Xolair (omalizumab) Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
06-16-2025

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Xolair® (omalizumab) Injection for subcutaneous use	Moderate to severe persistent asthma in adults and pediatric patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance Limitations of use: • Not indicated for the relief of acute bronchospasms, or status asthmaticus • Not indicated for the emergency treatment of allergic reactions, including anaphylaxis • Not indicated for treatment of other forms of urticaria		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Asthma	Asthma is a chronic inflammatory disorder of the airways. It is characterized by a history of respiratory symptoms along with variable expiratory airflow limitation, and is typically associated with bronchial hyperresponsiveness and underlying inflammation. Symptoms are variable and recurrent and include wheezing, coughing, shortness of breath, and chest tightness. Exercise, exposure to allergens and irritants, infections, and changes in the weather can be contributing factors to the variability in symptoms and airflow limitation.(3) Guidelines recommend evaluating respiratory symptoms, medical history, physical examination, and spirometry to determine a diagnosis of asthma.(2,3) Long-term goals for asthma management are to achieve control of symptoms, maintain normal activity level, and to minimize the future risk of exacerbations, decline in lung function, and medication side effects.(3)

	Different types of asthma and levels of severity exist. Moderate asthma is asthma that requires a low- or medium-dose inhaled corticosteroid (ICS) used in combination with a long-acting beta agonist (LABA) to be well controlled. Severe asthma is asthma that remains uncontrolled despite optimized treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA or biologic therapy to prevent it from becoming uncontrolled (e.g., asthma worsens when high-dose treatment is decreased). Severe asthma needs to be distinguished from difficult-to-treat asthma that remains symptomatic due to poor adherence, poor inhaler technique, comorbidities, and/or continued exposure to environmental agents since treatment and management differs between the two.(3) The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) define uncontrolled asthma for adults and pediatric patients 6 years of age and older as a patient having at least one of the following:(17) • Frequent severe exacerbations (i.e., two or more bursts of systemic corticosteroids within the past 12 months) • Serious exacerbations (i.e., at least one hospitalization, intensive care unit stay, or mechanical ventilation in the past 12 months) • Airflow limitation (i.e., FEV1 less than 80% predicted) • Asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids (or additional biologics) The Type 2 inflammatory asthma phenotype is found in the majority of people with severe asthma. Type 2 inflammation involves a systemic allergic response and elevated levels of Type 2 inflammatory cytokines such as interleukin (IL)-4, IL-5, and IL-13. Elevated eosinophils or an increased fractional exhaled nitric oxide (FeNO) are characteristics of the eosinophilic subtype of Type 2 inflammatory asthma, while the allergic asthma subtype is additionally characterized by elevated immunoglobulin E (IgE) levels and positive skin prick testing with common environmental allergens. Type 2 inflammation typically responds well to ICS treatment and rapidly improves, however, in severe asthma Type 2 inflammation may be relatively refractory to high-dose ICS. Maintenance oral corticosteroids (OCS) may elicit a response, but the risk of serious adverse effects with daily OCS use deters their usefulness and an alternative treatment should be sought.(3) Type 2 inflammation is considered refractory if any of the following are found while the patient is taking high dose ICS or daily OCS:(3) • Blood eosinophils greater than or equal to 150 cells/microliter • FeNO greater than or equal to 20 ppb • Sputum eosinophils greater than or equal to 2% • Asthma is clinically allergen-driven The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma. The 2024 GINA guidelines recommend all patients 6 years of age and older with asthma should receive ICS-containing controller medication to reduce the risk of serious exacerbation, even in patients with infrequent symptoms. It is recommended that patients with asthma symptoms most days should be started on low dose maintenance ICS-formoterol or an alternative ICS-LABA product. Patients' response to treatment should be reviewed after 2 to 3 months. If symptoms remain uncontrolled despite good adherence and correct inhaler technique, the next step up (Step 4) involves increasing controller therapy to medium or high dose ICS-formoterol (ICS-LABA). Other controller options that may be added on to ICS treatment at Step 4 include a long-acting muscarinic antagonist (LAMA), leukotriene receptor antagonist (LTRA), or theophylline. Both LTRA and theophylline are considered less efficacious than adding on a LABA or LAMA, and also come with safety concerns. Patients with uncontrolled symptoms and/or exacerbations despite being on Step 4 treatment for 3 to 6 months should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment, phenotyping, and potential add on biologic therapy. Maintenance oral corticosteroids (OCS) should be used only as last resort because short-term and long-term systemic side-effects are common and serious.(3)

