

# Wyoming Drug Utilization Review

## Chronic Obstructive Pulmonary Disease 1: Inhaler Therapy Options

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Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the world.<sup>1</sup> This disease is characterized by persistent respiratory symptoms and airflow limitation, which is due to airway and/or alveolar abnormalities. COPD can

afflict individuals with significant, long-term exposure to noxious particles or gases, especially tobacco smoke, and pre-disposing genetic factors. It is associated with significant morbidity and mortality. There is a direct relationship between the severity of COPD and cost of care. Inadequate disease state control with maintenance therapy can lead to exacerbations and/or disease progression.<sup>1</sup>

The two main goals of therapy for the management of stable COPD are to reduce symptoms and reduce the risk of future exacerbations.<sup>1</sup> The first goal entails improvement in symptom relief, exercise tolerance, and health status.<sup>1</sup> The second goal includes: preventing disease progression; preventing and/or treating exacerbations; and reducing mortality.<sup>1</sup>

These goals are accomplished primarily with inhaler therapy.<sup>1</sup> There are many inhaler therapy options available to choose from. However, the choice of which inhaler therapy to pursue can be difficult. Many factors have to be accounted for to ensure successful inhaler use to improve patient outcomes. Incorrect selection of drug class and inhaler device can lead to poor control.<sup>2</sup>

The first factor to address is which drug class to use, which is dependent on symptom severity and frequency of exacerbations.<sup>1</sup> The following drug classes are available: beta<sub>2</sub>-agonists; antimuscarinics; and inhaled corticosteroids (ICS). There are short- and long-acting beta<sub>2</sub>-agonists and antimuscarinics that are used as monotherapies, or in combination with each other or ICS. Beta<sub>2</sub>-agonists act directly on beta<sub>2</sub>-receptors, resulting in bronchial smooth muscle (BSM) relaxation. Antimuscarinics block the action of acetylcholine at parasympathetic sites in the BSM, causing bronchodilation. ICS inhibit the following processes: cytokine production; adhesion protein activation; inflammatory cell migration and activation; and microvascular leakage. Additionally, ICS reverse beta<sub>2</sub>-receptor downregulation. ICS are always used as part of combination therapy, never as monotherapies.

As with any therapy, advantages and disadvantages of the treatment agents should be considered. When used as monotherapy, long-acting beta<sub>2</sub>-agonists (LABA) and long-acting antimuscarinics (LAMA) have shown to significantly improve lung function, dyspnea, health status and rate of exacerbations. Disadvantages of long-acting monotherapy include resting sinus tachycardia, somatic tremor and hypokalemia for beta<sub>2</sub>-agonists and xerostomia, nasopharyngitis and cough for antimuscarinics. Short-acting beta<sub>2</sub>-agonists and antimuscarinics should only

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be used in patients with occasional symptoms and limited exacerbations. Combination therapy with LAMA and LABAs are more effective than either monotherapy in terms of improved lung function, symptoms, exacerbation rate and patient-reported outcomes. These combinations have proven to be superior to LABA and inhaled corticosteroid (ICS) combinations in preventing exacerbations in those with severe COPD. Disadvantages are similar to those with monotherapy. LABA/ICS combinations are also more effective than monotherapy and are the first choice in patients with a history of asthma or findings suggesting an asthma-COPD overlap. They may also be a consideration in patients with high eosinophil counts. Disadvantages of this combination include those associated with monotherapy LABA plus increased risk of pneumonia, oral candidiasis and skin bruises from the ICS component. There may also be a potential of decreased bone density leading to fractures and poor control of diabetes with LABA/ICS combinations. Finally, triple therapy with a LAMA/LABA/ICS has shown improved efficacy in lung function, symptoms and exacerbation rates over monotherapy and the LABA/ICS combinations. Disadvantages are similar to those listed for the agents above. Therapies within their respective drug classes are generally interchangeable.<sup>1</sup>

The second factor to address is which inhaler device to use. Currently, there are no specific recommendations on which inhaler device to use in which patient type to achieve optimal outcomes.<sup>3</sup> Unlike drug classes, inhaler devices are not created equal; and therefore, may not be interchangeable.<sup>2</sup> Each device has specific characteristics to achieve optimal inhalation of the medication, including how to prepare doses and deliver the medication.<sup>2</sup> As a result, individualization must be considered in all patients.<sup>2</sup> The following contributing factors should be weighed before prescribing a specific inhaler device: inspiratory ability; inhalation coordination; age; manual strength and/or dexterity; visual acuity; cognitive ability; patient preference; and cost.<sup>4</sup> There are three types of inhalers available: metered-dose (MDI), dry powder (DPI), and soft mist (SMI).<sup>4</sup>

Patients have to be able to inhale rapidly, regardless of coordination, with DPIs.<sup>5</sup> Use of SMIs requires coordination, regardless of inhalation speed.<sup>5</sup> Review Table 1 on page 3 for information regarding the advantages and disadvantages of each inhaler type.

