Xolair® (Omalizumab)

Policy Number: IEXD0033.14
Effective Date: October 1, 2025

Ü Instructions for Use

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Related Policies
None

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Massachusetts, Nevada, and New York.

Coverage Rationale

Ü See Benefit Considerations

This policy refers to Xolair (omalizumab) subcutaneous injection for administration by a healthcare professional. Xolair (omalizumab) for self-administered subcutaneous injection is obtained under the pharmacy benefit.

Moderate to Severe Persistent Asthma

Xolair for provider administration is proven and medically necessary for patients with moderate to severe persistent asthma when all of the following criteria are met:

- Diagnosis of moderate or severe asthma; **and**
- Classification of asthma as uncontrolled or inadequately controlled as defined by **at least one** of the following:
  - Poor symptom control [e.g., Asthma Control Questionnaire (ACQ) score consistently greater than 1.5 or Asthma Control Test (ACT) score consistently less than 20]
  - Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months
  - Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment)
  - Airflow limitation [e.g., after appropriate bronchodilator withhold forced expiratory volume in 1 second (FEV1) less than 80% predicted (in the face of reduced FEV1/forced vital capacity {FVC} defined as less than the lower limit of normal)]
  - Patient is currently dependent on maintenance therapy with oral corticosteroids for the treatment of asthma

  and
- Baseline (pre-omalizumab treatment) serum total IgE level greater than or equal to 30 IU/mL and less than or equal to 1300 IU/mL; **and**
- Positive skin test or in vitro reactivity to a perennial aeroallergen; **and**
- Used in combination with **one** of the following:
  - One maximally-dosed (appropriately adjusted for age) combination inhaled corticosteroid (ICS)/long-acting beta2-agonist (LABA) product [e.g., Advair/AirDuo Respiclick (fluticasone propionate/salmeterol), Symbicort (budesonide/formoterol), Breo Ellipta (fluticasone furoate/vilanterol)]

- Combination therapy including **both** of the following:
  - One maximally-dosed (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco®), mometasone furoate (Asmanex®), beclomethasone dipropionate (QVAR®)]; **and**
  - One additional asthma controller medication [e.g., LABA - olodaterol (Striverdi®) or indacaterol (Arcapta®); leukotriene receptor antagonist – montelukast (Singulair®); theophylline]

and

- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Prescribed by an allergist/immunologist or pulmonologist; **and**
- Initial authorization will be for no more than 12 months

Reauthorization/Continuation of Care Criteria

Xolair, for provider administration, for the treatment of moderate to severe persistent asthma, authorization for continued use will be approved based on all of the following criteria:

- Documentation of positive clinical response as demonstrated by **at least one** of the following:
  - Reduction in the frequency of exacerbations
  - Decreased utilization of rescue medications
  - Increase in percent predicted FEV1 from pretreatment baseline
  - Reduction in severity of frequency of asthma-related symptoms (e.g., wheezing, shortness of breath, coughing, etc.)

  and
- Used in combination with an ICS-containing maintenance medication [e.g., Advair/AirDuo (fluticasone/salmeterol), Breo Ellipta (fluticasone furoate/vilanterol), Symbicort (budesonide/ formoterol), Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)]; **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

Chronic Urticaria

Xolair for provider administration is proven and medically necessary for patients with chronic urticaria when all of the following criteria are met:

- Diagnosis of chronic urticaria; **and**
- **One** of the following:
  - Patient remains symptomatic despite at least a 2-week trial of, or history of contraindication or intolerance to, **two** H1-antihistamines [e.g., Allegra (fexofenadine), Benadryl (diphenhydramine), Claritin (loratadine)]*
  - Patient remains symptomatic despite at least a 2-week trial of, or history of contraindication or intolerance to **both** of the following taken in combination:
    - A second generation H1-antihistamine [e.g., Allegra (fexofenadine), Claritin (loratadine), Zyrtec (cetirizine)]; **and**
    - **One** of the following:
      - Different second generation H1-antihistamine [e.g., Allegra (fexofenadine), Claritin (loratadine), Zyrtec (cetirizine)]
      - First generation H1-antihistamine[e.g., Benadryl (diphenhydramine), Chlor-Trimeton (chlorpheniramine), Vistaril (hydroxyzine)]*
      - H2-antihistamine [e.g., Pepcid (famotidine), Tagamet HB (cimetidine), Zantac (ranitidine)]
      - Leukotriene modifier [e.g., Singulair (montelukast)]

  and
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

and

- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Prescribed by an allergist/immunologist or dermatologist; **and**
- Initial authorization will be for no more than 12 months

Reauthorization/Continuation of Care Criteria

Xolair, for provider administration, for the treatment of chronic urticaria, authorization for continued use will be approved based on all of the following criteria:

- Documentation of positive clinical response (e.g., reduction in exacerbations, itch severity, hives); **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

*__Note__: Patients 65 years of age and older in whom first generation H1-antihistamines are considered high risk medications to be avoided (e.g., Beers criteria, HEDIS) should be directed to try alternatives that are not considered high risk.