	Biologic agents should be considered as add-on therapy for patients with refractory Type 2 inflammation with exacerbations and/or poor symptom control despite taking at least high dose ICS-LABA, and who have allergic or eosinophilic biomarkers or need maintenance OCS, and only after treatment has been optimized.(3) Tezepelumab is considered a broad-acting biologic and may be considered in patients without a Type 2 inflammatory phenotype due to it binding to circulating thymic stromal lymphopoietin (TSLP), which is upstream on the inflammatory cascade.(3,12) Based on efficacy results from clinical trials, the indication of use for tezepelumab is not restricted to a biomarker-defined phenotype.(12) 2024 GINA guidelines recommend the use of biologics based on the following patient eligibility factors:(3)
	
	• Anti-IgE (omalizumab) for moderate to severe allergic asthma
	  ○ Sensitization to inhaled allergen(s) on skin prick testing for specific IgE
	  ○ Total serum IgE and body weight within dosing range
	  ○ Exacerbations within the last year
	• Anti-IL5 (mepolizumab, reslizumab) /Anti-IL5Ra (benralizumab) for severe eosinophilic asthma
	  ○ Blood eosinophils greater than or equal to 150 cells/microliter or greater than or equal to 300 cells/microliter
	  ○ Severe exacerbations within the last year
	• Anti-IL4Ra (dupilumab) for severe eosinophilic/Type 2 asthma or patients requiring maintenance OCS
	  ○ Blood eosinophil greater than or equal to 150 cells/microliter but less than or equal to 1500 cells/microliter, or FeNO greater than or equal to 25 ppb, or taking maintenance OCS
	  ○ Severe exacerbations within the last year
	• Anti-TSLP (tezepelumab) for severe asthma
	  ○ Severe exacerbations within the last year
	
	Patient response to biologic therapy should be evaluated 4 months after initiating therapy, and the patient should be re-evaluated every 3 to 6 months. If response is unclear after 4 months, the trial should be extended to 6-12 months.(3)
	
	2024 GINA guidelines recommend the following step-down therapy process in patients responding well to targeted biologic therapy:(3)
	
	• Re-evaluate the need for each asthma medication every 3 to 6 months, but inhaled therapy (e.g., ICS-containing therapy) should not be completely stopped
	• The order of reduction of treatments should be based on observed benefit, potential side-effects, cost, and patient preference. However, minimizing the use of OCS is a very high priority.
	• First, consider decreasing/stopping OCS due to their significant adverse effects. Then consider stopping other add-on asthma medications.
	• Then, if asthma is well controlled for 3-6 months, consider reducing maintenance ICS dose, but do not stop maintenance ICS-containing therapy (e.g., ICS-LABA)
	• Re-evaluate the need for ongoing biologic therapy, but a trial of withdrawal of the biologic should not be considered until after at least 12 months of treatment and only if asthma remains well controlled on medium-dose ICS-containing therapy
	  ○ For allergic asthma, also confirm there is no further exposure to an allergic trigger

Chronic Spontaneous Urticaria (CSU)	Chronic spontaneous urticaria (CSU) can be a debilitating condition that can significantly affect a patient's quality of life. Routine diagnostic work-up for CSU is limited to blood tests for complete blood count and inflammatory markers, such as C-reactive protein and/or erythrocyte sedimentation rate, mostly to rule out other potential diseases. Skin prick testing, typically used to identify specific allergens, is not

