Chronic Obstructive Pulmonary Disease (COPD)

A VA Clinician's Guide

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

PBM Academic Detailing Services

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Contents

This document aims to provide clarity in selecting optimal goals and evidence-based treatments for chronic obstructive pulmonary disease.

These materials were developed by:

VA Pharmacy Benefits Management Academic Detailing Services

Key Messages

Background

Did you know?

Almost 16 million Americans have been diagnosed with chronic obstructive pulmonary disease (COPD). The actual prevalence is likely much higher since many people with low pulmonary function are unaware of their condition and remain undiagnosed.[1–3] COPD was the 6th leading cause of death in the United States in 2020 and the 2nd most common cause of admission for an ambulatory care sensitive condition from 2022-2023.[4,5]

COPD has historically been a disease of men, however, more recently in North America the prevalence in women has surpassed men (8.1% women vs 7.3% men).[6] Prevalence of COPD is highest in rural areas with 8.2% of people in rural areas having COPD compared to 4.7% in large metro areas.[1] The goal in treating COPD is to improve symptoms and reduce acute exacerbations. An acute COPD exacerbation occurs when a patient has increased dyspnea and/or cough and sputum that worsens in less than 14 days. The risk of death increases as the number and severity of exacerbations increase.

Initial assessment and diagnosis

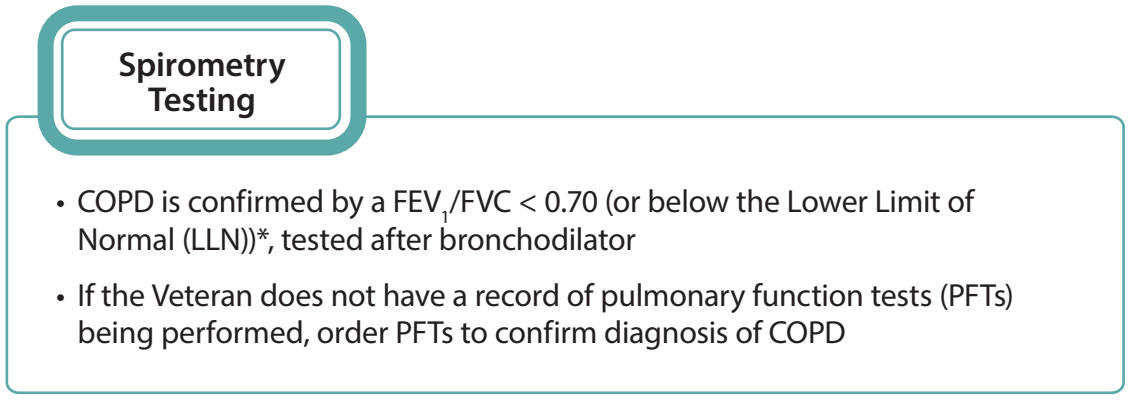
COPD should be considered in patients with any clinical indicators for COPD.[8] Airway obstruction is the hallmark of COPD. Spirometry is used to confirm the diagnosis of COPD.

Table 1.
Clinical indicators of COPD[8–11]

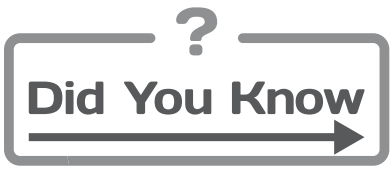
Clinical Indicators	
Dyspnea	Progressive over time; worsens with exertion; persistent
Chronic cough	Intermittent or persistent; productive or unproductive
Recurrent wheezing	
Recurrent lower respiratory tract Infections	
History of risk factors	Use or exposure to tobacco smoke; smoke from heating or cooking; occupational vapors, fumes, gases, dusts, etc.; host factors*

*Genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections, etc.

Figure 1.
Use spirometry to confirm diagnosis of COPD[8–11]



*Lower Limit Normal is based on age-appropriate cut-offs in post-bronchodilator spirometry. -



***Eliminating exposure to tobacco smoke and reducing air pollution exposure can prevent COPD in most individuals.*[6,8,11]**

KEY MESSAGE

Evaluate all patients with clinical indicators for COPD and diagnose with spirometry.

Developing a treatment plan for COPD

Simply prescribing an inhaler for a patient with COPD is not a treatment plan. Treatment decisions for COPD patients should be individualized, multi-modal, and guided by symptoms, symptom severity, comorbidities, and the frequency of acute exacerbations.[8,11]

Note: As part of the shared decision-making process, a patient's ability to use an inhaler device and their preference should be considered.

