Wyoming Drug Utilization Review

Monoclonal Antibodies for Asthma

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Asthma is a very common disease affecting nearly 25.1 million people in the United States (1). Of the 7.8% of the United States population that has asthma, 30% to 40% will develop chronic asthma, of which about 20% of patients go on to develop severe chronic asthma (1). The European Respiratory Society (ERS)/ American Thoracic Society (ATS) defines severe asthma as: "asthma which requires treatment with high dose inhaled corticosteroids (ICS)… plus a second controller (and/or systemic corticosteroids) to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy." (2). Patients with severe asthma experience "frequent shortness of breath, wheeze, chest tightness and cough [that] interfere with day-to-day living, sleeping, and physical activity, and patients often have frightening or unpredictable exacerbations." (3). Asthma is a heterogeneous disease and the phenotypes play an especially important role in severe asthma (4). Understanding the phenotypic heterogeneity is a key factor to providing "precision medicine" to patients with severe asthma (4). Many factors put a patient at risk for developing asthma, including familial history of asthma, cesarean section birth, formula feeding, community associated infections, lower socioeconomic status, smoking, obesity, and use of antibiotics (1). Alternatively, being the youngest sibling, natural birth, breastfeeding, higher socioeconomic status, healthy diet, low pollution rates, and exercise are all protective factors against developing asthma (1).

The monoclonal antibodies approved for asthma are mostly indicated for moderate to severe eosinophilic asthma. Eosinophilic asthma can be divided into two categories, allergic eosinophilic inflammation and non-allergic eosinophilic inflammation (1). The two groups present similarly with the presence of elevated eosinophils (specifically IgE, IL-4 and IL-5 for allergic and IL-5 and IL-33 for non-allergic), and airway smooth muscle mass, epithelial damage, and the absence of neutrophils (1). Before starting monoclonal therapy for these patients, they need to have their inflammatory phenotype for Type 2 inflammation identified (3). Type 2 inflammation is usually refractory to high dose ICS and presents with IL-4, IL-5, IL-13, Il-33, and IL-25. The presence of increased neutrophils often indicates non-Type 2 inflammation (3). Refractory Type 2 inflammation should be suspected when one of the following is met, "while the patient is taking high dose ICS or daily OCS [oral corticosteroids]: blood eosinophils >150/µl, and/ or [Fractional Exhaled Nitric Oxide] FeNO >20 ppb, and/or sputum eosinophils >2%, and/ or asthma is clinically allergen-driven." (3).

The 2022 Global Initiative for Asthma (GINA) guidelines (3) state that monoclonal antibodies should be considered only after "severe asthma" has been diagnosed. The phenotype should be assessed for Type 2 inflammation and only if Type 2 is suspected, non-biologics should be considered first, and then biologic therapy should be considered if an add-on is necessary and if this is an affordable option for the patient (3). The chart below summarizes the monoclonal antibodies available, the indication for use, and the mechanism of action (5).

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Medication	Brand Name	FDA Approved Asthma Indication	Mechanism of Action
Omalizumab	Xolair	Moderate to severe	Monoclonal antibody- inhibits IgE binding
Tezepelumab	Tezspire	Severe	Monoclonal antibody- reduces biomarkers and cytokines including blood eosinophils, IgE, FeNO, IL-5, and IL-13
Dupilumab	Dupixent	Moderate to severe eosinophilic	IL-4 receptor antagonist
Benralizumab	Fasenra	Severe eosinophilic	IL-5 receptor antagonist
Mepolizumab	Nucala	Severe eosinophilic	IL-5 antagonist
Reslizumab	Cinqair	Severe eosinophilic	IL-5 antagonist

The GINA guidelines help identify which monoclonal antibody would be best for each patient. In order to be eligible for anti-IgE therapy, the patient must have sensitization on the skin prick testing for specific IgE, a total IgE and weight within dosage range, and have had exacerbations within the last year (3). For both IL-4 and IL-5 receptor antagonists, patients must have had exacerbations in the last year and blood eosinophils >150/µl. More specifically, IL-4 antagonist should be chosen if FeNO > 25 ppb and IL-5 antagonists should be chosen if blood eosinophils >300/µl. In addition to the blood eosinophil and FeNO levels, the guideline further states that a predictor for good response for anti-IgE therapy is if the patient is experiencing allergen-driven symptoms or if the patient had childhood-onset asthma. For IL-5 receptor antagonist therapy, a patient may be a good responder if they have had more exacerbations in the last year, have adult-onset asthma or have nasal polyposis. With IL-4 receptor antagonist therapy, the patient may be a good responder if they present with higher blood eosinophils and/or FeNO. Whichever therapy is chosen, a trial of at least four months should be completed before making any changes to the therapy (3).