Nasal Polyps

Xolair for provider administration is proven and medically necessary for patients with nasal polyps when all of the following criteria are met:

- Diagnosis of nasal polyps
  - **Two or more** of the following symptoms for longer than 12 weeks duration:
    - Nasal mucopurulent discharge
    - Nasal obstruction, blockage, or congestion
    - Facial pain, pressure, and/or fullness
    - Reduction or loss of sense of smell

    and
  - **One** of the following findings using nasal endoscopy and/or sinus computed tomography (CT):
    - Purulent mucus or edema in the middle meatus or ethmoid regions
    - Polyps in the nasal cavity or the middle meatus
    - Radiographic imaging demonstrating mucosal thickening or partial or complete opacification of paranasal sinuses

    and
  - **One** of the following:
    - Patient has required prior sinus surgery
    - Patient has required systemic corticosteroids (e.g., prednisone, methylprednisolone) for nasal polyps in the previous 2 years
    - Patient has been unable to obtain symptom relief after trial of both of the following:
      - Intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone)
      - One other therapy used in the management of nasal polyps [i.e., nasal saline irrigations. antileukotriene agents (e.g., montelukast, zafirlukast, zileuton)]

  and
- Patient will receive Xolair as add-on maintenance therapy in combination with intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone); **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Prescribed by an allergist/immunologist/otolaryngologist/pulmonologist; **and**
- Initial authorization will be for no more than 12 months

Reauthorization/Continuation of Care Criteria

Xolair, for provider administration, for the treatment of nasal polyps, authorization for continued use will be approved based on all of the following criteria:

- Documentation of positive clinical response; **and**
- Patient will continue to receive Xolair as add-on maintenance therapy in combination with intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone); **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

IgE Mediated Food Allergy

Xolair for provider administration is proven and medically necessary when all of the following criteria are met:

- Diagnosis of IgE-mediated food allergy to one or more foods; **and**
- Patient is aged ≥ 1 year; **and**
- IgE-mediated food allergy to specific food(s) has been confirmed by **both** of the following:
  - History of type I allergic reactions (e.g., nausea, vomiting, cramping, diarrhea, flushing, pruritus, urticaria, swelling of the lips, face or throat, wheezing, lightheadedness, syncope); **and**
  - One of the following:
    - Food specific skin prick testing (SPT)
    - IgE antibody in vitro testing
    - Oral food challenge (OFC)

  and
- Xolair will be used in conjunction with food allergen avoidance; **and**
- Patient has access to epinephrine; **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Prescribed by an allergist or immunologist; **and**
- Initial authorization will be for no more than 12 months

Reauthorization/Continuation of Care Criteria

Xolair, for provider administration, for the treatment of IgE-mediated food allergy, authorization for continued use will be approved based on all of the following criteria:

- Documentation of positive clinical response to Xolair therapy (e.g., reduction in type I allergic reactions); **and**
- Xolair will be used in conjunction with food allergen avoidance; **and**
- Patient has access to epinephrine; **and**
- Patient is not receiving Xolair in combination with **any** of the following for treatment of the same indication:
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
  - Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

  and
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Prescribed by an allergist or immunologist; **and**
- Reauthorization will be for no more than 12 months

Unproven

Xolair for provider administration is unproven and not medically necessary in the following:

- Seasonal allergic rhinitis
- Perennial allergic rhinitis
- Atopic dermatitis

- Acute bronchospasm or status asthmaticus
- Emergency treatment of allergic reactions, including anaphylaxis

