Medical Benefit Drug Policy

Xolair (omalizumab) for injection, for subcutaneous use

Policy Number: MC/PC 052
Effective Date: June 1, 2025

Instructions for Use

Table of Contents **Page**

Related Policies

- N/A

Coverage Rationale

This policy is applicable to Xolair (omalizumab) for injection, for subcutaneous use only.

Allergic Asthma

For initial coverage of Xolair (omalizumab) injection for allergic asthma the following will be required:

- Diagnosis of moderate to severe persistent allergic asthma **and**
- Positive skin test or in vitro reactivity to a perennial aeroallergen **and**
- One of the following:
  - All of the following:
    - Patient is 6 years of age or older but less than 12 years of age **and**
    - Pre-treatment serum immunoglobulin (Ig)E level between 30 to 1300 IU/mL **and**
    - Patient is currently being treated with one of the following unless there is a contraindication or intolerance to these medications:
      - Both of the following:
        - Medium-dose inhaled corticosteroid (e.g., greater than 100 – 200 mcg fluticasone propionate equivalent/day)
        - Additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) **or**
      - One medium dosed combination ICS/LABA product (e.g., Advair Diskus [fluticasone propionate 100mcg/ salmeterol 50mcg], Symbicort [budesonide 80mcg/ formoterol 4.5mcg] Breo Ellipta [fluticasone furoate 50 mcg/ vilanterol 25 mcg]) **or**
  - All of the following:
    - Patient is 12 years of age or older **and**
    - Pre-treatment serum immunoglobulin (Ig)E level between 30 to 700 IU/mL **and**

- Patient is currently being treated with one of the follo n or intolerance to these medications:
    - Both of the following:
        - High-dose inhaled corticosteroid (ICS) (e.g., greater than 500 mcg fluticasone propionate equivalent/day)
        - Additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) **or**
    - One maximally-dosed combination ICS/LABA product (e.g., Advair [fluticasone propionate 500mcg/ salmeterol 50mcg], Symbicort [budesonide 160mcg/ formoterol 4.5mcg], Breo Ellipta [fluticasone 200mcg/ vilanterol 25mcg]) **and**
- Prescribed by or in consultation with one of the following:
    - Pulmonologist
    - Allergist/Immunologist

For reauthorization coverage of Xolair (omalizumab) injection for allergic asthma, the following will be required:

- Patient demonstrates positive clinical response to therapy (e.g., reduction in exacerbations, improvement in forced expiratory volume in 1 second [FEV1], decreased use of rescue medications) **and**
- Patient continues to be treated with an inhaled corticosteroid (ICS) (e.g., fluticasone, budesonide) with or without additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) unless there is a contraindication or intolerance to these medications **and**
- Prescribed by or in consultation with one of the following:
    - Pulmonologist
    - Allergist/immunologist

Chronic Spontaneous Urticaria (CSU)

For initial coverage of Xolair (omalizumab) injection for chronic spontaneous urticaria (CSU), the following will be required:

- Diagnosis of chronic spontaneous urticaria **and**
- Patient is 12 years of age or older **and**
- Persistent symptoms (itching and hives) for at least 4 consecutive weeks despite titrating to an optimal dose with a second generation H1 antihistamine (e.g., cetirizine, fexofenadine), unless there is a contraindication or intolerance to H1 antihistamines **and**
- Used concurrently with an H1 antihistamine, unless there is a contraindication or intolerance to H1 antihistamines **and**
- Patient has tried and had an inadequate response or intolerance to at least TWO of the following additional therapies:
    - Doxepin
    - H1 antihistamine
    - H2 antagonist (e.g., famotidine, cimetidine)
    - Hydroxyzine
    - Leukotriene receptor antagonist (e.g., montelukast) **and**
- Prescribed by or in consultation with one of the following:
    - Allergist/immunologist
    - Dermatologist

For reauthorization coverage of Xolair (omalizumab) injection for chroni following will be required:

- Patient's disease status has been re-evaluated since the last authorization to confirm the patient's condition warrants continued treatment **and**
- Patient has experienced at least one of the following:
    - Reduction in itching severity from baseline
    - Reduction in the number of hives from baseline