All of the monoclonal antibodies are subcutaneous injections, except for reslizumab, with the specific dosing listed in the chart below (3,5). These medications are contraindicated for anyone who has had a hypersensitivity reaction to any one of the specific drugs (5).

Medication	Dosing	Drug Interactions (Avoid combination)	Adverse Reactions	Monitoring
Omalizumab	≥6 years weight based dose every 2 to 4 weeks	Loxapine	Injection site reaction, anaphylaxis (0.2%), headache (3%-12%), nasopharyngitis (3%-9%)	Anaphylactic/ hypersensitivity reaction- observe for 2 hours after first 3 injections, then 30 minutes for any other injections
Tezepelumab	≥12 years 210 mg every 4 weeks	Live vaccines	Arthralgia (4%), back pain (4%), pharyngitis (4%)	FEV1, peak flow, and other pulmonary function tests, signs of injection
Dupilumab	≥12 years 200 or 300 mg every 2 weeks	Live vaccines	Injection site reactions, transient blood eosinophilia (rare cases of eosinophilic granulomatosis with polyangiitis (EGPA)), urticaria, angioedema, ocular surface disorders	Signs and symptoms of arthralgia, hypersensitivity, and ocular adverse reactions
Benralizumab	≥12 years 30 mg every 4 weeks for 3 doses, then every 8 weeks	No interactions that need to be avoided	Injection site reactions, headache (8%), pharyngitis (5%)	Pulmonary function test, signs of infection
Mepolizumab	6-11 years 40 mg every 4 weeks ≥12 years 100 mg every 4 weeks	No interactions that need to be avoided	Injection site reactions, headache (19%), oropharyngeal pain (8%)	Pulmonary function test
Reslizumab	≥18 years 3 mg/kg by IV infusion every 4 weeks	No interactions that need to be avoided	Injection site reactions, increased creatinine phosphokinase (20%)	Pulmonary function test, signs of infection, CBC with differential before initiating therapy

These monoclonal antibodies have shown to be effective in reducing the risk of exacerbations in patients with severe asthma. Agache et al. (6) reports in a systemic review, that included 19 randomized control trials from 28 publications, that all five of the approved monoclonal antibodies that were studied reduce the overall rate of exacerbations compared to the standard of care for severe eosinophilic asthma. The five medications that were evaluated were omalizumab, dupilumab, benralizumab, mepolizumab, and reslizumab. Due to differences in the baseline studies for each individual medication, direct comparisons cannot be derived from the analysis; however, results showed that each of the medications led to an approximately 50% decrease in exacerbations (6). Although there is strong evidence that supports the reduction of exacerbations with these biological medications when compared to the standard of care, "there is moderate certainty for improving asthma control, QoL [quality of life], FEV1." (6) This suggests more studies need to be performed to evaluate the efficacy, specifically regarding FEV1 function and patient's overall quality of life.

Monoclonal antibodies are reserved as one of the last-line treatments for those patients suffering from severe asthma; however, recent reviews of these medications show they are effective in reducing the number of exacerbations a patient will experience, which may lead to an overall better quality of life for the patient. Monoclonal antibodies should be considered for use for a patient that is eligible and meets the requirements.

References

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The P&T Committee met for its quarterly business meeting on May 9, 2024.

Highlights of this meeting include:

Change Healthcare has experienced a cyber threat-related outage. The pharmacy claims system was stood up on March 15, allowing pharmacies to process claims. The prior authorization system is expected to be stood up by the end of June. Six states have been affected by this outage.

Zilbrysq will require a trial and failure of one oral first-line agent for six months prior to approval for generalized myasthenia gravis.

Voydeya will be limited to indication and will require use of ravulizumab or eculizumab for the previous six months.

Wegovy will be approved for reduction of risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adult patients with established cardiovascular disease and either obesity or overweight.

Rezdiffra, Eohilia, Agamree, Duvyzat, Casgevy, and Lyfgenia were reviewed. All were limited to indication. Wainua, Vafseo, Zelsuvmi, and Winrevair were reviewed with no evidence of a significant difference in safety or efficacy versus the current products in their respective classes. All were referred to the Department of Health for cost analysis and Preferred Drug List placement.

All prior authorization criteria are open for public comment. Comments should be sent by email to alewis13@uwyo.edu by June 15, 2024.

The next P&T Committee meeting will be held August 8, 2024 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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