	useful for CSU as the condition is rarely caused by type 1 allergy. CSU is also referred to as chronic urticaria (CU) or chronic idiopathic urticaria (CIU).(13) Urticaria is characterized by the development of wheals (hives), angioedema, or both. Chronic urticaria is defined by the presence of urticaria that has been continuously or intermittently present for more than 6 weeks.(5,6) Treatment goals for CIU involves symptom control and improvement in quality of life that is acceptable to the patient.(6) The 2021 EAACI/GA LEN/EDF/WAO guidelines, endorsed by the American Academy of Allergy, Asthma, and Immunology, American Academy of Dermatology, American College of Asthma, and Allergy, and Immunology, recommend the following for the treatment of CIU:(6) • Recommend discontinuing medications suspected to worsen CIU (e.g., NSAIDs) • First line treatment: second-generation H-1 antihistamine (cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) dosed daily • Second-line treatment: Increase the dose up to 4 times the FDA max if inadequate control after 2-4 weeks of therapy at the FDA max • Third-line treatment: addition of omalizumab First-line treatment with second generation H-1 antihistamines is consistent in other guidelines but recommend omalizumab as second-line treatment and ciclosporin (off-label use) as third-line treatment.(13)

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)	Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory condition affecting the paranasal sinuses.(9) The exact cause of CRSwNP is unknown, but biopsies of nasal polyps have shown elevated levels of eosinophils. Sinus computed tomography (CT) and/or nasal endoscopy are needed to determine the presence of sinonasal inflammation and nasal polyps.(8)
	
	The International Consensus Statement on Allergy and Rhinology: Rhinosinusitis (ICAR-RS) indicates that the diagnostic criteria for CRSwNP consist of ALL the following:(11)
	
	• Symptoms greater than or equal to 12 weeks
	• Two of the following symptoms:
	  ○ Nasal discharge (rhinorrhea or post-nasal drainage)
	  ○ Nasal obstruction or congestion
	  ○ Hyposmia (loss or decreased sense of smell)
	  ○ Facial pressure or pain
	• One or more of the following findings:
	  ○ Evidence of inflammation on nasal endoscopy or computed tomography
	  ○ Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
	• Presence of nasal polyps
	
	Topical saline irrigation and intranasal corticosteroids (INCS) are recommended in the guidelines as initial treatment for CRSwNP.(7,9,11) Nasal saline irrigation used as adjunct treatment with other therapies improves symptoms and quality of life (QoL) outcomes and is considered an important aspect of management of CRSwNP. Saline irrigation can improve nasal mucosa function through the mechanical clearance of thick mucus and inflammatory mediators, including eosinophilic mucin.(7,11)
	
	INCS can have a positive impact on the disease and improve symptoms, reduce nasal polyp size, and improve sense of smell.(7,11) The ICAR-RS strongly recommends INCS before or after sinus surgery.(11) INCS are well tolerated and long term treatment is effective and safe. Many different INCS have been used in the treatment of CRSwNP, including triamcinolone, mometasone, fluticasone, and budesonide, but no

