

Wyoming Drug Utilization Review

Chronic Obstructive Disease 5: Exacerbations

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Chronic Obstructive Pulmonary Disease (COPD) is a respiratory illness characterized by persistent respiratory symptoms and airflow limitation. This is due to airway abnormalities caused by excessive exposure to noxious particles or gas (smoking, pollutants etc.). A COPD exacerbation is defined as an acute worsening of these pre-existing, chronic symptoms due to increased airway inflammation, mucous production, and gas trapping. The key symptom of an exacerbation is increased dyspnea, but other symptoms include increased sputum production, coughing, and wheezing (1).

Exacerbation risk is hard to determine since exacerbation rates vary greatly among patients, and many events are not reported to healthcare professionals. However, the one consistent predictor is a history of earlier treated events. This is due to each sequential exacerbation leading to increased airflow deterioration. This deterioration manifests as decreased lung function measured by forced expiratory volume (FEV₁) and forced vital capacity (FVC), putting patients at higher Global Initiative for Chronic Obstructive Lung Disease (GOLD) classes. Therefore, patients of higher GOLD classes have a higher risk for subsequent exacerbations (1). It is important then to control exacerbations, because the single best predictor of getting them is a history of prior exacerbations (2). It is also important to prevent exacerbations because events requiring hospitalization have a poor prognosis and a higher risk of death (1).

Primary prevention should be utilized in COPD patients to prevent exacerbations. There are many triggers to exacerbation that patients must be counseled on: the most common of which are respiratory viral infections. When caused by viral infections, exacerbations are often more severe, leading to more hospitalizations. The most common viral cause of COPD exacerbation is human rhinovirus, thus it is particularly important to counsel these patients on frequent handwashing and correct technique to avoid this very common trigger. It is also recommended to create a COPD exacerbation action plan. This will improve the response rate and the ability to recognize an exacerbation (1).

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Exacerbations require alternate additional therapy with the goal being to minimize the negative impact of the reaction and to prevent further exacerbations. The first step is assessing whether the exacerbation requires hospitalization. Some indications of a life-threatening exacerbation requiring hospitalization are severe sudden worsening of symptoms (especially dyspnea), respiratory failure, onset of new physical signs such as cyanosis or peripheral edema, failure to respond to treatment, presence of serious comorbidities, and/or insufficient home support. If none of these indications are present, or if they are not pronounced enough to warrant a hospital visit (non-life-threatening acute respiratory failure), then the patient can be managed in the outpatient setting with pharmacological intervention. The three most commonly used classes of medications for exacerbations are bronchodilators, glucocorticoids, and antibiotics (1).

Bronchodilators

Due to their rapid and local onset of action, short-acting beta₂ agonists (SABAs) such as albuterol and levalbuterol are recommended first-line agents. SABAs work by relaxing airway smooth muscles. These agents can also be easily self-administered through metered dose inhalers (MDIs) or nebulizers, making them ideal agents for patients experiencing an exacerbation with little or no support. There is no significant difference in FEV₁ when using an MDI vs. a nebulizer, so patients can use either one when administering these medicines. The patient should also take an inhaled short-acting muscarinic antagonist such as ipratropium first-line. Ipratropium works by antagonizing acetylcholine release and increased bronchoconstriction (3). It is important to continue long-term therapy while the patient is experiencing and immediately following an exacerbation. Long-acting muscarinic antagonists (LAMAs) including tiotropium and umeclidinium and long-acting beta₂ agonists (LABAs) including salmeterol and formoterol are integral in stabilizing a patient's COPD, and continued therapy with these can prevent further exacerbations (1).

Glucocorticoids

A steroid burst is also recommended for patients first-line (1). Prednisone 40 mg for 5 days has been shown to improve oxygenation and decrease the risk of relapse, likelihood of treatment failure, and length of hospital stay. Oral glucocorticoids have a myriad of side effects including myopathy, hyperglycemia, weight gain, and immune system suppression, so chronic use of these beyond 5 days is not recommended. If hospitalized, IV prednisolone has been shown to be just as effective. Another option is nebulized budesonide. This can be advantageous since the patient can administer this therapy themselves (1).

