COPD in BPS pharmacotherapy

An extensive exploration of the therapeutic options available for patients with COPD in BPS pharmacotherapy

Yasmeen Mustafa
Senior Clinical Pharmacist
Board certified pharmacotherapy specialist
57357 Children's Cancer Hospital
yasmeen.mustafa@57357.org

Guidelines

- Global Initiative for Chronic Obstructive Lung Disease (GOLD)
- Center of disease control and prevention (CDC)

Chronic obstructive pulmonary disease (COPD)

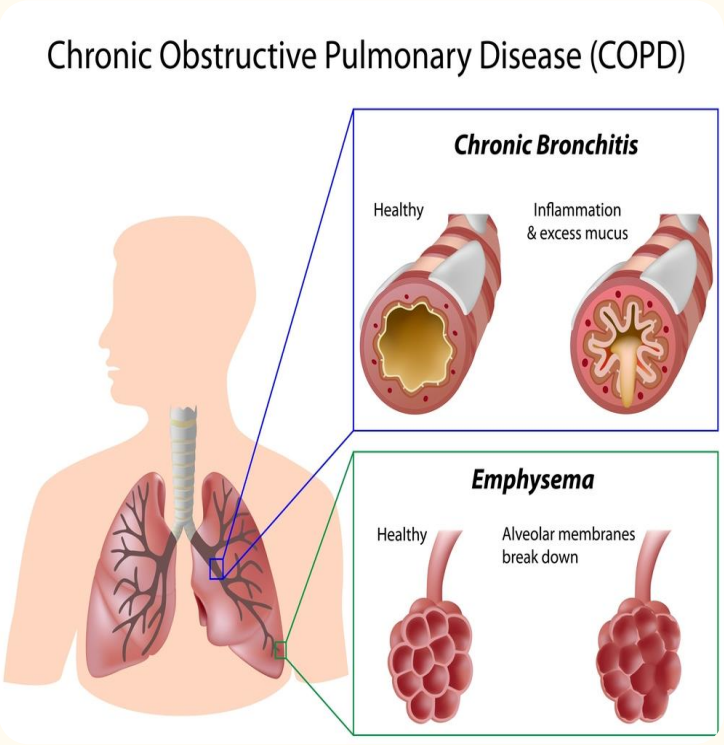
- Definition and prevalence
- Pathophysiology and symptoms
- COPD diagnosis
- Monitoring of lung function
- Pharmacologic options
- Classification of COPD stages
- Treatment algorithm
- Management of exacerbation

Definition

COPD is a common syndrome of persistent irreversible limitation in expiratory air flow which includes both emphysema and chronic bronchitis.

Chronic bronchitis is inflammation of the lining of the bronchial tubes, which carry air to and from the air sacs (alveoli) of the lungs. It's characterized by daily cough and mucus (sputum) production.

Emphysema is a condition in which the alveoli at the end of the smallest air passages (bronchioles) of the lungs are destroyed as a result of damaging exposure to cigarette smoke and other irritating gases and particulate matter



Who are at higher risk for COPD ?

- Women.
- People aged 65 to 74 years and ≥75 years.
- American Indians/Alaska Native.
- Current or former smokers.
- People with a history of asthma.

COPD Among Women

In the past, COPD was often thought of as a man’s disease, but things have changed in the past couple of decades. Since 2000, more women than men have died from COPD in the United States.

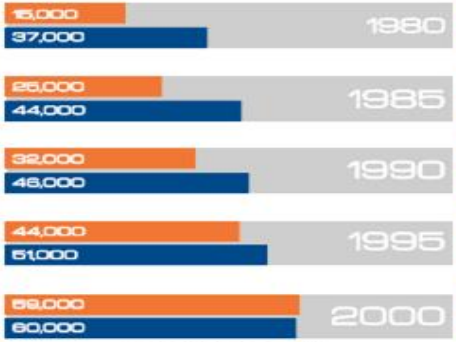
There are several reasons why COPD might affect women differently than men. Women tend to be diagnosed later than men, when the disease is more advanced and treatment is less effective. Women also seem to be more vulnerable to the effects of tobacco and other harmful substances, such as indoor air pollution.