	differences were shown to recommend a specific formulation.(7) For patients using INCS for at least 4 weeks and who continue to have high disease burden, biologics may be considered and preferred over other medical treatment choices.(9) Oral systemic corticosteroids (OCS), used as a short course, can result in a significant reduction in symptoms and nasal polyps for up to three months after the start of treatment. Up to 2 courses per year, taken in addition to INCS, can be useful for patients with partially or uncontrolled disease.(7) The ICAR-RS strongly recommends the use of OCS in the short term management of CRSwNP, but does not recommend longer term use due to the increased risk of adverse effects.(11) Endoscopic sinus surgery (ESS) is aimed at improving symptoms and creating better conditions for local treatment. Sinus surgery should be considered when disease is refractory and remains symptomatic despite trial of primary medical therapy (e.g., nasal sinus irrigation, INCS, oral corticosteroids). Based on current evidence, delaying surgical intervention can be detrimental to symptom improvement and outcomes.(7,11) After surgery, patients need to continue other treatments due to the chronic nature of the disease and nasal polyps potentially reoccurring despite surgery.(7,8) INCS can help to prevent nasal polyp recurrence.(7,11) Biologics can be considered in patients where their disease remains uncontrolled despite appropriate medical treatment and sinus surgery.(9,10) Biologics vary in their magnitude of benefits and harms and certainty of evidence across outcomes. Dupilumab and omalizumab are the most beneficial for most patient important outcomes when comparing with other biologics, followed by mepolizumab.(9)
IgE-Mediated Food Allergy	Food allergies have been increasing in prevalence in the past few decades affecting about 3-10% of children and up to 10% of adults. Food allergies can be classified based on the underlying mechanism as follows: IgE-mediated (type I hypersensitivity), non-IgE mediated (type III or type IV hypersensitivity), or mixed IgE and non-IgE mediated (combination of IgE and cellular mechanisms). The European Academy of Allergy and Clinical Immunology (EAACI) defines IgE-mediated food allergy as both of the following:(14) • Typical symptoms that usually develop within 2 hours of exposure to the allergen and are reproducible upon re-exposure • Evidence of IgE sensitization and/or effector cell response to the allergen Symptoms of IgE-mediated food allergy can be cutaneous, gastrointestinal, ocular, respiratory, cardiovascular, and/or neurological related. Signs and symptoms may clinically manifest in an isolated or concomitant manner, with the same timing or differing. Reactions can range from being mild and localized to being systemic and fatal, including anaphylaxis.(15) Diagnosing IgE-mediated food allergy typically involves a detailed allergy-focused clinical history as a first step. In patients with a history of suspected IgE-mediated food allergy, the EAACI strongly recommends IgE sensitizations tests, such as a skin prick test (SPT) and/or a serum specific IgE test, as first line to support the diagnosis. If the results are contradictory or equivocal with the clinical history, additional tests may need to be performed, including an oral food challenge (OFC). The EAACI strongly recommends a supervised OFC as the reference diagnostic procedure to confirm or exclude food allergy in patients with an unclear diagnosis despite IgE sensitization tests.(14) Due to patient and physician fears of severe reactions and logistic considerations, OFC should be reserved for cases that cannot be clarified with IgE sensitization tests.(14,15) Strict avoidance of trigger foods and training in the use of rescue medication for allergic reactions have been the main approach to manage food allergies. Strict avoidance of trigger foods can lead to reduced diet diversity, social restrictions impacting quality of life, potential risk of nutritional deficiencies, and anxiety over the possible accidental random exposure of the trigger food.(15) The Global Allergy and Asthma Excellence Network (GA2LEN) 2022 food allergy guidelines suggest that

	people with a documented food allergy avoid the offending food unless their individual circumstances and risks allow for some consumption, as advised by their healthcare professional.(16) When severe reactions occur, prompt administration of epinephrine should be used, which is the drug of choice for anaphylaxis. Allergen immunotherapy is an option for some food allergies as a disease-modifying therapy. Allergen immunotherapy uses sequential doses of increased amounts of the allergen in an attempt to desensitize the patient to the allergen.(15) The GA2LEN guidelines show that allergen immunotherapy can be a treatment option for some specific food allergies (i.e., peanut, hen's egg, cow's milk) for select children with substantial risk of severe reactions and/or substantially impaired quality of life. However, no recommendation was made for using allergen immunotherapy in adults, even though it may be useful for select adults if potential benefits outweigh the risks.(16)
Efficacy	**Asthma(1,4)** The safety and efficacy of Xolair in adult and adolescent patients 12 years of age and older were evaluated in three randomized, double-blind, placebo-controlled, multicenter trials. In all three trials, an exacerbation was defined as a worsening of asthma that required treatment with systemic corticosteroids or a doubling of the baseline inhaled corticosteroid dose. In two of these trials, patients had a forced expiratory volume in 1 second (FEV1) between 40 and 80% predicted. All patients had a FEV1 improvement of at least 12% following beta-2-agonist administration. All patients were required to have a baseline IgE between 30 and 700 IU/mL and a body weight not more than 150 kg. Dosing information includes weights of at least 30 kg. In both of these trials, the number of exacerbations per patient was reduced in patients treated with Xolair compared with placebo. In the third trial, there was no restriction on screening FEV1. The number of exacerbations in patients treated with Xolair was similar to that in the placebo-treated patients. The absence of an observed treatment effect may be related to differences in the patient population compared with the other two trials. In all three trials, a reduction of asthma exacerbations was not observed in the Xolair treated patients who had an FEV1 greater than 80% at the time of randomization. Reductions in exacerbations were not seen in patients who required oral steroids as maintenance therapy. The safety and efficacy of Xolair in pediatric patients 6 to less than 12 years of age with moderate to severe asthma is based on one randomized, double-blind, placebo controlled, multicenter trial and an additional supportive study. The primary efficacy variable was the rate of asthma exacerbations during the 24-week, fixed steroid treatment phase. An asthma exacerbation was defined as a worsening of asthma symptoms as judged clinically by the investigator, requiring doubling of the baseline inhaled corticosteroid dose for at least 3 days and/or treatment with rescue systemic (oral or IV) corticosteroids for at least 3 days. At 24 weeks, the Xolair group had a statistically significantly lower rate of asthma exacerbations (0.45 vs 0.64) with an estimated rate ratio of 0.69 (95% CI). Dosing for pediatric patients between the ages of 6 to less than 12 years is based on weight and IgE level with dosing available for weights less than or equal to 150 kg and IgE levels between 30 and 1300 IU/mL. **Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)(1)** The safety and efficacy of Xolair was evaluated in two randomized, multicenter, double-blind, placebo-controlled clinical trials that enrolled patients with CRSwNP with inadequate response to nasal corticosteroids. The co-primary endpoints in both trials were nasal polyp score (NPS) and average daily nasal congestion score (NCS) at Week 24. In both trials, patients who received Xolair had statistically significant greater improvement from baseline at Week 24 in NPS and weekly average NCS than patients who received placebo. **Chronic Spontaneous Urticaria (CSU)(1)** The safety and efficacy of Xolair for the treatment of CSU, previously referred to as chronic idiopathic urticaria (CIU) was assessed in two placebo-controlled, multiple-dose clinical trials of 24 and 12 weeks duration. Disease severity was measured by a

