

# Wyoming Drug Utilization Review

## Chronic Obstructive Pulmonary Disease and Stiolto Respimat, Seebri Neohaler and Utibron Neohaler

Ashley Francis, PharmD

Chronic Obstructive Pulmonary Disease (COPD) is a chronic and severe health issue that is linked to high mortality.<sup>1</sup> Lung function and airflow are limited by inflammation, obstructive bronchiolitis, and emphysema. As structural damage occurs, the lung tissue is not able to recoil back and air becomes trapped in the lungs. Patients

are treated for exacerbations and progression of this disease. The chronic inflammation can be linked to triggers including cigarette smoke and other “noxious particles or gases”. Additional risks for COPD include genetic factors, older age, diminished lung growth or infections as a child, particle exposure, poverty, and possibly asthma.<sup>1</sup>

The 2016 COPD guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) now suggest that diagnosis of COPD will be dependent on spirometry results.<sup>1</sup> After being given a bronchodilator medication, a positive diagnosis will be based on a  $Fev_1/FVC$  ratio less than 0.70. COPD is considered when an individual has an intermittent chronic cough, progressive dyspnea, chronic sputum production, known exposure to risk factors, or a family history of COPD. Other medical conditions that would need to be ruled out include asthma, lung

cancer, tuberculosis, bronchiectasis, left heart failure, interstitial heart disease, cystic fibrosis, idiopathic cough, chronic allergic rhinitis, upper airway cough syndrome, gastroesophageal reflux, and adverse effects of medications.<sup>1</sup>

When considering treatment for COPD, it is essential that patients avoid environmental triggers that can lead to possible exacerbations of the disease.<sup>1,2</sup> It is also recommended that individuals quit smoking, which can alter disease progression.<sup>1</sup> Other treatments include pulmonary rehabilitation, and long term oxygen therapy.<sup>1,2</sup>

There are several classes of medications that are used in the treatment of COPD. Treatments are necessary to limit “symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance”.<sup>1</sup> Bronchodilator medications open the airways and are used for a short or long term effect to improve or prevent symptoms. The short acting beta agonists include albuterol, levalbuterol, fenoterol, and terbutaline. The long acting beta agonists include salmeterol, formoterol, indacaterol, olodaterol, tulobuterol, and arformoterol. Anticholinergic medications may have a more extended effect and include ipratropium bromide, oxitropium bromide, aclidinium bromide, glycopyrronium bromide, tiotropium and umeclidinium. Many combination inhalers have been created to combine anticholinergic medications with either a short or long-acting beta agonist; which may limit side effects and better improve lung function. Methylxanthines such as aminophylline and theophylline are alternative medications if the long-acting bronchodilators are not effective, but are more toxic. Inhaled corticosteroid use is controversial and is limited to patients in GOLD group C or D. The inhaled corticosteroids include fluticasone, budesonide, and beclomethasone. In comparison, the systemic corticosteroids prednisone and methylprednisolone are used for acute exacerbations. Roflumilast is a phosphodiesterase-4 inhibitor that needs to be used with a long-acting bronchodilator to prevent more severe exacerbations.<sup>1</sup>

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**Wyoming Drug Utilization Review**  
University of Wyoming  
School of Pharmacy  
Dept. 3375  
1000 E. University Ave  
Laramie, WY 82071  
307-766-6750  
[www.uwyo.edu/DUR](http://www.uwyo.edu/DUR)

Edited by  
Aimee Lewis, PharmD, MBA  
Laura Miller, MS

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## *Chronic Obstructive Pulmonary Disease and Stiolto Respimat, Seebri Neohaler and Utibron Neohaler*

Stiolto Respimat is a combination inhaler of the anticholinergic medication – tiotropium, and a long acting beta agonist – olodaterol. The long acting anticholinergic component acts on the M1 and M3 muscarinic receptors to block acetylcholine binding and cause bronchodilation.<sup>1</sup> Beta agonists stimulate the beta<sub>2</sub> adrenergic receptors and block bronchoconstriction to allow relaxation of smooth muscle in the airways.<sup>1</sup> The synergistic effect causes bronchodilation and increases airflow.<sup>3</sup> This inhaler provides a long term maintenance therapy option for patients with COPD and airflow obstruction, and is a treatment of choice for those classified as GOLD 2-4.<sup>1,3</sup> Adverse reactions can include nasopharyngitis (12%), back pain (4%), or cough (4%).<sup>4</sup> Monitoring for this medication includes watching for anticholinergic side effects like increased blood pressure, increased heart rate, central nervous stimulation, narrow angle glaucoma, and urinary retention.<sup>5</sup> The contraindication for Stiolto Respimat is hypersensitivity to any of the components.<sup>4</sup> Precautions of this medication include concerns for bronchospasm, cardiovascular changes, prostatic hyperplasia, hypokalemia, CNS impacts, hyperthyroidism, seizure disorders, and renal impairment. Medications that will interact with Stiolto Respimat and should be avoided are acclidinium, other anticholinergic agents, non-selective beta blockers, cimetropium, eluxadoline, glucagon, glycopyrrolate, Iobenguane I 123, ipratropium, levosulpiride, other long-acting beta<sub>2</sub> agonists, loxapine, oral potassium chloride, and umeclidinium.<sup>4</sup>