Figure 2.
Elements of a COPD treatment plan[8,11]

Smoking Cessation	Quitting tobacco has the greatest impact on slowing COPD progression and improves mortality. (See **Tobacco Use Disorder (sharepoint.com)** for more information).
Vaccines	Influenza vaccination reduces COPD exacerbations and hospitalizations. Pneumococcal vaccinations reduce the rate of community-acquired pneumonia in patients with COPD. Routine vaccinations are recommended for patients with COPD as they are for the general population and include Zoster, tetanus/diphtheria/pertussis (Tdap), COVID-19, and respiratory syncytial virus (RSV).
Pharmacotherapy	Pharmacotherapy reduces symptoms, frequency, and severity of COPD exacerbations, and improves exercise tolerance and health status.
Non-Pharmacologic	Proper nutrition, exercise, and use of pulmonary rehabilitation therapies (if criteria are met) help improve quality of life and reduce exacerbations.
Treating Other Comorbidities	The most common cause of death in Veterans with COPD is cardiovascular disease. Addressing this, along with other common comorbidities, like depression, lung cancer, obesity, and osteoporosis, is vital to the overall health of patients with COPD.

Smoking cessation

Ask every patient with COPD if they smoke tobacco. If they do, smoking cessation should be addressed. Smoking cessation improves survival in patients with COPD, including older patients.[12,13] Veterans who say they are ready to quit in the next 30 days should receive pharmacotherapy support (e.g., nicotine replacement, bupropion, or varenicline).[14,15]

Figure 3.
Pathway for addressing tobacco use – The 5 A's[15–17]

Behavioral supports with evidence for benefit include individual sessions, group sessions, or provider support via telephone or Quitline (the VA National Quitline is: 1-855-QUIT-VET (1-855-784-8838). See the Academic Detailing Services (ADS) **Tobacco Use Disorder SharePoint Site (intranet)** for more detailed information on pharmacotherapy for tobacco cessation.

Note

Encourage a no smoking policy for home, car, and work settings to reduce exposure to secondhand smoke and prevent relapse.

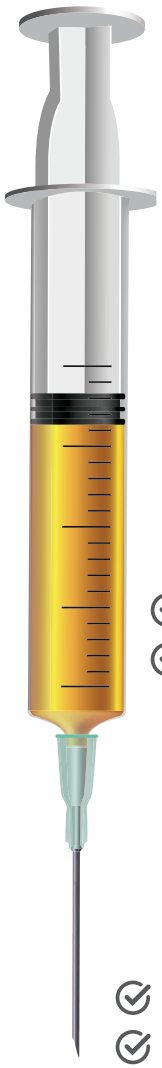
KEY MESSAGE

Encourage smoking cessation regardless of COPD severity.

Vaccines

Annual influenza vaccination can significantly reduce the incidence of lower respiratory infections and death in people with COPD.[8,18,19] Pneumococcal vaccination reduces the incidence of community-acquired pneumonia (CAP) and exacerbations in people with COPD.[20,21]

Figure 4.
Vaccine timing for adults with COPD*[8,20,21]



Influenza
- Annually

Zoster
- Indicated for ages 50+

Pneumococcal
- COPD patients 19 to 64 years old
- COPD patients ≥65 years old

RSV
- Adults ≥60 years old using shared clinical decision making

Tdap
- All adults need one booster of Tdap
- Then Td or Tdap booster every 10 years

COVID-19
- COVID-19 vaccine recommended
- See CDC for current recommendations

*Recommended CDC Vaccination and Immunization schedule: **www.cdc.gov/vaccines**.

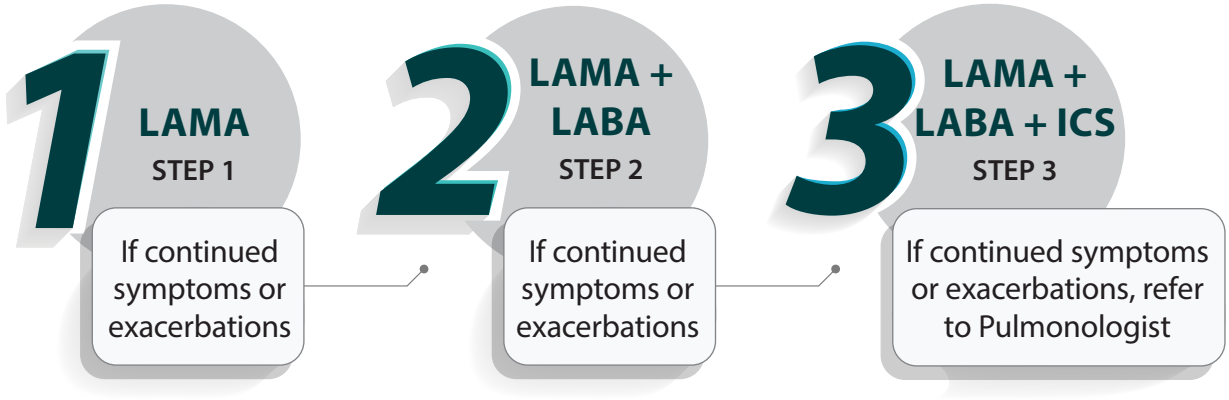
KEY MESSAGE

Vaccinate all Veterans with COPD with influenza vaccine annually and pneumococcal vaccine as recommended.