	weekly urticaria activity score (UAS7), which is a composite of the weekly itch severity score and the weekly hive count score. All patients were required to have a UAS7 of greater than or equal to 16 and a weekly itch severity score greater than or equal to 8 for the 7 days prior to randomization, despite having used an H1 antihistamine for at least 2 weeks. In both trials, patients who received Xolair 150 mg and 300 mg had greater decreases from baseline in weekly itch severity score and weekly hive count scores than placebo at week 12. **IgE-Mediated Food Allergy(1)** The safety and efficacy of Xolair was evaluated in a multi-center, randomized, double-blind, placebo-controlled Food Allergy (FA) trial (NCT03881696) in adult and pediatric patients 1 year of age to less than 56 years who were allergic to peanut and at least two other foods, including milk, egg, wheat, cashew, hazelnut, or walnut (i.e., studied foods). The FA trial enrolled patients who experienced dose-limiting symptoms (e.g., moderate to severe skin, respiratory, or gastrointestinal symptoms) to a single dose of less than or equal to 100 mg of peanut protein and less than or equal to 300 mg protein for each of the other two foods during the screening double-blind placebo-controlled food challenge (DBPCFC). Patients with a history of severe anaphylaxis (defined as neurological compromise or requiring intubation) were excluded from the study. Patients were randomized 2:1 to receive a subcutaneous dosage of Xolair (based on serum IgE level measured before the start of treatment and body weight) or placebo every 2 to 4 weeks for 16 to 20 weeks. After 16 to 20 weeks of treatment, each patient completed a DBPCFC consisting of placebo and each of their 3 studied foods. Efficacy of Xolair was based on 165 pediatric patients who were included in the efficacy analyses. The efficacy of Xolair in adults is supported by the adequate and well-controlled trial of Xolair in pediatric patients, disease similarity in pediatric and adult patients, and pharmacokinetic (PK) similarity. The primary efficacy endpoint was the percentage of patients who were able to consume a single dose of greater than or equal to 600 mg of peanut protein without dose-limiting symptoms (e.g., moderate to severe skin, respiratory, or gastrointestinal symptoms) during DBPCFC. Xolair treatment led to a statistically higher response rate (68%) than placebo (5%). The secondary efficacy endpoints were the percentage of patients who were able to consume a single dose of greater than or equal to 10000 mg of cashew, milk, or egg protein without dose-limiting symptoms during DBPCFC. The study met secondary endpoints and demonstrated that Xolair treatment led to statistically higher response rates than placebo for all three foods.
Safety	Omalizumab has a boxed warning due to risk of anaphylaxis. Because of the risk of anaphylaxis, therapy should be initiated in a healthcare setting and the patient closely observed for an appropriate period of time after administration. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur. Discontinue omalizumab in patients who experience severe hypersensitivity reaction. Selection of patients for self-administration should be based on criteria to mitigate risk from anaphylaxis. Patient-specific factors including the following criteria should be considered:(1) • Patient should have no prior history of anaphylaxis, including to omalizumab, or other agents such as foods, drugs, biologics, etc. ○ *For IgE-Mediated Food Allergy*: Patient should have no prior history of anaphylaxis to omalizumab or other agents (except foods), such as drugs, biologics, etc. • Patient should receive at least 3 doses of omalizumab under the guidance of a healthcare provider with no hypersensitivity reactions • Patient or caregiver is able to recognize symptoms of anaphylaxis • Patient or caregiver is able to treat anaphylaxis appropriately