WOMEN AND COPD

COPD, or Chronic Obstructive Pulmonary Disease, is an umbrella term used to describe progressive lung diseases including emphysema, chronic bronchitis, refractory (non-reversible) asthma, and some forms of bronchiectasis. This disease is characterized by increasing breathlessness.

COPD MORTALITY

MEN vs WOMEN



SYMPTOMS

- SHORTNESS OF BREATH
- CHRONIC COUGH
- CHEST TIGHTNESS
- FATIGUE
- MUCUS

COPD RELATED HOSPITALIZATIONS

There were 1.4 MILLION Emergency Room Visits

WOMEN ARE 2X LIKELY TO BE DIAGNOSED WITH CHRONIC BRONCHITIS THAN MEN

WOMEN WHO SMOKE ARE 13X AS LIKELY TO DIE FROM COPD

6%

OF U.S WOMEN HAVE COPD vs 4% OF MEN

COPD FOUNDATION

www.copdfoundation.org

What causes COPD?

In the United States, tobacco smoke is a key factor in the development and progression of COPD. Exposure to air pollutants in the home and workplace, genetic factors, and respiratory infections also play a role.

In the developing world, indoor air quality is thought to play a larger role than it does in the United States.

People with COPD are at increased risk of developing heart disease, lung cancer

Complications

- Respiratory infections. People with COPD are more likely to catch colds, the flu and pneumonia. Any respiratory infection can make it much more difficult to breathe and could cause further damage to lung tissue.
- Heart diseases. For reasons that aren't fully understood, COPD can increase your risk of heart disease, including heart attack
- Lung cancer. People with COPD have a higher risk of developing lung cancer.
- High blood pressure in lung arteries. COPD may cause high blood pressure in the arteries that bring blood to your lungs (pulmonary hypertension).
- Depression. Difficulty breathing can keep you from doing activities that you enjoy. And dealing with serious illness can contribute to the development of depression

Diagnosis of COPD

History & clinical presentation

Spirometry

Diagnosis of COPD

GOLD guidelines: perform spirometry and consider COPD if a patient is older than 40 yrs and has any of the following :

- Dyspnea that is progressive, persistent and worse with exercise or an exertion
- Chronic sputum production
- wheezing
- History of exposure to risk factors especially tobacco smoke (most common risk factor) , occupational dusts or chemicals

Diagnosis of COPD

For diagnosis and assessment of COPD, spirometry is the gold standard

Spirometry revealing FEV1/FVC < 70% is the hallmark of COPD

Bronchodilator reversibility test is no longer recommended

On the basis of spirometry results, a GOLD grade is assigned as follows:

- GOLD 1 **(mild)**: FEV1 80% or greater of predicted
- GOLD 2 **(moderate)** : FEV_1 50%-79% of predicted
- GOLD 3 **(severe)** : FEV_1 30%-49% OF predicted
- GOLD 4 **(very severe):** FEV_1 less than 30%

Initial assessment of COPD

Asses frequency of exacerbations in the past 12 months:

- Less severe : 0 or 1 exacerbation (not leading to hospitalization)
- More severe : 2 or more exacerbations or, 1 exacerbation leading to hospitalization

Use validated symptom scales or questionnaires:

- COPD assessment test **(CAT)** score (measure symptoms beyond breathlessness, such as cough, sputum production , limitation of activities, sleep and energy levels)
- Modified Medical Research Council breathlessness scale (**mMRC)** for assessing severity of breathlessness
- COPD control questionnaire **(CCQ)**

Validated symptom scales or questionnaires:

17.25 Modified Medical Research Council (MRC) dyspnoea scale

Grade	Degree of breathlessness related to activities
0	No breathlessness, except with strenuous exercise
1	Breathlessness when hurrying on the level or walking up a slight hill
2	Walks slower than contemporaries on level ground because of breathlessness or has to stop for breath when walking at own pace
3	Stops for breath after walking about 100 m or after a few minutes on level ground
4	Too breathless to leave the house, or breathless when dressing or undressing

