, which may have accounted for increased exacerbations in non-ICS groups.</li> <li>Higher incidence of pneumonia in ICS-containing groups.</li> </ul>
<b>Systemic Corticosteroids</b>				
<b>Prednisone</b> Generics Tablets: 1 mg, 5 mg, 50 mg	AECOPD: 30 to 50 mg PO once daily for 5 to 14 days	\$1/course (50 mg po daily x 5 days)	Regular Benefit	<ul style="list-style-type: none"> <li>Potential adverse effects: GI upset, fluid or electrolyte imbalance, hypertension, pituitary-adrenal suppression, skin effects (thinning, easy bruising, acne), hyperglycemia, weight gain, peptic ulcer, behavioural disturbances, insomnia, glaucoma, posterior subcapsular cataracts, myopathy, decreased bone mineral density, cushingoid syndrome.</li> <li>Increased risk of GI ulceration with concomitant NSAID.</li> <li>Increased risk of hypokalemia with concomitant diuretic (e.g., thiazide).</li> </ul>
<b>Macrolide – maintenance therapy to reduce AECOPD</b>				
<b>Azithromycin</b> Zithromax®, generics Tablets: 250 mg Oral suspension: 100 mg/5 ml, 200 mg/5 ml	To reduce risk of AECOPD: 250 mg daily or 250 mg three times per week	Tablets: \$0.45 to \$1.05/day (250 mg 3X weekly to 250 mg daily)  Suspension: \$1.79 to \$4.17/day (250 mg 3X weekly to 250 mg daily)	Regular Benefit	<ul style="list-style-type: none"> <li>Potential adverse effects: QT prolongation, hearing decrements, nasopharyngeal colonization with macrolide-resistant bacteria.</li> <li>Consider the risk of fatal cardiac arrhythmias in susceptible patients (e.g., patients with QT prolongation, electrolyte imbalance, arrhythmia, cardiac insufficiency, concurrent treatment with QT prolonging medications, elderly).</li> <li>Oral suspension contains 3.87 g of sucrose per 5 mL.</li> </ul>
<b>Phosphodiesterase 4 (PDE4) inhibitor</b>				
<b>Roflumilast</b> Daxas® Tablet: 500 mcg	500 mcg PO daily	\$75/30 tablets \$2.50 (1 tab daily)	Non-benefit	<ul style="list-style-type: none"> <li>Potential adverse effects: diarrhea, weight loss (average of 2 kg), nausea, headache, abdominal pain.</li> <li>Less common adverse events: suicide and/or suicidal ideation or behaviour, aspartate aminotransferase (AST) increase.</li> <li>Diarrhea, nausea and headache usually occur within the first 4 weeks of treatment and are typically resolved within 4 weeks while still on continued treatment.</li> <li>Contraindicated in moderate or severe hepatic impairment (Child-Pugh B or C).</li> <li>Do not use concurrently with theophylline.</li> </ul>

Generic Name Trade Name Dosage Forms and Strengths	Usual Adult Daily Dose	Cost per Device <i>Approx. cost per usual daily dose</i>	PharmaCare Coverage	Therapeutic Considerations
<b>Mucolytics</b>				
<b>N-acetylcysteine (NAC)</b> generics Solution: 200 mg/mL 10 mL, 30 mL vials	600 mg (3mL) PO BID	10 mL vial: \$10 30 mL vial: \$25 \$5/day (600 mg po bid)	Regular Benefit	<ul style="list-style-type: none"> <li>• Potential adverse effects of oral administration: nausea, vomiting, GI symptoms.</li> <li>• Solution must be diluted with cola or other soft drink to a final concentration of 5%. Water may be used as a diluent if administered via a gastric tube. Use dilutions within 1 hour of preparation.</li> <li>• The unpleasant, sulfur-like odour of the oral solution typically becomes less noticeable as treatment progresses. Administering the oral solution on ice, in a cup with a lid, and drinking through a straw may help.</li> <li>• Undiluted solutions in opened vials can be stored for up to 96 hours in the refrigerator.</li> <li>• Studies used NAC tablets; however, tablets are not readily available in Canada.</li> </ul>

**Abbreviations:** AECOPD = acute exacerbation of COPD; BID = twice daily; DPI = dry powder inhaler; G = generic; GI = gastrointestinal; HF = heart failure; IR = immediate-release; kg = kilogram; mg = milligram; pMDI = pressurized metered dose inhaler; QID = four times daily; TID = three times daily.