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

Diagnosis Code	Description
J33.0	Polyp of the nasal cavity
J33.1	Polypoid sinus degeneration
J33.8	Other polyp of sinus
J33.9	Nasal polyp, unspecified
J44.1	Chronic obstructive pulmonary disease with (acute) exacerbation
J44.9	Chronic obstructive pulmonary disease, unspecified
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.909	Unspecified asthma, uncomplicated
J45.998	Other asthma
L50.0	Allergic urticaria
L50.1	Idiopathic urticaria
L50.8	Other urticaria
Z91.010	Allergy to peanuts
Z91.0110	Allergy to milk products, unspecified
Z91.0111	Allergy to milk products with tolerance to baked milk
Z91.0112	Allergy to milk products with reactivity to baked milk
Z91.0120	Allergy to eggs, unspecified
Z91.0121	Allergy to eggs with tolerance to baked egg
Z91.0122	Allergy to eggs with reactivity to baked egg
Z91.013	Allergy to seafood
Z91.018	Allergy to other food

Background

Asthma is a common chronic inflammatory disease of the airways that affects an estimated 24 million adults and children. Although the disease is well controlled with inhaled therapy in most patients, approximately 1.2 to 2.4 million people have severe asthma (i.e., 5 to 10% of the asthma population) that is associated with substantial morbidity, mortality, and economic effects. Asthma has been divided into various clinical presentations or phenotypes. Key asthma phenotypes include allergic asthma, eosinophilic asthma, and non-eosinophilic asthma. Allergic asthma is characterized by a positive perennial aeroallergen skin test and/or increased levels of serum IgE.

Chronic spontaneous urticaria (CSU) is characterized by recurrent urticaria (e.g., hives, wheals), angioedema, or both for a period of six weeks or longer and have no apparent external trigger. It is estimated that approximately 1 percent of the adult population develops CSU at some point in their lives.

Chronic rhinosinusitis with nasal polyps is an inflammatory condition involving the paranasal sinuses and linings of the nasal passages, which persists for 12 weeks or longer, and affects approximately 2-4% of the population. Symptoms include mucopurulent drainage, nasal obstruction, facial pain/pressure/fullness, and decreased sense of smell.

Food allergy affects up to 8% of children and 10% of adults in the United States, and a large percentage (30 to 86%) of affected persons are allergic to multiple foods. Signs and symptoms can involve the skin, respiratory and gastrointestinal tracts, and cardiovascular system and are believed to be caused by mediator release from tissue mast cells and circulating basophils.

Omalizumab is a monoclonal antibody that binds to human immunoglobulin E (IgE)'s high affinity Fc receptor, thereby preventing the binding of IgE to a variety of cells associated with the allergic response. Preventing the bridging between IgE and cells associated with allergic response prevents degranulation of such cells and, thereby, the release of inflammatory mediators. Omalizumab has been found in clinical trials to reduce free serum IgE concentrations by more than 90%, considerably suppress eosinophils in induced sputum, and blunt both early and late phase allergic reactions.[33-34]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Allergic Asthma

Omalizumab is indicated for treatment of adults and adolescents 6 years of age and older, who have moderate to severe persistent asthma and a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Deschildre et al evaluated omalizumab efficacy and safety in a real-life setting in children aged 6 to 18 years (n = 104) with severe asthmas followed up in pediatric pulmonary tertiary care centers. Asthma control levels, exacerbations, inhaled corticosteroid dose, lung function and adverse events were evaluated over 1 year. Children were characterized by allergic sensitization to three or more allergens (66%), high IgE levels (mean 1125 kU · L(-1)), high rate of exacerbations (4.4 per year) and healthcare use during the previous year, and high inhaled corticosteroid dose (mean 703 µg equivalent fluticasone per day). Asthma control levels defined as good, partial, or poor, improved from 0%, 18% and 82% at entry to 53%, 30% and 17% at week 20, and to 67%, 25% and 8% at week 52, respectively ($p < 0.0001$). Reported exacerbation and hospitalization rates decreased by 72% and 88.5%, respectively. At 12 months, forced expiratory volume in 1 s (FEV1) improved by 4.9% ($p = 0.023$), and inhaled corticosteroid dose decreased by 30% ($p < 0.001$). Six patients stopped omalizumab for related significant adverse events. Omalizumab improved asthma control in children with severe allergic asthma and was generally well tolerated. Authors concluded that he observed benefit was greater than that reported in clinical trials.