Your name:

Today's date:

CAT
COPD Assessment Test

How is your COPD? Take the COPD assessment test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your well being and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

			Score
Example:	I am very happy 0 X 2 3 4 5	I am very sad	
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	
		Total score	

Initial assessment of COPD

Moderate to severe Exacerbation History

≥ 2 Or
≥ 1 leading to hospital admission

0 Or 1
Not leading to hospital admission

GOLD ABE Assessment Tool

E	
A	**B**
mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

Management of stable COPD

Description of level of evidence in GOLD guidelines

Evidence category	Source of evidence
A	Randomized clinical trials without any significant limitation or bias
B	Randomized clinical trials with important limitation
C	Nonrandomized trials & observational studies
D	Panel judgment consensus

Pharmacological therapy in COPD

1-Bronchodilators

- Inhaled bronchodilators in COPD are central to symptoms management and commonly given on regular basis to prevent or reduce symptoms (Evidence A)
- Regular or as needed use of SABA or SAMA improve FEV_1 and symptoms (Evidence A)
- Combinations of SABA and SAMA are superior compared to either medication alone in improving FEV_1 and symptoms (Evidence A)
- LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates (Evidence A)

1-Bronchodilators

- LAMAS have a greater effect on exacerbation reduction compared LABAS
- (evidence A) and decrease hospitalizations (Evidence B)
- Combination treatment with a LABA and LAMA increases FEV_1 and reduce symptoms compared to monotherapy (Evidence A)
- Combination treatment with a LABA and LAMA reduces exacerbations compared to monotherapy (Evidence B)
- Tiotropium improves the effectiveness of pulmonary rehabilitations in increasing exercise performance (Evidence B).
- Theophylline exerts a small bronchodilator effect in stable COPD (Evidence A) and that is associated with modest symptomatic benefits (Evidence B)

2-Inhaled corticosteroids (ICS)

- **Regular treatment with ICS increase risk of pneumonia & mortality** especially in those with severe disease (Evidence A)
- An **ICS combined with a LABA** is more effective than the in individual components in improving lung function and health status and **reducing exacerbation** in patients with exacerbations and moderate to very severe COPD. (Evidence A)
- **Triple inhaled therapy ICS/LAMA/LABA** improving lung function, symptoms and health status, and **reduces exacerbation**, compared to ICS/LABA, LABA/LAMA or LAMA monotherapy (Evidence A)

3-Phosphodiesterase-4 inhibitors

(Roflumilast)

Reduce inflammation through inhibition of breakdown of adenosine monophosphate, no direct bronchodilator effect

Contraindications:

Moderate to severe liver impairment & nursing mothers

Side effects:

weight loss & psychiatric events including suicidality

When to use:

In patients with chronic bronchitis, severe to very severe airflow limitation & history of exacerbations

PDE-4 inhibitors improve lung function & reduce moderate to severe exacerbation (Evidence A)

4-Antibiotics

Antibiotics (azithromycin & clarithromycin)

Anti- inflammatory and antibacterial effects

Daily dose of 250 mg of azithromycin orally for 1 year found to:

- Lengthen time to first exacerbation
- Decrease overall exacerbation rate
- Improve quality of life

Potential side effects:

- High incidence of bacterial resistance
- Hear loss & GI distubances
- QT prolongation

Macrolides are preferentially considered in former smokers with exacerbations (Evidence B)

5-Alpha-1-antitrypsin

In about 1% of people with COPD, the disease results from a genetic disorder that causes low levels of a protein called alpha-1-antitrypsin (AAt). AAt is made in the liver and secreted into the bloodstream to help protect the lungs. Alpha-1-antitrypsin deficiency can cause liver disease, lung disease or both.