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

For initial coverage of Xolair (omalizumab) injection for chronic rhinosinusitis with nasal polyps (CRSwNP), the following will be required:

- Diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP) **and**
- Patient is 18 years of age or older **and**
- Unless contraindicated, the patient has had an inadequate response to 2 months of treatment with an intranasal corticosteroid (e.g., fluticasone, mometasone) **and**
- Used in combination with another agent for chronic rhinosinusitis with nasal polyps (CRSwNP) **and**
- Prescribed by or in consultation with one of the following:
    - Allergist/Immunologist
    - Otolaryngologist
    - Pulmonologist

For reauthorization coverage of Xolair (omalizumab) injection for chronic rhinosinusitis with nasal polyps (CRSwNP), the following will be required:

- Patient demonstrates a positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS; 0-8 scale], improvement in nasal congestion/obstruction score [NCS; 0-3 scale]) **and**
- Used in combination with another agent for chronic rhinosinusitis with nasal polyps (CRSwNP) **and**
- Prescribed by or in consultation with one of the following:
    - Allergist/Immunologist
    - Otolaryngologist
    - Pulmonologist

IgE-Mediated Food Allergy

For initial coverage of Xolair (omalizumab) injection for IgE-Mediated Food Allergy, the following will be required:

- One of the following:
    - Both of the following:
        - Diagnosis of IgE Mediated Food Allergy as evidenced by one of the following:
            - Positive skin prick test (defined as ≥4 mm wheal greater than saline control) to food
            - Positive food specific IgE (≥6 kUA/L)
            - Positive oral food challenge, defined as experiencing dose-limiting symptoms at a single dose of ≤300 mg of food protein **and**
        - Clinical history of IgE Mediated Food Allergy **or**
    - Provider attestation that patient has a history of severe allergic response, including anaphylaxis, following exposure to one or more foods **and**
- Patient is 1 year of age or older **and**
- Used in conjunction with food allergen avoidance **and**
- Both of the following:
    - Baseline (pre-Xolair treatment) serum total IgE level is greater than or equal to 30 IU/mL and less than or equal to 1850 IU/mL

    - Dosing is according to serum total IgE levels and body weight
- Prescribed by or in consultation with one of the following:
    - Allergist
    - Immunologist

For reauthorization coverage of Xolair (omalizumab) injection for IgE-Mediated Food Allergy, the following will be required:

- Patient demonstrates positive clinical response to therapy (e.g., reduction of type 1 allergic reactions, including anaphylaxis, following accidental exposure to one or more foods) **and**
- Used in conjunction with food allergen avoidance **and**
- Dosing will continue to be based on body weight and pretreatment total IgE serum levels **and**
- Prescribed by or in consultation with one of the following:
    - Allergist
    - Immunologist

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J2357	Injection, omalizumab, 5 mg

ICD-10 Code	Description
J33.0	Polyp of nasal cavity
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.42	Moderate persistent asthma with status asthmaticus
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.52	Severe persistent asthma with status asthmaticus
L50.1	Idiopathic urticaria
L50.6	Contact urticaria
L50.8	Other urticaria
L50.9	Urticaria, unspecified
T78.40XA	Allergy, unspecified, initial encounter
T78.40XD	Allergy, unspecified, subsequent encounter
T78.40XS	Allergy, unspecified, sequela
Z91.010	Allergy to peanuts
Z91.011	Allergy To Milk Products
Z91.012	Allergy To Eggs
Z91.013	Allergy To Seafood

ICD-10 Code	Description
Z91.014	Allergy To Mammalian Meats
Z91.018	Allergy To Other Foods

Background

Respiratory and allergy biologics are a mainstay of treatment for severe asthma, chronic idiopathic urticaria (CIU) and chronic rhinosinusitis with nasal polyposis. Asthma is a chronic lung disease that inflames and narrows the airways, making it difficult to breathe. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. In 2020, asthma affected an estimated 21 million adults and 4.2 million children in the United States (U.S.). Current pharmacologic options for asthma management are categorized as: (1) controller medications to achieve and maintain control of persistent asthma or prevent exacerbations, and (2) reliever medications for symptom relief and before exercise to prevent exercise-induced asthma symptoms (*Cloutier et al 2020, NHLBI 2007, Global Initiative for Asthma [GINA] 2024*). Severe asthma is defined as asthma that is uncontrolled despite adherence to maximal optimized high-dose ICS/LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased *(GINA 2024).*