Pharmacotherapy for stable (non-exacerbating) COPD

Pharmacotherapy can reduce symptoms, decrease the risk and severity of exacerbations, and improve health status and exercise tolerance.[8,11,23–26] Long-acting bronchodilators used in patients with symptomatic COPD have been shown to decrease dyspnea, improve quality of life, and decrease exacerbations when compared to placebo.[11] Long-acting bronchodilators are preferred over short-acting agents for initial treatment in patients with persistent symptoms because they improve lung function, dyspnea, and health status as well as reduce exacerbations. Short-acting agents only improve dyspnea and temporarily improve lung function.[8,27–30]

Figure 5.
Pharmacotherapy for COPD based on VA/DoD Guidelines[11]



Management of Chronic Obstructive Pulmonary Disease (COPD) (2021) - VA/DoD Clinical Practice Guidelines

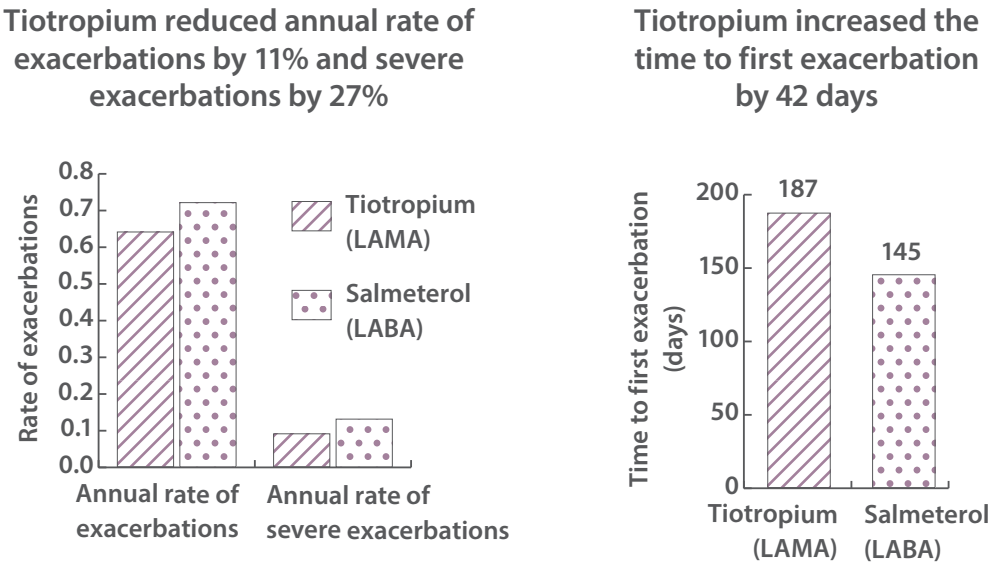
STEP 1

Initial treatment in most patients with persistent symptoms is starting with a long-acting muscarinic antagonist (LAMA). Evidence shows LAMA to reduce exacerbations and increase time to first exacerbation compared to long-acting beta agonists (LABA).[11,27–32]

- Short-acting bronchodilators can be considered in patients with intermittent symptoms
  - Short-acting muscarinic antagonists (SAMA) and short-acting beta agonists (SABA) have comparable efficacy.

- SABA can be added to LAMA therapy in patients who need immediate relief, prescribed on an as-needed schedule. SAMA should not be used in patients on LAMA due to increased risk of anticholinergic side effects.

Figure 6.
Reduced annual rate of exacerbations and increased time to first exacerbation with tiotropium (LAMA) monotherapy compared to salmeterol (LABA)[31]



POET-COPD trial comparing tiotropium to salmeterol in patients with moderate-to-very-severe - COPD and a history of exacerbations in the previous year ($p < 0.05$ for all comparisons in figures). -