For adults with COPD related to AAt deficiency, treatment options include those used for people with more-common types of COPD. In addition, some people can be treated by replacing the missing AAt protein, which may prevent further damage to the lungs

Non Pharmacological therapy

1-Oxygen therapy

Long-term oxygen therapy (LTOT) is indicated for stable patients who have: Pao2 of 55 mm Hg Or Sao2 ≤ 88% with or without hypercapnia, confirmed twice during a 3-week period

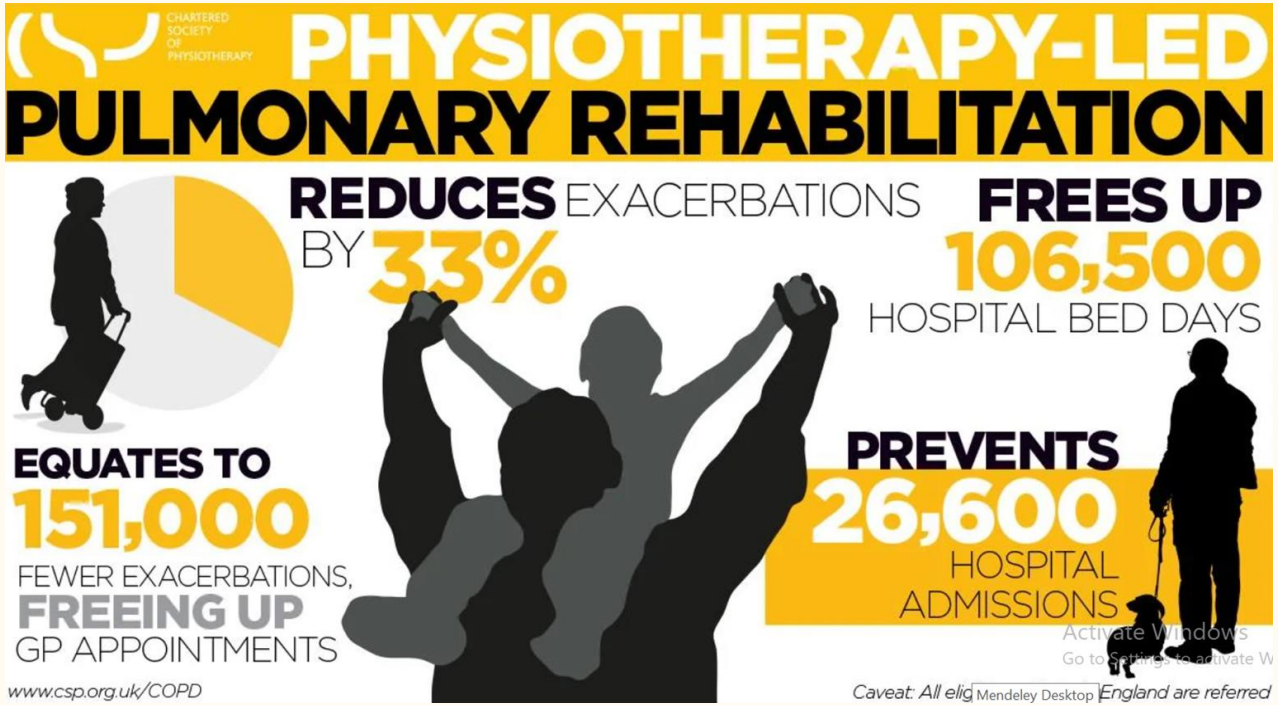
Or

Pao2 between (55-60 mmHg), or SaO2 of 88%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive heart failure or polycythemia (hematocrit >55%)

Once placed on LTOT the patient should be re-evaluated after 60 to 90 days with repeat arterial blood gas (ABG) or oxygen saturation while inspiring the same level of oxygen or room air to determine if oxygen is therapeutic and still indicated.

Long-term (>15 hours/day) use in patients with chronic respiratory failure improves survival.

2- Pulmonary rehabilitation



Includes exercise training, nutrition counseling, and education

Improves many outcomes in COPD, including quality of life and survival

Initial pharmacologic treatment

≥2 moderate exacerbation or ≥1 leading to hospitalization

Group E
LAMA or
LAMA+LABA*(consider if highly symptomatic)
LABA+ICS**(consider if eos ≥300)

0 or 1 moderate exacerbation not leading to hospitalization

Group A

A bronchodilator

mMRC 0-1
CAT <10

Group B

Long acting bronchodilator (LAMA or LABA)

mMRC ≥2
CAT≥ 10

Exacerbations Of COPD

1. Definition

An event characterized by dyspnea and/or cough and sputum that worse suddenly.