The Seebri Neohaler is the new formulation of glycopyrronium bromide. This long-acting anticholinergic is a reversible and competitive inhibitor of acetylcholine primarily on the M1 and M3 receptors in the bronchial smooth muscle.<sup>4</sup> Common side effects of this medication are constipation, flushing, headache, urinary retention, sinusitis, and xerostomia.<sup>6</sup> Infrequent adverse effects include abdominal pain, agitation, bronchial secretions, dysgeusia, emotional lability, flatulence, hyperglycemia, infection, insomnia, nasal congestion, nasal dryness, nausea, nystagmus, pallor, pharyngitis, pruritis, rash, restlessness, seizures, vomiting, and xerosis. Rare side effects have been noted to be atrial fibrillation, cough, or dysuria.<sup>6</sup> This inhaler is an once-daily option that provides long acting bronchodilation for maintenance of COPD.<sup>7</sup> Pulmonary function tests can be conducted to monitor this medication. Use of Seebri Neohaler is contraindicated in those with hypersensitivity to any of the ingredients including lactose.<sup>4</sup> Cautions include monitoring for signs of bronchospasm, urinary retention, glaucoma, cardiovascular

disease, renal function and drowsiness or blurred vision. Drug interactions that should be avoided are the use with acclidinium, other anticholinergic agents, cimetropium, eluxadoline, glucagon, ipratropium, levosulpiride, oral potassium chloride, or umeclidinium. Therapy modification should be considered if Seebri Neohaler is used with pramlintide or secretin.<sup>4</sup>

Utibron Neohaler is a combination of glycopyrrolate and a long-acting beta<sub>2</sub> agonist, indacaterol. As described above, glycopyrrolate is a long-acting anticholinergic that blocks the binding of acetylcholine to muscarinic receptors.<sup>4</sup> Indacaterol acts on the beta<sub>2</sub> receptors in the lung to relax bronchial smooth muscle.<sup>4</sup> Infrequent adverse effects of this inhaler have included back pain, diarrhea, gastroesophageal reflux, headache, hyperglycemia, hypertension, infection, pharyngitis, and rhinitis.<sup>6</sup> Rare side effects include atrial fibrillation, chest pain, dizziness, dyspepsia, edema, fatigue, insomnia, palpitations, pruritis, rash, and sinus tachycardia.<sup>6</sup> This particular combination appears to have a place in therapy for those with advanced COPD<sup>8</sup>, and has been more effective at improving lung function than monotherapy with either component<sup>7</sup>. Patient monitoring with this medication includes checking pulmonary function, and watching for increased use of a short acting beta<sub>2</sub> agonist inhaler.<sup>6</sup> While taking this medication patients also need to be evaluated for hypokalemia, hyperglycemia, and cardiovascular changes. This inhaler is contraindicated if patients have hypersensitivity to any of the components. Cautions include bronchospasm and CNS depression. This medication should be used cautiously in patients with cardiovascular disease, diabetes, hyperthyroidism, hypokalemia, bladder neck obstruction, seizure disorders, renal impairment, or hepatic impairment. It may be necessary to avoid the concomitant use of the following medications: acclidinium, other anticholinergic agents, non-selective beta blockers, cimetropium, eluxadoline, glucagon, ipratropium, levosulpiride, other long acting beta agonists, loxapine, oral potassium chloride, or umeclidinium. Therapy changes should be considered with the use of secretin, mifepristone, linezolid, and agents that have a high risk of prolonging QTc.<sup>6</sup>

These three new inhalers for treatment of COPD have been shown to be safe and effective maintenance medications for moderate to very severe disease. Stiolto Respimat and Utibron Neohaler are combination inhalers that have also shown better efficacy than each medication individually.

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## P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on May 10, 2017.

Highlights of this meeting include:

The new Pharmacy Benefit Management system implementation has been delayed until July 24, 2017. As a result, the new long and short-acting narcotic dose limits will be implemented on September 1, 2017.

New language will be added to the Suboxone prior authorization form regarding counseling about neonatal abstinence syndrome and use of birth control in women of child bearing age. 86% of pregnancies in women taking narcotics are unintended. Seventeen Wyoming Medicaid babies had a diagnosis of neonatal abstinence or withdrawal at birth in 2016.

The Nuedexta criteria will be updated to require a diagnosis of pseudobulbar affect with an underlying diagnosis of multiple sclerosis, amyotrophic lateral sclerosis, traumatic brain injury, stroke or dementia.

Emflaza will be limited to use in those with a diagnosis of Duchenne's Muscular Dystrophy.

Nucala and Cinqair will require a diagnosis of eosinophilic asthma as well as a trial and failure of a medium or high potency inhaled corticosteroid in combination with a long-acting beta agonist, per asthma guidelines.

The proposed prior authorization criteria will be posted for public comment at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR). Comments may be sent by email to [alewis13@uwyo.edu](mailto:alewis13@uwyo.edu) or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to July 1, 2017.

The next P&T Committee meeting will be held August 10, 2017 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

### P & T Committee Meetings

Thursday, August 10, 2017  
Thursday, November 9, 2017

P & T Committee meetings are held quarterly in Cheyenne at Laramie County Community College, 10 am - 1 pm. Visit the WY-DUR website at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR) for meeting details.

#### References:

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**Wyoming Drug Utilization Review  
University of Wyoming  
School of Pharmacy  
Dept. 3375  
1000 E. University Avenue  
Laramie, WY 82071**

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**P&T Committee Meeting Update**

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