KEY MESSAGE

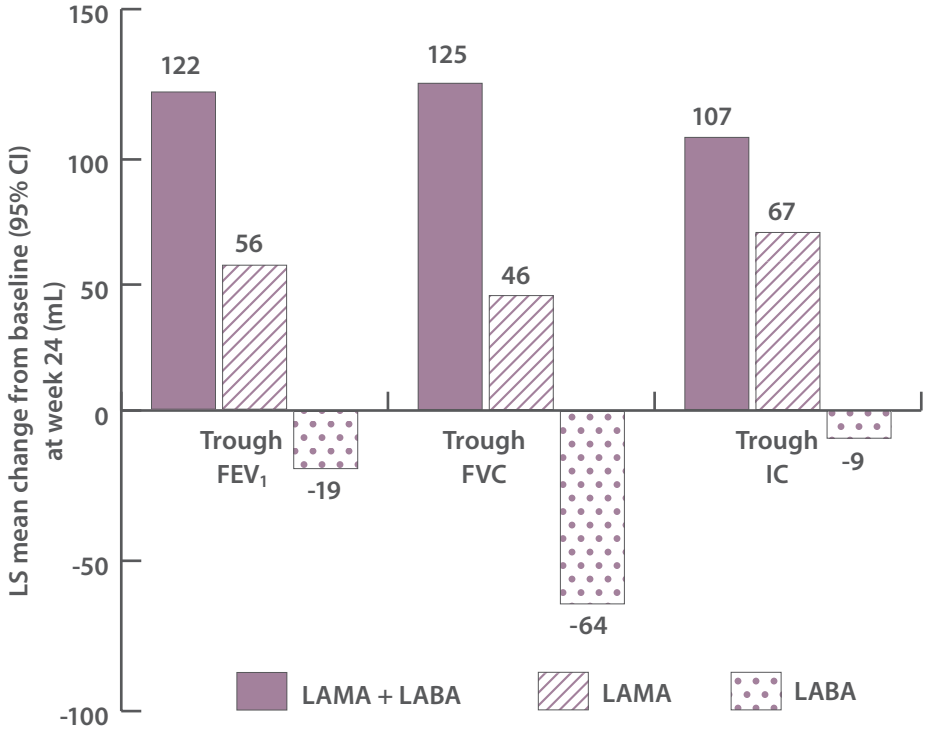
Use a LAMA as initial therapy for patients with persistent symptoms.

STEP 2

If symptoms persist or if the Veteran experiences an exacerbation, add LABA.

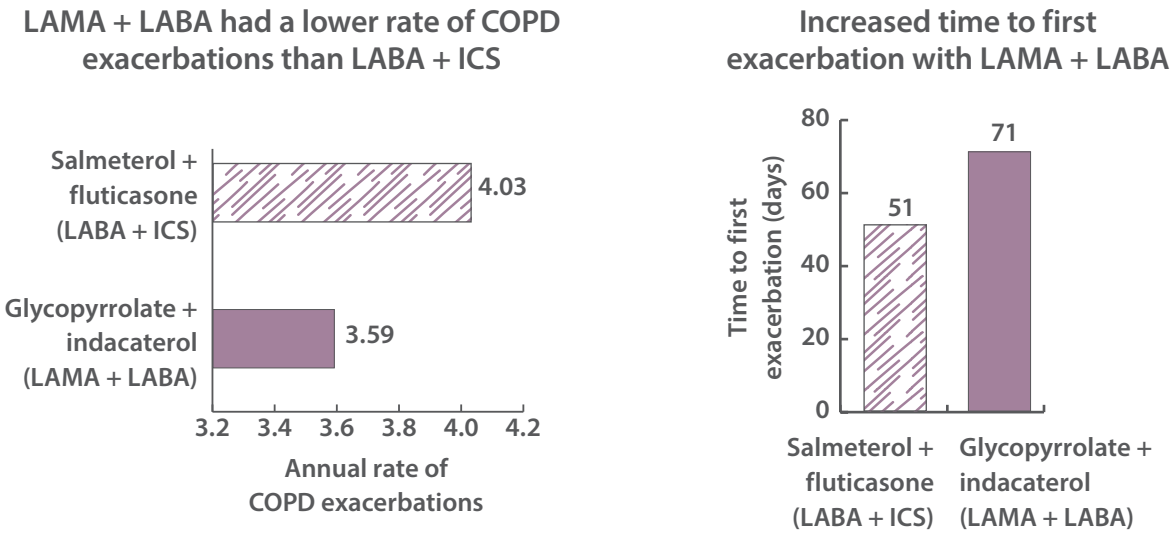
- Combination of LAMA + LABA reduces COPD exacerbations and increases the time to first exacerbation compared to LABA + ICS.[33,34]
- Assess adherence with therapy and inhaler technique.

Figure 7.
Mean change from baseline in trough FEV_1 at week 24 with umeclidinium + vilanterol (LAMA + LABA) compared to umeclidinium (LAMA) and salmeterol (LABA) monotherapies.[33]



EMAX trial evaluating umeclidinium/vilanterol (LAMA + LABA), umeclidinium (LAMA) and salmeterol (LABA) for improving COPD stability in patients at low exacerbation risk not receiving inhaled corticosteroids. Primary endpoint was trough forced expiratory volume in 1 second (FEV_1) at Week 24.

Figure 8.
Combination of LAMA + LABA reduced COPD exacerbations and increased the time to first exacerbation compared to LABA + ICS[34]



FLAME trial evaluating Glycopyrrolate + indacaterol (LAMA + LABA) compared to salmeterol-fluticasone (LABA + ICS) in patients with COPD and a history of at least one exacerbation in the previous year. The trial was designed to evaluate the annual rate of all COPD exacerbations ($p < 0.001$ for all comparisons in figure).