	• Patient or caregiver is able to perform subcutaneous injections with omalizumab prefilled syringe or autoinjector with proper technique according to the prescribed dosing regimen and Instructions for Use Omalizumab is contraindicated in patients with severe hypersensitivity reaction to omalizumab or any ingredient of the omalizumab product.(1)

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POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J2357	Xolair	omalizumab for inj ; omalizumab subcutaneous soln auto-injector ; omalizumab subcutaneous soln prefilled syringe	150 MG ; 150 MG/ML ; 300 MG/2ML ; 75 MG/0.5ML	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Xolair	omalizumab for inj ; omalizumab subcutaneous soln auto-injector ; omalizumab subcutaneous soln prefilled syringe	150 MG ; 150 MG/ML ; 300 MG/2ML ; 75 MG/0.5ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All Target Agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. BOTH of the following: 1. ONE of the following: A. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following: 1. ONE of the following: A. The patient is 6 to less than 12 years of age AND BOTH of the following: 1. The patient's pretreatment IgE level is 30 IU/mL to 1300 IU/mL **AND** 2. The patient's weight is 20 kg to 150 kg **OR** B. The patient is 12 years of age or over AND BOTH of the following: 1. The patient's pretreatment IgE level is 30 IU/mL to 700 IU/mL **AND** 2. The patient's weight is 30 kg to 150 kg **AND** 2. Allergic asthma has been confirmed by a positive skin test or in vitro reactivity test to a perennial aeroallergen **AND** 3. The patient has a history of uncontrolled asthma while on asthma control therapy as demonstrated by ONE of the following:

Module	Clinical Criteria for Approval
	A. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months **OR** B. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months **OR** C. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered **OR** D. The patient has baseline (prior to therapy with the requested agent) Forced Expiratory Volume (FEV1) that is less than 80% of predicted **OR** B. The patient has a diagnosis of chronic spontaneous urticaria (CSU) (otherwise known as chronic idiopathic urticaria [CIU]) AND ALL of the following: 1. The patient has had over 6 weeks of hives and itching **AND** 2. If the patient is currently treated with medications known to cause or worsen urticaria, then ONE of the following: A. The prescriber has reduced the dose or discontinued any medications known to cause or worsen urticaria (e.g., NSAIDs) **OR** B. There is support that a reduced dose or discontinuation of any medication(s) known to cause or worsen urticaria is NOT appropriate **AND** 3. ONE of the following: A. The patient has tried and had an inadequate response to the FDA labeled maximum dose of a second-generation H-1 antihistamine (e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) after at least a 2-week duration of therapy AND ONE of the following: 1. The patient has tried and had an inadequate response to a dose titrated up to 4 times the FDA labeled maximum dose of a second-generation H-1 antihistamine **OR** 2. There is support that the patient cannot be treated with a dose titrated up to 4 times the FDA labeled maximum dose of a second-generation H-1 antihistamine **OR** B. The patient has an intolerance or hypersensitivity to therapy with a second-generation H-1 antihistamine **OR** C. The patient has an FDA labeled contraindication to ALL second-generation H-1 antihistamines **OR** C. The patient has a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP) AND ALL of the following: 1. BOTH of the following: A. The patient's pretreatment IgE level is 30 IU/mL to 1500 IU/mL **AND** B. The patient's weight is 30 kg to 150 kg **AND** 2. The patient has at least TWO of the following symptoms consistent with chronic rhinosinusitis (CRS): A. Nasal discharge (rhinorrhea or post-nasal drainage) B. Nasal obstruction or congestion C. Loss or decreased sense of smell (hyposmia) D. Facial pressure or pain **AND**