Chronic spontaneous urticaria (CSU), is defined by the presence of hives on most days of the week for 6 weeks or longer, with or without angioedema. The hives are circumscribed, raised, erythematous plaques, often with central pallor and variable in size. No external allergic cause or contributing disease process can be identified in 80 to 90% of adults and children with CIU (*Khan 2023, Saini 2024*). CIU affects up to 1% of the general population in the U.S. and is more common in adults than children and typically begins in the third to fifth decades of life. Non-sedating H1-antihistamines are the cornerstone of therapy for CIU and limited courses of oral glucocorticoids are often used in combination with antihistamines for refractory symptoms. Other pharmacologic options for patients who do not respond to H1-antihistamines include the use of H2-antihistamines, leukotriene modifiers, cyclosporine, tacrolimus, mycophenolate, hydroxychloroquine, sulfasalazine, dapsone, and omalizumab (*Khan 2023, Maurer et al 2013, Sabroe et al 2021, Zuberbier et al 2022*).

Chronic rhinosinusitis with nasal polyps (CRSwNP) has a prevalence of approximately 2.7% in adults, and peaks in the sixth decade of life. Symptoms include nasal obstruction, reduced sense of smell, and sleep disturbance, all of which can substantially impact the quality of life. The majority of cases are idiopathic but may be due to genetic, metabolic, or immunologic causes, resulting in inflammation characterized by eosinophilia and elevated levels of IL-4, IL-5, and interleukin-13 (IL-13) (*Hopkins 2019*). Common treatment options for CRSwNP include saline irrigation and intranasal glucocorticoids in patients with mild symptoms, and short-term systemic glucocorticoids, surgery, and biologic agents in patients with severe symptoms (*Hopkins 2019*). Biologic agents in this review that are FDA-approved for CRSwNP include dupilumab, mepolizumab, and omalizumab.

IgE-mediated food-allergic disease differs from non-IgE-mediated disease because the pathophysiology results from activation of the immune system, causing a T helper 2 response which results in IgE binding to Fc ε receptors on effector cells like mast cells and basophils (*Anvari et al 2019*). The activation of these cells causes release of histamine and other preformed mediators, and rapid symptom onset, in contrast with non-IgE-mediated food allergy which is more delayed in onset. Symptoms of IgE-mediated food allergies range from mild to severe. The severity of symptoms is not predicted by the level of specific IgE or skin test wheal size, but the likelihood of symptom onset is directly related. Anaphylaxis is the most severe form of the clinical manifestation of IgE-mediated food allergy, and injectable epinephrine is the first-line treatment. Management of food allergies requires strict avoidance measures, counseling of the family about constant vigilance, and prompt treatment of allergic reactions with emergency medications.

Xolair (omalizumab) is an anti-IgE antibody which prevents binding of IgE to FcεRI (high-affinity IgE receptor) on basophils and mast cells, thereby reducing the amount of free IgE that is available to trigger the allergic cascade. Treatment of atopic subjects with omalizumab resulted in a marked down-regulation of FcεRI receptors on basophils.

Clinical Evidence

Asthma
The original FDA approval of omalizumab was based on the results of 3 randomized, double-blind, placebo-controlled, multicenter trials conducted in patients ≥ 12 years of age with moderate to severe asthma for ≥ 1 year and a positive skin test reaction to a perennial aeroallergen. All patients were required to have a baseline IgE between 30 and 700 international unit (IU)/mL and body weight not more than 150 kg. Patients were treated according to a dosing table to administer at least 0.016 mg/kg/IU (IgE/mL) of omalizumab or placebo over each 4-week period. A meta-analysis of 3 of the previously mentioned trials (*Busse et al 2001, Holgate et al 2004, Solèr et al 2001*) and their extension studies assessed the efficacy of omalizumab in a subgroup of 254 patients at high risk of serious asthma-related mortality and morbidity. The primary outcome was an annualized rate of acute exacerbation episodes based on data from the initial 16-week stable steroid phase for high-risk patients. Two kinds of acute exacerbation episodes were considered as endpoints: significant acute exacerbation episodes and all acute exacerbation episodes (i.e., all episodes recorded by the investigator). Significant acute exacerbation episodes were defined as those requiring a doubling of baseline ICS dose (*Busse et al 2001, Solèr et al 2001*) or use of systemic steroids (all 3 studies). During the stable steroid phase, mean significant acute exacerbation episode rates were 1.56 and 0.69/patient-year, respectively, a reduction of 56% with omalizumab (p = 0.007). Similar reductions in exacerbations in favor of omalizumab were observed for the whole study period and for all acute exacerbation episodes. The authors concluded that 113 significant acute exacerbation episodes were prevented for every 100 patients treated with omalizumab for 1 year (*Holgate et al 2001*).