KEY MESSAGE

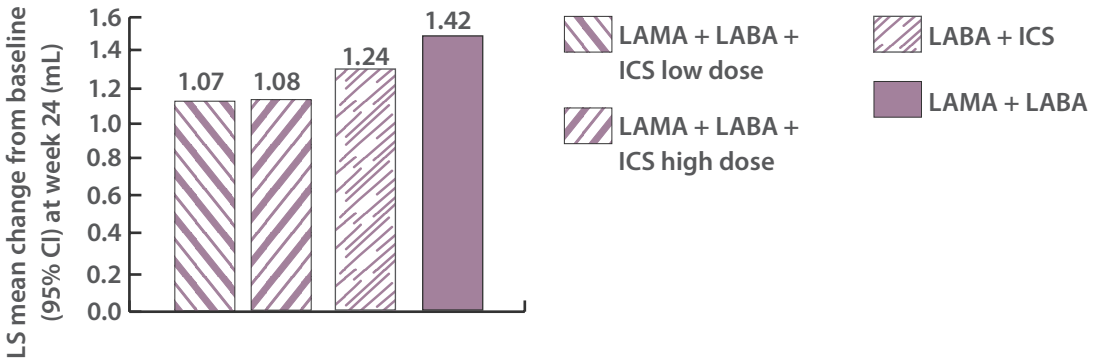
Use LAMA + LABA for patients with continued symptoms or exacerbations on LAMA monotherapy.

STEP 3

If symptoms persist or if the Veteran experiences exacerbations, add inhaled corticosteroid (ICS).

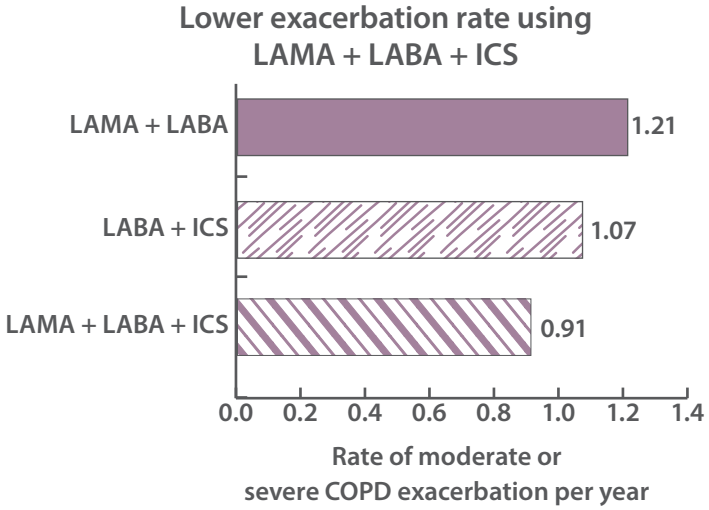
- LAMA + LABA + ICS
  - Use LAMA + LABA and a separate ICS inhaler or LABA + ICS and a separate LAMA first line. If Veteran is unable to use multiple inhalers then consider triple therapy single LAMA + LABA + ICS inhaler.

Figure 9.
Rates of moderate or severe exacerbations were lower using LAMA + LABA + ICS compared to LAMA + LABA or LABA + ICS in patients with moderate to very severe COPD[35]



ETHOS trial evaluated the use of annual rate of moderate or severe COPD exacerbations in patients taking triple therapy at two dose levels of ICS compared to LAMA + LABA and LABA + ICS. Both triple therapy regimens had lower rates of exacerbations. + LAMA + LABA + ICS low dose = glycopyrrolate formoterol + budesonide 160 µg; LAMA + LABA + ICS high dose = glycopyrrolate + formoterol + budesonide 320 µg LABA + ICS = formoterol + budesonide 320 µg; LAMA + LABA = glycopyrrolate + formoterol.

Figure 10.
Triple therapy versus dual therapy in patients with moderate to severe COPD[36]



Greatest reduction in exacerbation rate with LAMA + LABA + ICS (triple therapy) was seen in patients with eos ≥150cells/µL

IMPACT trial evaluated the use of umeclidinium+vilanterol (LAMA + LABA), vilanterol + fluticasone furoate (LABA + ICS), and umeclidinium + vilanterol + fluticasone furoate (LAMA + LABA + ICS) in patients with moderate to severe COPD. LAMA + LABA + ICS had the lowest rate of exacerbations. -

KEY MESSAGE

Add ICS to LAMA + LABA therapy when symptoms persist, or Veteran has an exacerbation on LAMA + LABA therapy.

VA/DoD Clinical Practice Guidelines Management of Chronic Obstructive Pulmonary Disease compared to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report.

VA/DoD Clinical Practice Guidelines are based on a systematic review of both clinical and epidemiological evidence developed by multidisciplinary experts. On the other hand, GOLD reports are not guidelines with measures of strength of evidence or certainty of recommendations, nor are they specific to United States or Veteran populations. The VA/DoD guidelines are designed to provide information and assist in decision making but are not intended to define a standard of care.