Exacerbation of COPD are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.

2. Diagnosis

Diagnosis is based purely on clinical presentation.

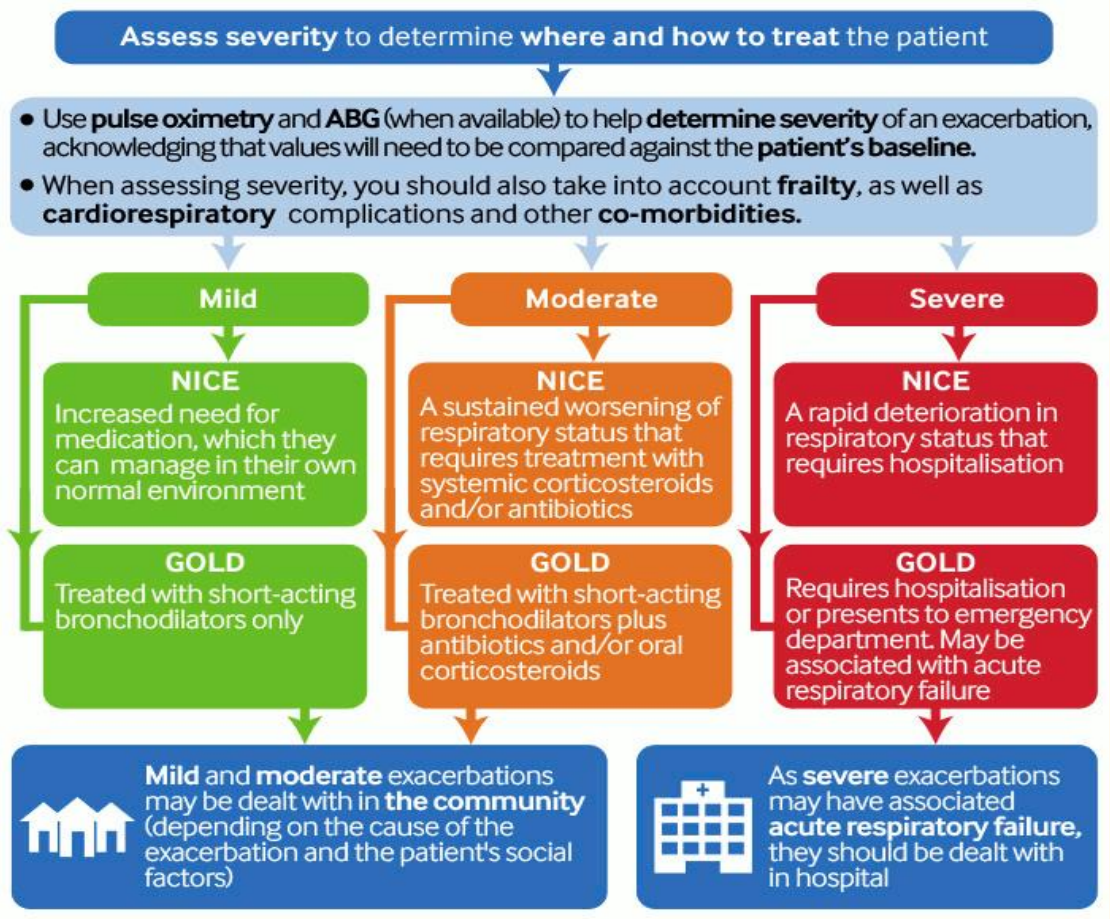
Spirometry isn't accurate during an exacerbation and isn't recommended.

3. Classification

a. **Mild**:Treated with Short Acting bronchodilators only (SAMA/SABA)

b. **Moderate:** Treated with SA bronchodilators plus antibiotics and/or oral corticosteroids

c. **Severe:** patient requires hospitalization or visits the Emergency room.