Module	Clinical Criteria for Approval
	3. The patient has had symptoms consistent with chronic rhinosinusitis (CRS) for at least 12 consecutive weeks **AND** 4. The patient's diagnosis was confirmed by ONE of the following: A. Anterior rhinoscopy or endoscopy **OR** B. Computed tomography (CT) of the sinuses **AND** 5. ONE of the following: A. The patient has tried and had an inadequate response to ONE intranasal corticosteroid therapy (e.g., fluticasone nasal spray, mometasone nasal spray, Sinuva) after at least a 4-week duration of therapy **OR** B. The patient has an intolerance or hypersensitivity to ONE intranasal corticosteroid therapy (e.g., fluticasone nasal spray, mometasone nasal spray, Sinuva) **OR** C. The patient has an FDA labeled contraindication to ALL intranasal corticosteroids **OR** D. The patient has a diagnosis of IgE-mediated food allergy AND ALL of the following: 1. BOTH of the following: A. The patient's pretreatment IgE level is 30 IU/mL to 1850 IU/mL **AND** B. The patient's weight is 10 kg to 150 kg **AND** 2. The patient has a confirmed IgE-mediated food allergy confirmed by an allergy diagnostic test (e.g., skin prick test, serum specific IgE test, oral food challenge) **AND** 3. The requested agent will NOT be used for the emergency treatment of allergic reactions, including anaphylaxis **OR** E. The patient has another FDA labeled indication for the requested agent **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **OR** C. The patient has another indication that is supported in compendia for the requested agent **AND** 2. If the patient has a diagnosis of moderate to severe persistent asthma, then ALL of the following: A. ONE of the following: 1. The patient is NOT currently treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months AND has been adherent for 90 days within the past 120 days **OR** 2. The patient is currently treated with the requested agent AND ONE of the following: A. The patient is currently treated with an inhaled corticosteroid for at least 3 months that is adequately dosed to control symptoms AND has been adherent for 90 days within the past 120 days **OR** B. The patient is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months AND has been adherent for 90 days within the past 120 days **OR** 3. The patient has an intolerance or hypersensitivity to therapy with an inhaled corticosteroid **OR** 4. The patient has an FDA labeled contraindication to ALL inhaled corticosteroids **AND** B. ONE of the following: 1. The patient is currently treated for at least 3 months AND has been adherent for 90 days within the past 120 days with ONE of the following:

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	A. A long-acting beta-2 agonist (LABA) **OR** B. A long-acting muscarinic antagonist (LAMA) **OR** C. A Leukotriene receptor antagonist (LTRA) **OR** D. Theophylline **OR** 2. The patient has an intolerance or hypersensitivity to therapy with a long-acting beta-2 agonist (LABA), a long-acting muscarinic antagonist (LAMA), a leukotriene receptor antagonist (LTRA), or theophylline **OR** 3. The patient has an FDA labeled contraindication to ALL long-acting beta-2 agonists (LABA) AND long-acting muscarinic antagonists (LAMA) **AND** C. The patient will continue asthma control therapy (e.g., ICS, ICS/LABA, LTRA, LAMA, theophylline) in combination with the requested agent **AND** D. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 375 mg every 2 weeks **AND** 3. If the patient has a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP), then ALL of the following: A. The patient is currently treated with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone nasal spray, mometasone nasal spray, Sinuva]) **AND** B. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone nasal spray, mometasone nasal spray, Sinuva]) in combination with the requested agent **AND** C. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **AND** 4. If the patient has a diagnosis of chronic spontaneous urticaria (CSU) (otherwise known as chronic idiopathic urticaria [CIU]), the requested dose is within FDA labeled dosing AND does NOT exceed 300 mg every 4 weeks **AND** 5. If the patient has a diagnosis of IgE-mediated food allergy, then ALL of the following: A. The patient will avoid known food allergens while treated with the requested agent **AND** B. The patient has epinephrine on hand for emergency treatment **AND** C. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **AND** 6. If the patient has another FDA labeled indication for the requested agent, the requested quantity (dose) is within FDA labeled dosing for the requested indication **AND** 7. If the patient has another indication that is supported in compendia for the requested agent, the requested quantity (dose) is supported in compendia for the requested indication **AND** 8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 9. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 10. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Module	Clinical Criteria for Approval
	Length of Approval: 6 months for moderate to severe persistent asthma, chronic spontaneous urticaria (CSU), IgE-mediated food allergy, and chronic rhinosinusitis with nasal polyps (CRSwNP); 12 months for all other indications **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. ONE of the following: A. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following: 1. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. Increase in percent predicted Forced Expiratory Volume (FEV1) **OR** B. Decrease in the dose of inhaled corticosteroid required to control the patient's asthma **OR** C. Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma **OR** D. Decrease in the number of hospitalizations, need for mechanical ventilation, or visits to the emergency room or urgent care due to exacerbations of asthma **AND** 2. The patient is currently treated within the past 90 days and is compliant with asthma control therapy (e.g., inhaled corticosteroids [ICS], ICS/long-acting beta-2 agonist [ICS/LABA], leukotriene receptor antagonist [LTRA], long-acting muscarinic antagonist [LAMA], theophylline) **AND** 3. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 375 mg every 2 weeks **OR** B. The patient has a diagnosis of chronic spontaneous urticaria (CSU) (otherwise known as chronic idiopathic urticaria [CIU]) AND BOTH of the following: 1. The patient has had clinical benefit with the requested agent **AND** 2. The requested dose is within FDA labeled dosing for the requested indication AND does NOT exceed 300 mg every 4 weeks **OR** C. The patient has a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP) AND ALL of the following: 1. The patient has had clinical benefit with the requested agent **AND** 2. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids [e.g., fluticasone nasal spray, mometasone nasal spray, Sinuva]) in combination with the requested agent **AND** 3. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **OR** D. The patient has a diagnosis of IgE-mediated food allergy AND ALL of the following: 1. The patient will avoid known food allergens while treated with the requested agent **AND** 2. The patient has epinephrine on hand for emergency treatment **AND** 3. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **OR** E. The patient has a diagnosis other than moderate to severe persistent asthma, CSU/CIU, CRSwNP, or IgE-mediated food allergy AND BOTH of the following:

Module	Clinical Criteria for Approval
	1. The patient has had clinical benefit with the requested agent **AND** 2. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 12 months

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Avtozma (tocilizumab-anoh) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab) Cyltezo (adalimumab-adbm) Dupixent (dupilumab) Ebglyss (lebrikizumab-lbkz) Enbrel (etanercept) Entyvio (vedolizumab) Fasenra (benralizumab) Hadlima (adalimumab-bwwd) Hulio (adalimumab-fkjp) Humira (adalimumab) Hyrimoz (adalimumab-adaz) Idacio (adalimumab-aacf) Ilaris (canakinumab) Ilumya (tildrakizumab-asmn) Imuldosa (ustekinumab-srlf) Inflectra (infliximab-dyyb) Infliximab Kevzara (sarilumab) Kineret (anakinra)

Contraindicated as Concomitant Therapy
Leqselvi (deuruxolitinib)
Litfulo (ritlecitinib)
Nemluvio (nemolizumab-ilto)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omlyclo (omalizumab-igec)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Otulfi (ustekinumab-aauz)
Pyzchiva (ustekinumab-ttwe)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Saphnelo (anifrolumab-fnia)
Selarsdi (ustekinumab-aekn)
Siliq (brodalumab)
Simlandi (adalimumab-ryvk)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Spevigo (spesolimab-sbzo) subcutaneous injection
Stelara (ustekinumab)
Steqeyma (ustekinumab-stba)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tofidence (tocilizumab-bavi)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tyenne (tocilizumab-aazg)
Tysabri (natalizumab)
Ustekinumab
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yesintek (ustekinumab-kfce)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)