Table 2.
Comparing VA/DoD Guidelines to the Global Initiative for COPD (GOLD) Report.

VA/DoD CPG 2021[11]	GOLD Report 2024[8]
Step 1: LAMA tiotropium (Spiriva®)	Group A: LAMA or LABA* mMRC 0–1 or CAT <10 and 0–1 moderate exacerbation**
Step 2: LAMA + LABA tiotropium + olodaterol (Stiolto®)	Group B: LAMA + LABA mMRC ≥2 or CAT ≥10 and 0–1 moderate exacerbation**
Step 3: LAMA + LABA + ICS tiotropium + olodaterol (Stiolto®) + mometasone HFA (Asmanex®)	Group E: LAMA + LABA Consider LAMA + LABA + ICS with history of asthma, blood eosinophils ≥300, or frequent and severe exacerbations Any score on mMRC or CAT and ≥2 moderate exacerbations or ≥1 leading to hospitalization

CAT = COPD Assessment Test; mMRC = Modified Medical Research Council Breathlessness Scale; See **Appendix A** for the full questionnaires. *LAMA or LABA for patients with persistent symptoms. SAMA or SABA can be used instead for Group A if only occasional dyspnea. **Not leading to hospitalization.

Use of inhaled corticosteroids

Monotherapy with ICS is not recommended in patients with COPD since it does not improve FEV_1 or decrease exacerbations.[8] If the Veteran has COPD in addition to asthma and an ICS is indicated, a LAMA should be provided with or without LABA. Blood eosinophil counts (eos) may help predict response to ICS (eos >300 cells/µL (0.3 cells/nL) = greater likelihood to respond, eos <100 cells/µL (0.1 cells/nL) = lower likelihood to respond).[8,36–41]

ICS inhalers have adverse effects which need to be considered and discussed before prescribing. ICS adverse effects include:[8,42–44]

- Oral candidiasis
- Hoarse voice
- Skin bruising
- Pneumonia

Patients at highest risk of pneumonia related to ICS include patients:

Note

- ✓ **Who smoke**
- ✓ **Are >55 years of age**
- ✓ **Have a history of pneumonia**
- ✓ **Have a body mass index <25 kg/m²**
- ✓ **Have severe airflow limitation**

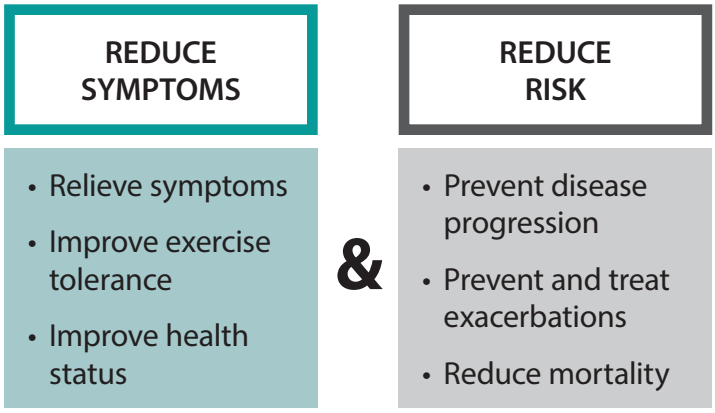
Withdrawal of inhaled corticosteroids

Corticosteroid inhalers may need to be discontinued. In some cases, corticosteroids can be discontinued without tapering. For some patients, tapering may be needed, particularly if they are using high dose ICS or have a history of exacerbations after discontinuing ICS.[37–38] When tapering, the dose should be slowly tapered from high dose ICS to moderate dose ICS, to low dose ICS every 6 weeks to avoid worsening of symptoms. Caution should be used when withdrawing ICS in patients with blood eosinophils ≥300 cells/µL (0.3 cells/nL) due to a higher risk of experiencing more exacerbations after stopping ICS.[8,42–46]

Possible candidates for ICS discontinuation include patients with:[8]

- Pneumonia
- Inappropriate original indication for ICS
- No symptom improvement while taking ICS
- Stable COPD without exacerbation in the past 2 years[11]
- Eosinophil count <300 cells/µL (0.3 cells/nL)

Goals of treatment for stable COPD[8,11]



Follow up assessment and treatment of COPD

Follow up treatment is based on how the patient responded[8]

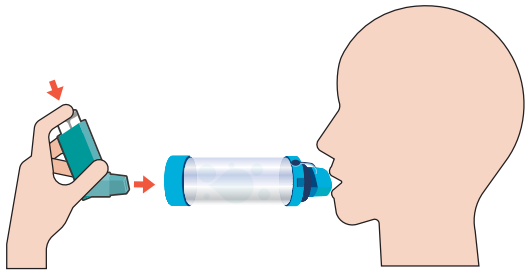
- If the patient had an adequate response to the initial treatment, then maintain it.
- If not, modify treatment as indicated.