**Footnotes:** Pricing is approximate (rounded up to nearest \$5) as of June 10, 2020 and does not include dispensing fee or additional markups.

**Note:** Please review product monographs at [hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php](http://hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) and regularly review current Health Canada advisories, warnings and recalls at [www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index\\_e.html](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html)

**PharmaCare Coverage Definitions:** **G:** generic(s) are available; **Regular Coverage:** also known as regular benefit; does not require Special Authority. Regular benefits may be fully or partially covered.\*; **Limited Coverage:** requires Special Authority for coverage. Limited Coverage benefits approved by Special Authority may be fully or partially covered.\*; **RDP:** Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. Patients receive full coverage of drugs designated as the Reference Drug(s) of the therapeutic class. Other drugs in the same RDP category are covered up to the price of the Reference Drug; **Non-benefit:** also known as no coverage; does not fit the above categories.

\* Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search ([www.health.gov.bc.ca/pharmacare/benefitslookup/](http://www.health.gov.bc.ca/pharmacare/benefitslookup/)). In all cases, coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: [www.health.gov.bc.ca/pharmacare/plans/index.html](http://www.health.gov.bc.ca/pharmacare/plans/index.html) and [www.health.gov.bc.ca/pharmacare/policy.html](http://www.health.gov.bc.ca/pharmacare/policy.html) for further information.

## References

1. CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2015 [cited 2016 Apr 4]. Available from: <http://www.e-therapeutics.ca>.
2. McIvor R. Chronic Obstructive Pulmonary Disease. In: Jovaisas, Barbara, editor. Therapeutics [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2016 [updated Jul 2015; cited 2016 Apr 15]. Available from: <http://www.e-therapeutics.ca>.
3. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; April 4, 2016.
4. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Updated 2020. Available at: [www.goldcopd.org/](http://www.goldcopd.org/).
5. Lipson et al. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. *N Engl J Med* 2018;378;18:1671-1680.
6. Crawley A, Jensen B, Regier L. COPD: Drug Comparison Chart. RxFiles. 11th ed. Saskatoon, SK: Saskatoon Health Region; 2020. p. 193–194. Available from: [www.RxFiles.ca](http://www.RxFiles.ca). Accessed online 2020 June 11 at <https://www.rxfiles.ca/RxFiles/uploads/documents/members/CHT-COPD-Tx.pdf>.



## Appendix B: Antibiotic Treatment Recommendations for Acute Exacerbations of COPD (AECOPD)

CATEGORY	RECOMMENDED EMPIRIC THERAPY (ALPHABETICAL ORDER)	NOTES
<p>&lt; 4 exacerbations/year and at least 2 of the following:</p> <ul style="list-style-type: none"> <li>• increased sputum purulence</li> <li>• increased sputum volume</li> <li>• increased dyspnea</li> </ul>	<p><b>First line agents:</b></p> <p style="text-align: center;"><b>amoxicillin</b> 1 g PO TID or <b>doxycycline</b> 200 mg PO once, then 100 mg PO BID or <b>sulfamethoxazole-trimethoprim</b> 1 DS (800-160 mg) tablet PO BID</p> <p><b>Failure of first line agents: see below</b></p>	<p>Treat for 5 to 7 days. Evidence indicates that 5 days of treatment may be as effective as 7 to 10 days.</p>
<p>≥ 4 exacerbations/year and at least 2 of the following:</p> <ul style="list-style-type: none"> <li>• increased sputum purulence</li> <li>• increased sputum volume</li> <li>• increased dyspnea</li> </ul> <p>or</p> <p><b>Failure of first line agents above<sup>1</sup></b></p> <p>or</p> <p><b>Antibiotics in the past 3 months<sup>2</sup></b></p>	<p><b>First line agents:</b></p> <p style="text-align: center;"><b>amoxicillin-clavulanate</b> 875-125 mg PO BID for 5 to 10 days or <b>cefuroxime axetil</b> 500 to 1000 mg PO BID for 5 to 10 days or <b>levofloxacin<sup>3</sup></b> 750 mg PO once daily for 5 days</p> <p><b>Alternatives:</b></p> <p style="text-align: center;"><b>azithromycin<sup>4</sup></b> 500 mg PO BID for 3 days or <b>clarithromycin<sup>4</sup></b> 500 mg PO BID or 1000 mg extended-release (XL) PO once daily for 5 to 10 days</p>	<ol style="list-style-type: none"> <li>1. Failure of first line agents: no improvement in symptoms following completion of antibiotic therapy OR clinical deterioration after 72 hours of antibiotic therapy.</li> <li>2. Use a different antibiotic class than was used previously.</li> <li>3. Due to the broad spectrum of levofloxacin, potential for increasing resistance and risk of <i>C. difficile</i> infection, reserve this medication for beta-lactam allergies or failure to first line antibiotic therapy.</li> <li>4. Macrolides have poor <i>Haemophilus</i> coverage and significant <i>S. pneumoniae</i> resistance. The benefit of macrolides may be due more to anti-inflammatory properties than to antibacterial activity.</li> </ol>