Antibiotics

Antibiotics are indicated when there is evidence of a bacterial infection (increased sputum purulence) and are not to be used liberally in all patients experiencing an exacerbation (4). When infected, antibiotic therapy has been shown to decrease short-term mortality, treatment failure, and sputum purulence. Detecting bacterial infections through sputum production and biomarker detection are not recommended due to cost, time to see results, and unreliability. Therefore antibiotic use should be initiated based off of clinical presentation. A patient must exhibit two of the three cardinal symptoms in order to be started on antibiotic therapy, which includes increased dyspnea, sputum volume, and sputum purulence. Empiric therapy should be initiated with either a moxifloxacin-clavulanate, a macrolide, or a tetracycline until therapy can be narrowed down from sputum cultures, if they are taken. The recommended duration of therapy is 5–7 days (4).

Oxygen

If hospitalized, the patient should be given supplemental oxygen in order to improve oxygen saturation. A target level for these patients is 88–92% (1). Oxygen should be titrated to this level, as it results in less mortality than high flow (non-titrated) oxygen due to the increased risk for respiratory acidosis (5). Blood gases should be checked frequently to avoid acidosis. Non-invasive ventilation should be utilized for improved gas exchange, and it also decreases the effort needed to breathe, the likelihood of intubation, the duration of hospital stay, and mortality (1).

Follow-up

If hospitalized, the patient should undergo a full review of all their clinical data, have their oxygen therapy need assessed, and have a management plan created for future exacerbations at discharge. There should be follow-up with these patients at 4 and 12 weeks. After 4 weeks their inhaler technique should be assessed, their oxygen need should be reassessed, and their comorbidities and capacity for physical activity should be determined and documented. After 12 weeks these elements should be reassessed. It is important the patient be informed and understand not only every aspect of their treatment regimen but also the dangers of subsequent exacerbations and how they can lead to further exacerbations and ultimately a decline in their overall health status (1). COPD exacerbations are a potentially life-threatening situation that, if managed correctly, can be treated and prevented in the future. This is based on the patient's ability to recognize an exacerbation and notify a health professional. It is also up to that health professional to properly treat that exacerbation based on the patient-specific symptoms. A combination of bronchodilators, glucocorticoids, antibiotics (if warranted) and oxygen support should be initiated in these patients in combination with their chronic medications to treat and prevent further exacerbations.

References

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P&T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on November 14, 2019.

Highlights of this meeting include:

- Based on comment from a local provider, the Sunosi criteria for patients with a diagnosis of fatigue associated with sleep apnea was updated as follows: Sunosi will be limited to indication. Patients must show compliance with their sleep apnea treatment defined as 70% or greater use of the CPAP machine for more than four hours at a time for one month prior to approval. In addition, patients must have an Apnea-Hypopnea Index (AHI) of 10 or less.
- The Immune Modulator criteria will be simplified to require a trial and failure of Humira and Enbrel for Rheumatoid Arthritis, Psoriatic Arthritis, Plaque Psoriasis, Ankylosing Spondylitis, and Juvenile Idiopathic Arthritis. Consideration will be given to prior authorization requests for any agents that have evidence of superiority to the preferred agents.
- Clopidogrel will no longer be limited to one year treatment duration.
- Dupixent will be limited to treatment of severe eosinophilic asthma.
- Showing no evidence of a difference in safety or efficacy against existing agents, Baqsimi, Gvoke, Rybelsus, Duaklir, Wakix, and Fasentra will be referred to the Department of Health for cost analysis and PDL placement.
- Nayzilam, Descovy and letrozole will be limited to indication.

The proposed prior authorization criteria and draft 2020 PDL will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to 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 January 3, 2020.

The next P&T Committee meeting will be held February 13, 2019 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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December 2019

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