COPD is a complex, progressive disease state with significant morbidity and mortality. Adequate disease state control can help to prevent exacerbations and disease progression. The decision on which inhaler therapy to use should take drug class and type of inhaler into consideration. It is important to critically evaluate each individual patient and engage him/her in shared decision-making, when selecting an inhaler to prescribe to optimize outcomes.

#### References:

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2. Rogliani P, Calzetta L, Coppola A, et al. Optimizing drug delivery in COPD: the role of inhaler devices. *Respir Med.* 2017;124:6-14.
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4. Self TH, Ellingson S. New treatment option for chronic obstructive pulmonary disease: two long-acting bronchodilators in a single metered-dose inhaler. *Am J Med.* 2017;130:1251-1254.
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## P&T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on August 9, 2018. Highlights of this meeting include:

Change Healthcare has implemented a new Pharmacy Care Management program which will initially focus on hemophilia and hepatitis C compliance.

The Statewide Health Information Exchange, WYFI, is operational. Cheyenne Regional Medical Center and its Physician Group are connected currently. The plan is to connect all 27 hospitals. This system will provide real-time notifications on admissions, discharges and transfers and will allow practitioners to see everything that happens with their patients, including an updated medication list.

Opiate medications will be limited to a 7-day supply for opiate naïve patients only, defined as anyone who has not had a claim for an opiate product in the previous 45 days.

Dr. Del Real provided significant public comment regarding the buprenorphine prior authorization criteria. Additional information will be provided for further discussion at the November meeting.

Jynarque, Samsca, Crysvida, and Tavalisse will be limited to indication. Rhopressa, cyclosporine in Klarity, Osmolex

ER and isotretinoin agents will be added to the preferred drug list following cost analysis by the Department of Health.

Aimovig will require a three-month trial and failure of three generic prophylactic agents from different classes including divalproex, tricyclic antidepressants, beta blockers and topiramate. Botox is not included in required trials.

Long-acting injectable antipsychotics will be limited to 150% of labeled maximum dose immediately. Additional information will be provided regarding the appropriateness of the 150% level for oral and injectable products at the November meeting.

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 October 1, 2018.

The next P&T Committee meeting will be held November 8, 2018 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

Table 1. Advantages & Disadvantages of Different Types of Inhaler Devices

	Metered-Dose Inhalers (MDIs)	Dry Powder Inhalers (DPIs)	Soft Mist Inhalers (SMIs)
Advantages	<ul style="list-style-type: none"> <li>- Multi-dose device<sup>2,5</sup></li> <li>- Consistent dosing and rapid delivery<sup>2,5</sup></li> <li>- Not dependent on PIFR</li> <li>- Dose counter may be available<sup>2</sup></li> <li>- Spacer or holding chamber can be used in conjunction to ease coordination and improve drug delivery<sup>2,5</sup></li> <li>- Relatively cheap<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li>- Some multi-dose devices<sup>5</sup></li> <li>- Do not require hand strength and/or coordination of inhalation with activation (i.e. breath actuation)<sup>2</sup></li> <li>- Some have feedback systems for ensuring correct technique<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li>- Multi-dose device<sup>2,5</sup></li> <li>- Does not possess the level of limitations found with MDIs (i.e. coordination) and DPIs (i.e. PIFR)<sup>2</sup></li> </ul>
Disadvantages	<ul style="list-style-type: none"> <li>- Difficult to use for those with poor dexterity or weak grip strength<sup>2,5</sup></li> <li>- Greatly reduced doses with lack of proper hand-breath coordination<sup>2,5</sup></li> <li>- Less portable with spacer or holding chamber<sup>2,5</sup></li> </ul>	<ul style="list-style-type: none"> <li>- A PIFR of at least 60 L/min is required to optimize dose inhaled</li> <li>- May be inappropriate in emergency situations (e.g. exacerbations)<sup>2</sup></li> <li>- Incorrect use possible, especially in elderly patients with cognitive and psychomotor impairments<sup>2,5</sup></li> <li>- Manual dexterity required for single-dose DPIs<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li>- Hand grip strength for loading cartridge required<sup>5</sup></li> <li>- Hand-breath coordination required<sup>5</sup></li> <li>- Relatively expensive<sup>5</sup></li> </ul>

PIFR: peak inspiratory flow rate

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**P&T Committee Meeting Update**

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