In July 2016, the FDA expanded the indication of omalizumab to patients 6 to 11 years of age with moderate to severe persistent asthma. The approval was based primarily on a 52-week, randomized, double-blind, placebo-controlled, multicenter trial. The study evaluated the safety and efficacy of omalizumab as add-on therapy in 628 pediatric patients 6 to < 12 years of age with moderate to severe asthma inadequately controlled despite the use of an ICS (*Lanier et al 2009*). Over the 24-week fixed-steroid phase, omalizumab reduced the rate of clinically significant asthma exacerbations (worsening symptoms requiring doubling of baseline ICS dose and/or systemic steroids) by 31% vs placebo (0.45 vs 0.64; RR, 0.69; p = 0.007). Over a period of 52 weeks, the exacerbation rate was reduced by 43% (p < 0.001).

Chronic spontaneous urticaria
The safety and efficacy of omalizumab for the treatment of CSU was assessed in 2 placebo-controlled, multiple-dose clinical studies. Patients received omalizumab 75, 150, or 300 mg or placebo by SC injection every 4 weeks in addition to their baseline level of H1 antihistamine therapy for 24 or 12 weeks, followed by a 16-week washout observation period. In both studies, patients who received omalizumab 150 mg or 300 mg had greater decreases from baseline in weekly itch severity scores and weekly hive count scores than placebo at week 12 (*Kaplan et al 2013, Maurer et al 2013*).

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
The efficacy and safety of omalizumab for the treatment of CRSwNP in adult patients with an inadequate response to intranasal corticosteroids were based on results from 2 randomized, multicenter, double-blind, placebo-controlled, Phase 3 studies, POLYP 1 (n = 138) and POLYP 2 (n = 127) (*Gevaert et al 2020*). Patients were randomly assigned to omalizumab 75 to 600 mg SC every 2 or 4 weeks (based upon pretreatment serum total IgE level and body weight) or placebo for 24 weeks. All patients received background intranasal mometasone therapy. Results from both studies revealed that omalizumab was associated with a significantly greater improvement from baseline at week 24 in Nasal Polyp Score (NPS) and weekly average Nasal Congestion Score (NCS) as compared to placebo.

IgE-Mediated Food Allergy
The approval of Xolair for the IgE-mediated food allergy indication was based on a randomized, double-blind, placebo-controlled study in patients who were allergic to peanut and at least two other foods, including milk, egg, wheat,

cashew, hazelnut, or walnut (i.e., studied foods) (*Xolair Prescribing Informatio* Xolair or placebo for 16 to 20 weeks. The efficacy analysis included 165 pediat s the percentage of patients who were able to consume a single dose of ≥ 600 mg of peanut protein without dose-limiting symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) during a double-blind placebo-controlled food challenge (DBPCFC). The secondary endpoints were the percentage of patients who were able to consume a single dose of ≥ 1000 mg of cashew, milk, or egg protein without dose-limiting symptoms during DBPCFC. Xolair treatment led to a statistically higher response rate than placebo for the primary and secondary endpoints. The effectiveness 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 similarity. While efficacy cannot be established from uncontrolled, open-label studies, for 38 pediatric patients who continued Xolair for 24 to 28 weeks in an open-label extension, the percentage of patients who were able to consume ≥ 600 mg of peanut protein and ≥ 1000 mg of egg, milk, and/or cashew protein without moderate to severe dose-limiting symptoms was maintained.