### References

- Blondel-Hill E, Fryters S. Bugs & Drugs 2012. 2012 edition. Edmonton, AB: Alberta Health Services; 2012.  
Canadian Pharmacists Association. Chronic Obstructive Pulmonary Disease. Revised: July 2015.



## Appendix C: BC Home Oxygen Program Medical Eligibility

Medical eligibility criteria may vary slightly between health authorities. Refer to health authorities for more details on local criteria and application forms. All Home Oxygen Program applicants are expected to seek and be compliant with optimal medical or adjunctive treatment prior to use of oxygen therapy.

	CRITERIA	NOTES
1. RESTING OXYGEN	<b>PaO<sub>2</sub> ≤ 55mmHg on room air</b>	Client must be breathing room air and seated at rest for at least 10 minutes prior to taking an arterial blood gas sample or beginning to monitor oximetry.
	<b>OR</b>	
	<b>SpO<sub>2</sub> &lt; 88% sustained continuously for 6 minutes<sup>1</sup></b>	
	<b>OR</b>	
	<b>PaO<sub>2</sub> ≤ 60 mmHg</b> <b>-AND-</b> <b>Evidence<sup>2</sup> of one of the following co-morbid diseases:</b> i. Heart failure ii. Pulmonary hypertension <sup>3</sup>	
2. AMBULATORY OXYGEN	<b>Short-term ambulatory oxygen therapy criteria<sup>4</sup></b> <b>SpO<sub>2</sub> &lt; 88% sustained continuously for one minute during the patient's usual type of ambulation on a level surface.</b>	If the client is unable to walk one minute or more, ambulatory oxygen will not be useful and will not be funded.
	<b>Long-Term ambulatory oxygen therapy criteria</b> (outpatient portable oxygen applications): <b>SpO<sub>2</sub> &lt; 88% sustained continuously for a minimum of one minute while breathing room air and a measured improvement within a 6-minute walk test as tolerated on oxygen compared to room air showing 1) the distance traveled increases by at least 25% AND 2) at least 30 meters (100 feet).</b> <b>-OR-</b> <b>SpO<sub>2</sub> &lt; 80% with ambulation for a minimum of one minute.</b>	Ambulatory testing is to be performed on a flat surface only; no exercise equipment (e.g. treadmills) is permitted. Clients should be tested with their usual mobility devices (e.g. walkers, canes, etc.).
3. NOCTURNAL OXYGEN	<b>SpO<sub>2</sub> must be &lt; 88% for &gt; 30% of a minimum 4 hour nocturnal oximetry study while breathing room air.</b>  In the absence of co-morbidities (heart failure, pulmonary hypertension), <sup>3</sup> daytime desaturation must be present at rest or with ambulation according to sections 1 or 2 for nocturnal oxygen therapy to be funded.	Sleep disordered breathing (i.e. sleep apnea) will only be treated with supplemental oxygen if the nocturnal criteria are met despite optimal CPAP treatment.
4. PALLIATIVE	Palliative clients must have hypoxemia according to sections 1, 2, or 3 above to be funded.	

### Notes

1. Island Health and Vancouver Coastal Health indicate that this criterion is only accepted in exceptional circumstances.
2. Information to support the co-morbid diseases is required (e.g. consultation note, discharge summary, spirometry, etc.).
3. Vancouver Coastal Health also accepts evidence of polycythemia or cor pulmonale.
4. Northern Health does not have specific short-term ambulatory oxygen therapy criteria.