Figure 11.
Proper inhaler technique is critical for effective COPD pharmacotherapy[8,11]

✓ *Provide instructions and demonstrate proper technique when prescribing an inhaler device.*

✓ *Spacers may improve drug delivery when used with metered dose inhalers (MDI).*

✓ *Inhaler technique and adherence to therapy should be assessed before considering dose adjustments and/or changing therapy. (Links to VA Instructional Videos in the Veteran Health Library:* **Combivent Respimat**, **Pressurized Metered Dose Inhaler**, **HandiHaler**, **Mometasone Twisthaler**, **How to Use a Nebulizer**, **Wixela Inhub Inhaler***)*



When inhalers are not enough

In patients with continued exacerbations despite maximizing inhaler therapy, a referral to a pulmonologist is recommended. Roflumilast or azithromycin may be indicated.[8,47–49]

Table 3.
Comparing roflumilast and macrolide antibiotic (azithromycin)

Roflumilast*	Macrolide antibiotic
Indicated for patients with FEV_1 < 50% with ≥ 1 recorded exacerbation requiring systemic steroids, unscheduled healthcare contact, or hospitalization in the previous year.	Azithromycin is the macrolide of choice for this indication. Best evidence is for use in patients who are former smokers. May reduce exacerbation rates in some patients.
Patients should be on optimal bronchodilator therapy (LAMA + LAMA) +/- ICS. Prescribing should be done by a pulmonologist or designated expert.	Patients should be on optimal bronchodilator therapy (LAMA + LABA) +/- ICS. Prescribing should be done by a pulmonologist or designated expert.
Avoid use in patients with depression, may increase risk of suicide. Contraindicated in patients with moderate to severe liver impairment.	Associated with an increased incidence of bacterial resistance, prolongation of QTc interval, and impaired hearing tests.
Roflumilast 500 mg tablet orally once daily; may initiate at 250 mg daily for 4 weeks to reduce adverse effects.	Azithromycin 250 mg orally once daily or 500 mg three times weekly. No data showing benefit beyond one year of treatment. Patients should be re-assessed annually.

Criteria for use of roflumilast is available at **https://www.va.gov/formularyadvisor/**. See ADS COPD Quick Reference Guide for more detailed medication information.

Non-pharmacologic interventions

Non-pharmacologic interventions are an important part of the treatment plan for all patients with COPD.

Step 1

- Smoking Cessation
- Physical Activity
- Vaccinations
- Self-management education/written plan

Step 2

- Add pulmonary rehabilitation

Step 3

- Add end of life and palliative care support

Pulmonary rehabilitation

Pulmonary rehabilitation is an evidence-based, multidisciplinary intervention for patients with chronic respiratory disease who are symptomatic and have a reduction in daily life activities.[8,11,52,53]

Pulmonary rehabilitation

- Reduces symptoms, optimizes functional status, increases participation in care, and reduces healthcare costs
- May benefit patients with moderate to severe COPD[8]
- Should be provided at diagnosis, at discharge after hospitalization for an exacerbation, or when symptoms are progressively deteriorating.[8] Check with your local facility about the referral process for pulmonary rehabilitation.

Oxygen therapy

Using supplemental oxygen long-term (>15 hours a day) increases survival in patients with chronic respiratory failure and severe chronic resting hypoxemia.[54] Long-term oxygen does not prolong survival or time to first hospitalization or provide sustained benefit in health status, lung function, or 6-minute walk distance in patients with stable COPD and moderate resting or exercise-induced arterial desaturation.[55]

Oxygen is indicated when oxygen saturation (SaO_2) falls below 88% to keep SaO_2 > 90%[8,11]

- PaO_2 at or below 55 mmHg (7.3 kPa) or $SaO_2 \leq 88\%$, or
- PaO_2 between 56 mmHg (7.3 kPa) and 59 mmHg (8.0 kPa), or SaO_2 of > 88% and < 90%, with evidence of tissue hypoxia (hematocrit > 55%, pulmonary hypertension, or cor pulmonale).

Recheck SaO_2 60 to 90 days after starting oxygen therapy to decide if:

- Supplemental oxygen is still indicated
- Prescribed supplemental oxygen is effective

See **VHA Directive 1173.13(1) Home Oxygen Program** for additional information. **Centers for Medicare and Medicaid Services** has information on coverage for home oxygen therapy.

