Piedmont WellStar HealthPlans, Inc.
COPD Clinical Guideline

Relevance to Population: COPD affects 12 million people in the United States, making it the 4th leading cause of mortality and the 2nd leading cause of disability. It is predicted that these statistics will increase by 30% by 2020 due to the aging population and prevalence of tobacco use (Buist 2005). Although COPD cannot be cured, use of the following evidence-based guidelines for management of COPD can control symptoms, slow disease progression, and improve quality of life.

Definition: Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with both pulmonary and extra-pulmonary effects. Its pulmonary component is characterized by chronic airflow limitation that is not fully reversible. It is usually progressive and associated with an inflammatory response of the lung to noxious particles or gases. The extra-pulmonary effects, which include weight loss, nutritional abnormalities, skeletal muscle dysfunction, and increased risk for cardiovascular disease, may contribute to the severity of COPD in individual patients.

Clinical Indicators Measured by Piedmont WellStar HealthPlans, Inc.:

1. The percentage of members 40 years of age and older with a new diagnosis or newly active chronic obstructive pulmonary disease (COPD) who received appropriate spirometry testing to confirm the diagnosis. HEDIS®
2. The percentage of COPD exacerbations for members 40 years of age and older who had an acute inpatient discharge or ED encounter during the measurement year and who were dispensed appropriate medications
    - Dispensed a systemic corticosteroid within 14 days of the event
      AND
    - Dispensed a bronchodilator within 30 days of the event. HEDIS®

Population Covered by Guideline: All adult members with stable COPD and acute exacerbations of COPD.

Goals of Therapy for COPD Management:

- Prevent disease progression - Smoking cessation has the greatest capacity to reduce the decline in lung function in COPD. (GOLD 2011)
- Improve symptoms and health status - Pharmacologic therapy can reduce symptoms and exacerbations and improve health status and exercise tolerance in COPD. (GOLD 2011)

Spirometry – KEY POINTS:

- Spirometry is required to establish a diagnosis of COPD. (GOLD 2011 & Qaseem 2011)
- COPD is diagnosed when spirometry shows airway obstruction that is not completely reversible.
- Spirometry should be performed after administration of an adequate dose of a short-acting inhaled bronchodilator in order to minimize variability of results. (GOLD 2011)
- Spirometry recommendations from the 2011 COPD Guideline of ACP, ACCP, ATS, ERS (Qaseem 2011):
    - Spirometry should only be used to screen for COPD in people with respiratory symptoms, who may benefit from inhaled pharmacotherapy.
    - Spirometry should not be used to screen for COPD in asymptomatic people; evidence does not support treatment without symptoms, even with airflow obstruction.
    - Routine periodic spirometry in COPD after initiation of therapy is not recommended, since symptomatic improvement may not correlate with spirometric responses to therapy.

- Spirometry is used to determine the severity of airflow obstruction, but other factors including symptoms, exacerbations, and comorbid conditions are used in the determination of treatment of COPD.
- Worsening spirometric stages of airflow obstruction correlate with increased risk of exacerbations, hospitalizations and death. (GOLD 2011)

Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV_1 (GOLD 2011)			
COPD Severity Category	**Degree of Airflow Limitation**	**FEV_1 (% predicted)**	**FEV_1/FVC Ratio (% predicted)**
I: Mild	Mild	$FEV_1 \geq 80\%$	$FEV_1/FVC < 70\%$
II: Moderate	Worsening	$50\% \leq FEV_1 < 80\%$	$FEV_1/FVC < 70\%$
III: Severe	Further worsening	$30\% \leq FEV_1 < 50\%$	$FEV_1/FVC < 70\%$
IV: Very Severe	Severe	$FEV_1 < 30\%$ OR $FEV_1 < 50\%$ plus chronic respiratory failure	$FEV_1/FVC < 70\%$

Smoking Cessation – KEY POINT:

- Smoking cessations is the single most effective intervention to prevent COPD and to slow its progression (GOLD 2011 and Qaseem 2011)

Pharmacological Treatment of COPD – KEY POINTS:

- Inhaled therapy is preferable to systemic therapy for COPD. (GOLD 2011)
- Roflumilast (Daliresp), a Selective Phosphodiesterase 4 Enzyme Inhibitor (PDE4), has been shown to reduce exacerbations in select patients with severe or very severe COPD with repeated exacerbation and chronic bronchitis (GOLD 2011). It is best reserved for patients who do not respond to other therapies. (The Medical Letter)
- Mucolytic therapy has overall demonstrated very small benefits in COPD and its routine use is not recommended. (GOLD 2011)
- Antibiotic therapy in COPD:
  - Prophylactic, continuous use of antibiotics is not recommended in COPD. (GOLD 2011)
    - Older studies showed no effect on COPD exacerbations.
    - A recent trial demonstrated reduced exacerbations with maintenance azithromycin, but is not recommended due to an adverse profile of side effects vs. benefits.
  - Antibiotics are indicated for the acute management of infectious exacerbations of COPD.