Clinical Guidelines

Asthma

The National Asthma Education and Prevention Program (NAEPP) guideline from the NHLBI states that the initial treatment of asthma should correspond to the appropriate asthma severity category, and it provides a stepwise approach to asthma management. Long-term control medications such as ICSs, long-acting bronchodilators, leukotriene modifiers, cromolyn, and immunomodulators should be taken daily on a long-term basis to achieve and maintain control of persistent asthma. ICSs are the most potent and consistently effective long-term asthma control medication. Quick-relief medications such as SABAs and anticholinergics are used to provide prompt relief of bronchoconstriction and accompanying acute symptoms such as cough, chest tightness, and wheezing. Systemic corticosteroids are important in the treatment of moderate or severe exacerbations because these medications prevent progression of the exacerbation, speed recovery, and prevent relapses (*NHLBI 2007*). The 2024 GINA report also provides a stepwise approach to asthma management (*GINA 2024*). Treatment recommendations are based on patient age, and stepping down should be considered when asthma symptoms have been well-controlled and lung function have been stable for ≥ 3 months. ICS/beta2-agonist combination products are recommended for both controller (i.e., maintenance treatment) and reliever use in patients ≥ 6 years of age, while the preferred controller option in patients ≤ 5 years of age consists of low-dose ICS plus as-needed SABA as a reliever. In patients ≥ 6 years of age diagnosed with severe asthma and uncontrolled on Step 4 treatment phenotyping for Type 2 inflammation into categories such as severe allergic, aspirin-exacerbated, allergic bronchopulmonary aspergillosis, chronic rhinosinusitis, nasal polyposis, atopic dermatitis, or eosinophilic asthma is recommended. Add-on treatment with a biologic agent should be considered as follows:

- Severe allergic asthma: Anti-IgE treatment with omalizumab is recommended for patients ≥ 6 years of age.
- Severe eosinophilic asthma: Add-on anti-IL-5 therapy is recommended for patients ≥ 6 years of age (mepolizumab and benralizumab), or ≥ 18 years of age (reslizumab).
- Severe eosinophilic/Type 2 asthma: Anti-IL4 therapy (dupilumab) is recommended for patients ≥ 6 years of age.
- Adults or adolescents requiring oral corticosteroids for maintenance therapy: Anti-IL4 therapy (dupilumab) is recommended.
- Severe asthma: Anti-TSLP therapy (tezepelumab-ekko) is recommended for patients ≥ 12 years of age.
- Prior to initiation of a biologic agent, several factors should be considered including cost, insurance eligibility criteria, evaluation of predictors of response, delivery route, dosing frequency, and patient preference.

The European Respiratory Society/American Thoracic Society guideline on the management of severe asthma suggests the use of anti-IL-5 therapy as an add-on in adults with severe uncontrolled eosinophilic asthma or severe corticosteroid-dependent asthma. A blood eosinophil count of ≥ 150 cells/µL is suggested as a cut-point to guide initiation of anti-IL-5 therapy in adults with severe asthma and prior exacerbations. A blood eosinophil count of ≥ 260 cells/µL or an exhaled nitric oxide level of 19.5 parts per billion or greater may be used to identify adolescents and adults with severe allergic asthma who are likely to benefit from anti-IgE treatment (*Holguin et al 2020*).

Chronic spontaneous urticaria
Guidelines developed by the American Academy of Allergy, Asthma & Immuno , Asthma & Immunology, and the Joint Council of Allergy, Asthma & Immunology recommend a stepwise treatment approach for CSU. Treatment with omalizumab is recommended in patients inadequately controlled with antihistamines and a LTRA (*Bernstein et al 2014*). Joint guidelines by the European Academy of Allergy and Clinical Immunology, the Global Allergy and Asthma European Network, the European Dermatology Forum, and the World Allergy Organization recommend treatment with omalizumab in patients with symptoms despite treatment with a 4-fold dose of modern second-generation antihistamines. This is a change from previous guidelines in which use of either omalizumab or cyclosporine after failure of high-dose antihistamines was recommended. However, due to adverse effects and the lack of an approved indication, the new recommendation was that cyclosporine should only be considered if omalizumab does not provide an adequate response (*Zuberbier et al 2022*). Guidelines published by the British Association of Dermatologists similarly recommend omalizumab as a potential second-line agent in patients inadequately controlled on first-line second-generation antihistamines (*Sabroe et al 2021*).