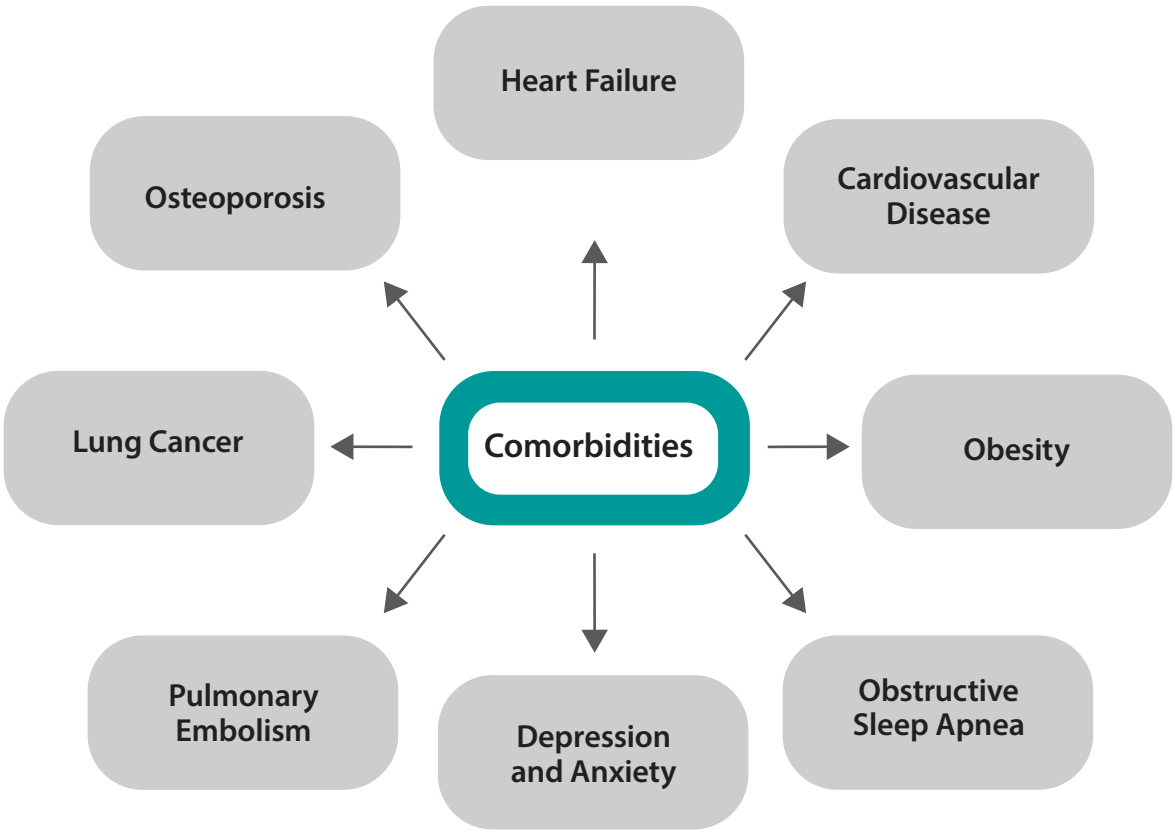
Did You Know

Participation in the VA COPD CARE team-based service led by Clinical Pharmacist Practitioners (CPP) resulted in greater access to health care, increased receipt of COPD management best practices, and readmission reduction compared to treatment as usual.[56]

Treating other comorbidities

Treating comorbidities is very important for optimal management of COPD.

Figure 12.
Conditions that are of greatest concern



Appendix A

Your name:_____

Today's date:_____

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional to measure the impact that COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing 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 gain the greatest benefit from the treatment.

For each item below, place a mark (X) in the box that best describes your current situation. Please ensure that you only select one response for each question.

Example: I am very happy | 0 | X | 2 | 3 | 4 | 5 | I am very sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) on my chest at all	0 1 2 3 4 5	My chest is 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 a flight of stairs I am not out of breath	0 1 2 3 4 5	When I walk up a hill or a flight of stairs I am completely out of breath	
I am not limited to doing any activities at home	0 1 2 3 4 5	I am completely limited to doing all activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not confident leaving my home at all because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I do not 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 | | |

A COPD assessment test was developed by an interdisciplinary group of international COPD experts with support from GSK. GSK's activities in connection with the COPD assessment test are monitored by a supervisory council that includes external, independent experts, one of which is chair of the council.

Appendix B

Table 1.
Modified medical research council breathlessness scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

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Abbreviations

COPD: chronic obstructive pulmonary disease

EOS: eosinophils

FEV_1: forced expiratory volume in one second

FVC: forced vital capacity

GOLD: Global Initiative for Chronic Obstructive Lung Disease

IC: inspiratory capacity

ICS: inhaled corticosteroid

Kg: kilograms

kPa: kilopascal; a unit of pressure

LABA: long-acting beta-2 agonist

LAMA: long-acting muscarinic antagonist

LLN: lower limit of normal

m^2: meters squared

mg: milligrams

mmHg: millimeters of mercury

nL: nanoliter

PaO_2: partial pressure of oxygen in arterial blood

PFT: pulmonary function tests

QTc: corrected QT interval; represents the duration of ventricular depolarization and repolarization

RSV: respiratory syncytial virus

SABA: short-acting beta-2 agonist

SAMA: short-acting muscarinic antagonist

SaO_2: arterial oxygen saturation

Tdap: tetanus diphtheria pertussis

µL: microliter

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