- **2011 ACP, ACCP, ATS, ERS Guideline Update (Qaseem 2011):**
  http://www.thoracic.org/statements/resources/respiratory-disease-adults/copd-guideline-acp-ats-ers-accp%20-abstract.pdf

Guideline Update: Recommendations for Treatment of Stable COPD				
Patient Description	**FEV_1/FVC Ratio**	**FEV_1**	**Treatment Recommendation**	**Strength of Recommendation**
Asymptomatic, with or without airflow obstruction	< 0.70 or > 0.70	> 50%	No evidence for benefit of treatment	Recommend against treatment
Stable symptomatic COPD	< 0.70	60-80%	Inhaled therapy may be used	Weak recommendation
Stable symptomatic	< 0.70	< 60%	Inhaled therapy is	Strong

COPD			recommended	recommendation
Stable symptomatic COPD	< 0.70	< 60%	Inhaled monotherapy with LABA or Anti- Cholinergic	Strong recommendation
Stable symptomatic COPD	< 0.70	< 60%	Inhaled combination therapies may be used	Weak recommendation

KEY POINTS:

- Most trials have demonstrated that long-acting inhaled monotherapy reduces COPD exacerbations, but are inconclusive regarding reduction in mortality. (Qaseem 2011)
- Monotherapy with inhaled long-acting anticholinergics, long-acting B-agonists (LABA) or inhaled corticosteroids (ICS) appears to be equally efficacious. (Qaseem 2011)
- Between inhaled anticholinergic medications, tiotropium is superior to ipratropium in COPD.
- Benefits of inhaled combination therapy compared to monotherapy have shown mixed results; it remains unclear whether combination therapy is preferred over monotherapy. (Qaseem 2011)

- **Recommendation of the 2011 GOLD COPD Guideline:**
  - GOLD recommends placing patients into 4 treatment categories (A, B, C, D) based on the following:
    - Validated patient questionnaires to assess symptoms in COPD patients, using the:
      - Modified British Medical Research Council (mMRC) Questionnaire: measures 5 levels of breathlessness and predicts future mortality risk (copd.about.com/od/copdbasics/a/MMRCdyspneascale.htm)

      OR
      - COPD Assessment Test (CAT): 8 item measure (score 0-40) of health status impairment in COPD. (www.catestonline.org)
    - Spirometric severity level (mild, moderate, severe, or very severe)
    - Assessment of exacerbation risk (based on the previous number of exacerbations per year).
  - GOLD association between Symptoms, Spirometric Classification, and Exacerbation Risk:
    - Patient Group A – Low Risk, Less Symptoms: Mild or moderate airflow obstruction and/or 0-1 exacerbations/year, and mMRC grade 0-1 or CAT score < 10.
    - Patient Group B – Low Risk, More Symptoms: Mild or moderate airflow obstruction and/or 0-1 exacerbations/year, and mMRC grade ≥ 2 or CAT score ≥ 10.
    - Patient Group C – High Risk, Less Symptoms: Severe or very severe airflow obstruction and/or ≥ 2 exacerbations/year, and mMRC grade 0-1 or CAT score < 10.
    - Patient Group D – High Risk, More Symptoms: Severe or very severe airflow obstruction and/or ≥ 2 exacerbations/year, and mMRC grade ≥ 2 or CAT score ≥ 10.

Initial Pharmacological Management of COPD* (GOLD 2011)			
Patient Group	**First Choice**	**Second Choice**	**Alternative Choice****
A	Short-acting anticholinergic prn *or* Short-acting beta$_2$-agonist prn	Long-acting anticholinergic *or* Long-acting beta$_2$-agonist *or* Short-acting beta$_2$-agonist and short-	Theophylline
B	Long-acting anticholinergic	Long-acting anticholinergic	Short-acting beta$_2$-agonist *and/or*
	or Long-acting beta$_2$-agonist	and long-acting beta$_2$-agonist	Short-acting anticholinergic Theophylline
C	Inhaled corticosteroid + long-acting beta$_2$-agonist *or* Long-acting anticholinergic	Long-acting anticholinergic and long-acting beta$_2$-agonist	Phosphodiesterase-4 inhibitor Short-acting beta$_2$-agonist *and/or* Short-acting anticholinergic
D	Inhaled corticosteroid + long-acting beta$_2$-agonist *or* Long-acting anticholinergic	Inhaled corticosteroid and long-acting anticholinergic *or* Inhaled corticosteroid + long-acting beta$_2$-agonist and long-acting anticholinergic *or* Inhaled corticosteroid + long-acting beta$_2$-agonist and phosphodiesterase-4 inhibitor *or* Long-acting anticholinergic and long- acting beta$_2$-agonist *or* Long-acting anticholinergic	Carbocysteine Short-acting beta$_2$agonist *and/or* Short-acting anticholinergic Theophylline

*Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order or preference.
**Medications in this column can be used alone or in combination with other options in the First and Second columns.

Non-Pharmacological Treatment of COPD – KEY POINTS:

- Influenza and pneumococcal immunization should be offered to every COPD patient. (GOLD 2011)
- Pulmonary Rehabilitation:
  - Should be prescribed for symptomatic patients with FEV_1 < 50% predicted (strong recommendation). (Qaseem 2011)
  - May be considered for symptomatic or exercise-limited patients with FEV_1 > 50% predicted (weak recommendation). (Qaseem 2011)
  - Benefits of pulmonary rehabilitation (level A evidence) (GOLD 2011):
    - Improves exercise capacity
    - Reduces the perceived level of breathlessness
    - Improves health-related quality of life
    - Reduces hospitalizations and the number of days in the hospital
- Long-term Oxygen Therapy:
  - Oxygen (O_2) therapy (> 15 hours/day) has been shown to increase survival in patients with hypoxemia
  - Continuous O_2 therapy should be prescribed in COPD patients with severe resting hypoxemia ($PaO_2 \leq 55$ mmHg/$SaO_2 \leq 88\%$ on room air) (strong recommendation). (Qaseem 2011)
- Lung Volume Reduction Surgery (LVRS): (GOLD 2011)
  - Patients should be referred to the LVRS coordinator (412-647-5266) for more detailed radiographic, cardiac, and exercise evaluation to determine candidacy.
  - Removing hyper-inflated parts of the lung improves respiratory muscle function, increases elastic recoil pressure of the lung, and improves expiratory flow rates.
  - LVRS is most effective among patients with severe, predominantly upper-lobe emphysema and low exercise capacity prior to treatment.
  - LVRS has been demonstrated to reduce COPD exacerbations, but has also been shown to improve survival in selected COPD patients as compared to medical therapy (54% vs. 39%).

Brief Strategy to Help Patients Willing to Quit Smoking (GOLD 2011):

- **ASK:** Systemically identify all tobacco users at every visit.
- **ADVISE:** Strongly urge all tobacco users to quit.
- **ASSESS:** Determine willingness to make a quit attempt.
- **ASSIST:** Aid the patient in quitting.
- **ARRANGE:** Schedule follow-up contact.

Pharmaceutical Interventions for Inhaled Agents and Dosing Information (GOLD 2011)			
Generic Name	**Brand Name**	**Drug Category**	**Dosing Information & Comments**
Beta2-Agonists, *Short-acting*			
Albuterol (Salbutamol)	Ventolin HFA®, Proventil HFA®, Proair HFA®	Short-acting β2 agonist	2 puffs as needed every 4-6 hours
Levalbuterol	Xopenex HFA®	Short-acting β2 agonist	2 puffs every 4-6 hours (theoretical benefits over Albuterol not demonstrated; 3rd line after Albuterol & Ipratropium in COPD)
Terbutaline	Brethine	Short-acting β2 agonist	5 mg three times a day, taken P.O.
Beta2-Agonists, *Long-acting*			
Arformoterol	Brovana®	Long-acting β2 agonist	15 mcg via a standard jet nebulizer connected to an air compressor twice a day
Salmeterol	Serevent Discus®	Long-acting β2 agonist	1 puff BID; higher and longer bronchodilation effect than other β2 agonists
Formoterol	Foradil®	Long-acting β2 agonist	1 puff BID; similar to Salmeterol, but has quicker onset of action
Indacaterol	Arcapta Neohaler	24-hour long-acting β2 agonist	75 mcg once daily, dry powder capsule for inhalation with the Neohaler
ANTICHOLINERGICS			
Ipratropium	Atrovent®	Short-acting anticholinergic	2-4 puffs QID; maintenance only, not PRN for acute symptoms
Tiotropium	Spiriva®	Long-acting anticholinergic	1 capsule inhaled daily; replaces Ipratropium