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
Treatment of CRSwNP is addressed in guidelines from the American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma & Immunology, and the Joint Council of Allergy, Asthma & Immunology; the International Forum of Allergy & Rhinology; and the European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA) (*Orlandi et al 2016, Peters et al 2014, Rosenfeld et al 2015, Rank et al 2023*). Routine treatment recommendations include saline irrigation and/or intranasal glucocorticoids in patients with mild symptoms, and short-term systemic glucocorticoids and surgery in patients with severe or refractory symptoms. Biologics rather than no biologics are recommended for patients with CRSwNP and dupilumab is specifically recommended by ICAR-RS *(Orlandi et al 2021, Rank et al 2023)*.

IgE-mediated food allergy
Food allergy is an important public health problem affecting children and adults and may be increasing in prevalence (*Boyce et al 2010)*. Despite the risk of severe allergic reactions and even death, there is no current treatment for food allergy. The disease can only be managed by allergen avoidance or treatment of symptoms. Anaphylaxis is the most severe form of the clinical manifestation of IgE-mediated food allergy. Current clinical guidelines including those from the National Institute of Allergy and Infectious Diseases (NIAID), American Academy of Pediatrics, the World Allergy Organization, and the Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma, and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology consistently recommend epinephrine as the first-line medication of choice for the treatment of anaphylaxis due to its life-saving effects. It is suggested that patients who have a history of anaphylaxis or systemic reaction to allergens, including insect stings or foods, be prescribed an injectable epinephrine agent, and be advised to carry it with them at all times. Consideration may also be given to patients who do not have a history of anaphylaxis but are at high risk of an anaphylactic reaction (*Boyce et al 2010, Campbell et al 2014, Cardona et al 2020, Golden et al 2017, Kemp et al 2008, Lieberman et al 2015, Sampson et al 2014, Shaker et al 2020, Sicherer et al 2017, Simons et al 2015).* Antihistamines, glucocorticoids, and bronchodilators may be used as adjunctive therapy to epinephrine but should not be used as initial or sole therapy as these agents do not have any life-saving properties *(Lieberman et al 2015, Shaker et al 2020, Sicherer et al 2017, Simons et al 2015).*

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Xolair is an anti-IgE antibody indicated for:

- 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 te response to nasal corticosteroids, as add-on maintenance 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
- Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

References

1. Anvari S, Miller J, Yeh CY, Davis CM. IgE-Mediated Food Allergy. Clin Rev Allergy Immunol. 2019 Oct;57(2):244-260. doi: 10.1007/s12016-018-8710-3. PMID: 30370459.
2. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014;133:1270-1277.
3. Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010;126(6):S1-58.
4. Busse W, Corren J, Lanier BQ, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol. 2001;108(2):184-90.
5. Campbell RL, Li JT, Nicklas RA, et al. Emergency department diagnosis and treatment of anaphylaxis: a practice parameter. Ann Allergy Asthma Immunol. 2014;113:599-608.
6. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. World Allergy Organ J. 2020;13(10):100472.
7. Cloutier MM, Dixon AE, Krishnan JA, et al. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program. JAMA. 2020;324(22):2301-2317. doi: 10.1001/jama.2020.21974.
8. Gevaert P, Omachi TA, Corren J, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. J Allergy Clin Immunol. 2020;146(3):595-605. doi: 10.1016/j.jaci.2020.05.032.
9. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. 2024. http://www.ginasthma.org. Accessed April 15, 2025.
10. Golden DB, Demain J, Freeman T, et al. Stinging insect hypersensitivity: a practice parameter update 2016. Ann Allergy Asthma Immunol. 2017;118(1):28-54.
11. Holgate S, Bousquet J, Wenzel S, et al. Efficacy of omalizumab, an anti-immunoglobulin E antibody, in patients with allergic asthma at high risk of serious asthma-related morbidity and mortality. Curr Med Res Opin. 2001;17(4):233-240.
12. Holgate ST, Chuchalin AG, Hébert J, et al. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. Clin Exp Allergy. 2004;34(4):632-8
13. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020;55(1). pii: 1900588. doi: 10.1183/13993003.00588-2019.
14. Hopkins C. Chronic Rhinosinusitis with Nasal Polyps. N Engl J Med. 2019;381(1):55-63. doi: 10.1056/NEJMcp1800215.
15. Kaplan A, Ledford D, Ashby M, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. J Allergy Clin Immunol. 2013;132:101-9.
16. Kemp SF, Lockey RF, Simons FE; World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: the drug of choice for anaphylaxis-a statement of the World Allergy Organization. World Allergy Organ J. 2008;1(Suppl 2):S18-26.
17. Khan DA. Chronic spontaneous urticaria: treatment of refractory symptoms. UpToDate Web site. https://www.uptodate.com/. Updated November 17, 2023. Accessed April 15, 2025. Lanier B, Bridges T, Kulus M, Taylor AF, Berhane I, Vidaurre CF. Omalizumab for the treatment of exacerbations in children with inadequately controlled allergic (IgE-mediated) asthma. J Allergy Clin Immunol. 2009;124(6):1210-6.
18. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis--a practice parameter update 2015. Ann Allergy Asthma Immunol. 2015;115(5):341-384.

