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## **Indiana Medicaid Therapeutics Committee** **Therapeutic Class Review Summary**

### **Therapeutic Class:**

Respiratory Immunomodulators

### **Overview:**

Asthma is a chronic respiratory condition characterized by bronchial inflammation, episodes of airflow obstruction, and airway hyperresponsiveness. Immunohistopathological features of asthma include denudation of airway epithelium, collagen deposition beneath the basement membrane, edema, mast-cell activation, and inflammatory cell infiltration of neutrophils, eosinophils, and lymphocytes. Inflammation of the airways contributes to, respiratory symptoms, airway hyperresponsiveness, and airflow limitation, ultimately leading to bronchial obstruction. Asthma severity can be diagnosed by assessing the symptoms and their severity, the patient's exercise tolerance, and the patient's medications.

Viruses, allergens, and occupational exposures can contribute to the development of asthma. Atopy, a term often used interchangeably with allergy, is a genetically determined predisposition for the development of an immunoglobulin E (IgE)-mediated response to common aeroallergens and is the most identifiable predisposing factor for the development of asthma. IgE is the antibody responsible for the immediate immune response that occurs within minutes of exposure to an antigen and for the late-phase reaction that may occur two to eight hours afterward. It is closely associated with allergic inflammatory disorders, such as allergic asthma. IgE antibodies bind to high-affinity receptors (Fc<sub>ε</sub>RI receptors) located on tissue mast cells or circulating basophils to initiate the release of histamine and other mediators responsible for allergic disease.

Pharmacologic therapy consists of both long-term control medications, used daily to achieve and maintain control of persistent asthma, and relief or rescue medications used to treat acute exacerbations. The most effective are those that attenuate the underlying inflammation characteristic of asthma. Long-term control medications include corticosteroids, mast cell stabilizers, immunomodulators, leukotriene inhibitors, long-acting beta-agonists (LABAs), and methylxanthines. Quick-relief medications include anticholinergics, short-acting beta-agonists, and systemic corticosteroids. The inhaled corticosteroids, short and long-acting beta-agonists, and leukotriene inhibitors are discussed in separate reviews. Allergen immunotherapy has been shown to suppress free IgE levels in the serum. The monoclonal antibody, Xolair<sup>®</sup> (omalizumab), binds to human IgE's high affinity Fc receptor (Fc<sub>ε</sub>RI), preventing the binding of IgE to cells associated with the allergic response (mast cells, monocytes, eosinophils, dendritic cells, epithelial cells, platelets), and preventing the release of inflammatory mediators.



According to the National Heart, Lung, and Blood Institute (NHLBI) and the National Institutes of Health (NIH), asthma severity is classified as intermittent, mild persistent, moderate persistent, and severe persistent. Guidelines developed by NHLBI and NHI recommend a stepwise approach for managing asthma to gain and maintain control, and for patients  $\geq 12$  years of age, omalizumab is recommended as adjunctive therapy for those who have sensitivity to relevant allergens, and who require step 5 or 6 care (severe persistent asthma). Omalizumab may also be considered for patients who require steps 2-4 care (mild persistent, moderate persistent) that have allergic asthma. Clinical studies have shown that suppression of free IgE levels in the serum with Xolair<sup>®</sup> use can improve quality of life (QOL) and reduce the dosage of inhaled corticosteroids. Xolair<sup>®</sup> is indicated for adults and adolescents  $\geq 12$  years of age with moderate to severe persistent asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. The most common adverse effects reported with Xolair<sup>®</sup> use are injection site reaction, viral infection, upper respiratory tract infection, and sinusitis. Clinicians who administer Xolair<sup>®</sup> should be prepared and equipped to identify and treat anaphylaxis that may occur. Due to a lack of head-to-head comparative trials, comparative efficacy data are limited.

<b>Generic Name</b>	<b>Brand Name</b>	<b>Manufacturer</b>	<b>Generic Available</b>
Omalizumab	Xolair <sup>®</sup>	Genentech	N

**Summary:**

Omalizumab is recommended by NHLBI and NIH as adjunctive therapy for those who have sensitivity to relevant allergens, and who require step 5 or 6 care (severe persistent asthma). Omalizumab may also be considered for patients who require steps 2-4 care (mild persistent, moderate persistent) that have allergic asthma. Clinical studies have shown that suppression of free IgE levels in the serum with Xolair<sup>®</sup> use can improve quality of life (QOL) and reduce the dosage of inhaled corticosteroids. Comparative efficacy data are limited due to the lack of head-to-head comparative trials; however, data suggests that omalizumab is effective in treating severe persistent asthma in patients whose symptoms are inadequately controlled with inhaled corticosteroids. The preferred drug list should be based upon FDA-approved indications, efficacy, and cost.