N.B

NICE guidelines are evidence-based recommendations for health and care in England. They set out the care and services suitable for most people with a specific condition or need, and people in particular circumstances or settings. Our guidelines help health and social care professionals to: prevent ill health

4. Common precipitating factors

Include infection of tracheobronchial tree and viral upper respiratory tract infections (most common) and air pollution.

However, the cause of one-third of exacerbations cannot be determined.

5. Key points in Management

- SABA+SAMA are recommended as the initial bronchodilators to treat an acute exacerbation.
- Systemic corticosteroids can improve lung function (FEV1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy shouldn't be more than 5-7 days.
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5-7 days.
- Methylxanthines are not recommended due to increased side effect profiles.

6. Antibiotic treatment

a. The most common pathogens in COPD exacerbations:

- Streptococcus pneumoniae (pneumococcus) (Gram + ve diplococci)
- Haemophilus influenzae (Gram - ve bacilli)
- Moraxella catarrhalis (Gram- ve diplococci)

b. In patients with GOLD 3 and 4 severity:

Pseudomonas aeruginosa infection becomes an important pathogen. (Gram -ve bacilli)

c. The 3 cardinal symptoms in COPD exacerbations are:

- increased dyspnea
- increased sputum volume
- increased sputum purulence

When to give antibiotics?

d. Antibiotics should be given if

- All 3 cardinal symptoms are present.
- 2 of the 3 cardinal symptoms are present and if ↑ sputum purulence is one of the symptoms.
- Severe exacerbation requiring mechanical ventilation.

e. The recommended duration of antibiotic treatment is usually 5 to 7 days (level of evidence B)

Recommended Antibiotics

Empiric treatment consists of:

- Amoxicillin with clavulanic acid, Macrolide (azithromycin) or Tetracycline (doxycycline).

  If antibiotics have been used recently (in the last 3 months), use an alternative class.

In complicated COPD with risk factors:

- Amoxicillin/clavulanate, levofloxacin, moxifloxacin.

Risk factors:

- Comorbid diseases
- severe COPD (FEV1 < 50% of predicted)
- > 3 exacerbations/year
- antibiotic use in past 3 months

If at risk of **Pseudomonas** infection:

High-dose levofloxacin (750 mg) or ciprofloxacin; obtain sputum culture.

Risk factors:

- ≥ 4 courses of antibiotics in past year
- History of pseudomonas/ previous pseudomonas isolation
- Recent hospitalization (past 90 days)

Is it Asthma or COPD ?

	Asthma	ACO	COPD
history	● Symptoms vary over time & in intensity ● Triggers:laugh, exercise and allergens ● Onset < 40 yrs		● Persistent symptoms on most days ● Onset > 40 yrs ● Bronchodialtor provide limited relief ● H/O smoking, low birth weight or respiratory illness (TB)
Lung function	● Symptoms improvement by bronchodialators		● Persistent airflow limitation ● No bronchodialator reversibility
Initial treatment	● ICS is cornerstone. ● Do not give LABA/ LAMA alone. ● Avoid maintenance OCS.		● LAMA is cornerstone (as per GOLD guidelines). ● Reliever containing ICS is not recommended. ● Avoid maintenance OCS.

Patient case:

A 64-year old woman was recently given a diagnosis of COPD. spirometry reveals an FEV1/FVC 60%of predicted,pre-bronchodilator FEV1 70% of predicted, and post-bronchodilator FEV1 72% of predicted. Her symptoms are quite bothersome. she reports walking more slowly than others because of shortness of breath (mMRC score 2) he had 1 exacerbation in the past year that did not require hospitalization.

Which is the most appropriate patient group classification according to GOLD guidelines?

1. GOLD 1, group A
2. GOLD 2, group B
3. GOLD 3, group E
4. GOLD 4, group E

Patient case :

In addition to albuterol 2 puffs every 4-6 hours as needed, which pharmacotherapy option is most appropriate to initiate?

1. No additional therapy needed
2. Salmeterol 50 mcg 1 puff twice daily
3. tiotropium/olodaterol 2.5/2.5 2 puffs once daily
4. salmeterol/fluticasone 50/500 1 puff twice daily plus roflumilast 500 mcg orally once daily

Thank you for listening!