19. Maurer M, Rosen K, Hsieh HJ, et al. Omalizumab for the treatment of c
urticaria. N Engl J Med. 2013;368:924-935.
20. National Heart, Lung, and Blood Institute. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma (guideline on the Internet). 2007. https://www.ncbi.nlm.nih.gov/books/NBK7232/. Accessed April 22, 2024.
21. Orlandi RR, Kingdom TT, Hwang PH, et al. International Consensus Statement on Allergy and Rhinology: Rhinosinusitis. Int Forum Allergy Rhinol. 2016;6 Suppl 1:S22-209. doi: 10.1002/alr.21695.
22. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. Ann Allergy Asthma Immunol. 2014;113(4):347-85. doi: 10.1016/j.anai.2014.07.025.
23. Rank MA, Chu DK, Bognanni A, et al. The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. J Allergy Clin Immunol. 2023;151(2):386-398. doi:10.1016/j.jaci.2022.10.026.
24. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015;152(2 Suppl):S1-S39. doi: 10.1177/0194599815572097.
25. Sabroe RA, Lawlor F, Grattan CEH, et al. British Association of Dermatologists guidelines for the management of people with chronic urticaria 2021. Br J Dermatol. 2022;186(3):398-413. doi:10.1111/bjd.20892
26. Saini S. Chronic spontaneous urticaria: clinical manifestations, diagnosis, pathogenesis, and natural history. UpToDate Web site. https://www.uptodate.com/. Updated June 6, 2024. Accessed April 15, 2025.
27.
28. Saini SS, Bindslev-Jensen C, Maurer M, et al. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: a randomized, placebo-controlled study. J Invest Derm. 2015;135:67-75.
29. Sampson HA, Aceves S, Bock A, et al for the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma & Immunology, and the Joint Council of Allergy, Asthma & Immunology. Food allergy: a practice parameter update – 2014. J Allergy Clin Immunol. 2014;134(5):1016-1025.
30. Shaker MS, Wallace DV, Golden DBK, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and grading of recommendations, assessment, development and evaluation (GRADE) analysis. J Allergy Clin Immunol. 2020;145(4):1083-1123.
31. Sicherer SH, Simons FER, AAP section on allergy and immunology. Epinephrine for first-aid management of anaphylaxis. Pediatrics. 2017;139(3):e20164006.
32. Simons FE, Ebisawa M, Sanchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J. 2015;8(1):32.
33. Solèr M, Matz J, Townley R, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. Eur Respir J. 2001;18(2):254-61.
34. Xolair [package insert], South San Francisco, CA: Genentech, Inc. and East Hanover, NJ: Novartis Pharmaceuticals; February 2024.
35. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA/LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022;77(3):734-766.doi: 10.1111/all.15090.

Policy History/Revision Information

Date	Summary of Changes
11/16/2023	Approved by OptumRx P&T Committee
04/17/2024	New indication added. Updates to all sections
05/16/2024	Annual Review. Updated criteria language in coverage rationale section in line with other drugs in same class. Updated references.

Date	Summary of Chang
05/15/2025	Annual Review. Added age criterion for CRSwNP in Covera Background & Clinical Guidelines sections. Updated references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).