Pharmaceutical Interventions for Inhaled Agents and Dosing Information (GOLD 2011)			
Generic Name	**Brand Name**	**Drug Category**	**Dosing Information & Comments**
Aclidinium*	Tudorza™	Long-acting anticholinergic	1 inhalation twice a day
Combination short-acting beta2-agonists plus anticholinergic in one inhaler			
Albuterol + Ipratropium*	Combivent®	Short-acting β2 agonist + short-acting anticholinergic	2 puffs QID; greater bronchodilation effect than each alone, but similar effect probably achieved by doubling the dose of each drug
METHYLXANTHINES			
Aminophylline		Methylxanthines	300-600 mg every 6 to 8 hours dependent on weight and tolerability
Theophylline (SR)	Theo-Dur, Theo-24	Methylxanthines	300-600 mg once or twice daily depending on the formulation, weight, and tolerability
INHALED CORTICOSTEROID			
Beclomethasone	Qvar®	Inhaled Corticosteroid	1-8 puffs (40-320mcg) twice daily
Budenoside DPI	Pulmicort®	Inhaled Corticosteroid	1 – 8 puffs (180-1440 mcg) daily divided in 2 doses
Flunisolide*	Aerobid®	Inhaled Corticosteroid	2 – 8 puffs (500 – 2000 mcg) daily divided in 2 doses
Fluticasone 44	Flovent 44®	Inhaled Corticosteroid	2 – 6 puffs (88 – 264 mcg) daily divided in 2 doses
Fluticasone 110	Flovent 110®	Inhaled Corticosteroid	2 – 16 puffs (220 – 1760 mcg) daily divided in 2 doses
Fluticasone 220	Flovent 220®	Inhaled Corticosteroid	2– 8 puffs (440– 1760 mcg) daily divided in 2 doses
Mometasone*	Asmanex®	Inhaled Corticosteroid	1-2 puffs (220-440 mcg) once or twice daily
Ciclesonide*	Alvesco®	Inhaled Corticosteroid	1-4 puffs (80mcg-320mcg) twice daily
Fluticasone 100 + Salmeterol 50	Advair 100/50®	Combination long-acting β2 agonist + Inhaled Corticosteroid	1 puff (100 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs
Fluticasone 250 + Salmeterol 50	Advair 250/50®	Combination long-acting β2 agonist + Inhaled Corticosteroid	1 puff (250 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs
Fluticasone 500 + Salmeterol 50	Advair 500/50®	Combination long-acting β2 agonist + Inhaled Corticosteroid	1 puff (500 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs
Formoterol/ Budesonide	Symbicort®	Combination long-acting β2 agonist + Inhaled Corticosteroid	2 puffs(80-160mg/4.5mg) twice daily
System Corticosteroids			
Prednisone	Deltasone	Corticosteroid	Variable dosing, short term use if exacerbation to shorten recovery time
Methyl-prednisolone	Medrol	Corticosteroid	Variable dosing, short term use if exacerbation to shorten recovery time
Phosphodiesterase 4 Enzyme (PDE4) Inhibitor - systemic/oral therapy			

Pharmaceutical Interventions for Inhaled Agents and Dosing Information (GOLD 2011)			
Generic Name	**Brand Name**	**Drug Category**	**Dosing Information & Comments**
Roflumilast	Daliresp	PDE4 Inhibitor	500 mcg once daily, taken P.O.

*=not listed in GOLD treatment guidelines
Shaded drugs are new to this table

It is important to note, the pharmacy coverage can vary based on the members plan. Therefore it is recommended that the office confirm coverage through the pharmacy to determine covered plan benefits.

For additional information go to www.pwplans.org.

Clinical practice guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients.

Additional Resources for Piedmont Wellstar HealthPlans, Inc. Members

- ***My*Health Advice Line** is staffed by experienced Registered Nurses and is available 24/7 to provide telephone support to members. Call 855-514-3679.

- **Online** interactive preventive health programs and resources are available in partnership with WebMD by logging in at www.pwplans.org/individuals,

Scientific Evidence Sources:

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Deltasone [package insert]. New York, NY: Pfizer, Inc.; August 2006.

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Qaseem A et al. "Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease: A Clinical Practice Guideline Update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society." *Annals of Internal Medicine.* August 2, 2011; 155(3):179-191. Available at: http://www.thoracic.org/statements/resources/respiratory-disease-adults/copd-guideline-acp-ats-ers-accp%20-abstract.pdf

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Ventolin HFA [package insert]. Research Triangle Park, NC: GlaxoSmithKline; March 2010.