Sorkness et al conducted a post-hoc analyses which examined patient characteristics of those eligible and ineligible for omalizumab; described onset of effect after initiation of omalizumab and offset of treatment effect after stopping therapy; and determined whether the efficacy differs by age, asthma severity, dosing regimen, and pre-specified biomarkers. Inner-city children and adolescents with persistent allergic asthma enrolled in the Inner-City Anti-IgE Therapy for Asthma (ICATA) trial that compared omalizumab with placebo added to guidelines-based therapy for 60 weeks were eligible for the evaluation (a significant portion of children and adolescents particularly suited for omalizumab because of asthma severity status were ineligible due to IgE > 1300 IU/mL). Two hundred ninety-three of 889 participants (33%) clinically suitable for omalizumab were ineligible for dosing according to a modified dosing table specifying IgE level and body

weight criteria. Baseline symptoms were comparable among those eligible and ineligible to receive omalizumab, but other characteristics (rate of health care utilization and skin test results) differed. Patients receiving biweekly injections experienced a greater reduction in both exacerbations (OR = 2.54) and inhaled corticosteroids (ICS) usage (−204.8 μg/day) compared to patients receiving monthly injections (1.42 and −50.2 μg/day; p = 0.08 and p = 0.02, respectively). Omalizumab efficacy for symptom days per 2 weeks did not differ by dosing regimen (p = 0.62). Patients with total IgE ≥ 700 IU/mL had the greatest reduction in ICS usage (−504.6 μg/day) because of treatment with omalizumab. The time of onset of omalizumab effect was < 30 days and time of offset was between 30 and 120 days. No difference in efficacy was noted by age or asthma severity, but high exhaled nitric oxide, blood eosinophils, and body mass index predicted efficacy. Researchers concluded that results of this analysis showed that efficacy for exacerbations and ICS treatment was comparable in children 6 to 12 years of age compared with older children (> 12 years). Additionally, the data suggested that omalizumab may be efficacious in both severe disease (steps 5-6 treatments) and more moderate disease (steps 1-4). Certain subgroups of persons, for example, those with higher exhaled nitric oxide, blood eosinophils, and BMI were more likely to benefit from omalizumab according to the secondary analysis.

The Inner-City Anti-IgE Therapy for Asthma (ICATA) Study was a 60-week, randomized, double-blind, placebo-controlled, parallel-group trial (n = 419) which evaluated the effectiveness of omalizumab (75-375 mg subcutaneously every 2-4 weeks), as compared with placebo, when added to guidelines-based therapy. The primary outcome was reduction in symptoms and exacerbations of asthma. Inner-city patients 6 to 20 years of age with persistent asthma (receiving long-term therapy for disease control and having symptoms of persistent asthma or evidence of uncontrolled disease as indicated by hospitalization or unscheduled urgent care in the 6 to 12 months preceding study entry), at least one positive skin test for a perennial allergen, weight between 20 and 150 kg, and having total serum levels of IgE between 30 and 1300 IU per milliliter were eligible for enrollment. Additionally, patients not receiving long-term control therapy were eligible for enrollment only if they had both persistent symptoms and uncontrolled asthma. The primary outcome defined as reduction in symptoms (number of days with symptoms during the previous two weeks) and exacerbations of asthma was evaluated every 4 weeks. Omalizumab as compared with placebo significantly reduced the number of days with asthma symptoms, from 1.96 to 1.48 days per 2-week interval, a 24.5% decrease (p < 0.001). Similarly, the percentage of participants with exacerbations (one or more) during the study was 48.8% in the placebo group as compared with 30.3% in the omalizumab group (p < 0.001), and the percentage who were hospitalized because of asthma was 6.3% as compared with 1.5%, respectively (p = 0.02). Improvements occurred with omalizumab despite reductions in the use of inhaled glucocorticoids and long-acting beta-agonists.

In a further pre-specified, subgroup (Lanier 2009) analysis, Kulus et al. evaluated efficacy and safety of omalizumab as compared to placebo in children (n = 235) with severe, persistent allergic asthma. Over the 24-week fixed-steroid phase, omalizumab reduced the rate of clinically significant asthma exacerbations (worsening symptoms requiring doubling of baseline inhaled corticosteroid dose and/or systemic steroids) by 34% versus placebo (0.42 vs 0.63, p = 0.047). Over 52 weeks, the exacerbation rate was reduced by 50% (p < 0.001). The overall incidence of adverse events (AEs) was similar in both omalizumab and placebo groups (93.4% vs 95.0%, p = 0.779), serious AEs were less frequent in the omalizumab group (3.6% vs 10.0%, p = 0.073), and no new safety concerns were evident. Researchers noted that the sample size was not based on providing statistical power in the severe subgroup, and no corrections were made for multiple comparisons; however, outcomes consistently favored omalizumab.

Milgrom et al. evaluated the safety of omalizumab in children (n = 926) ages 6-12 with allergic (IgE-mediated) asthma in a pooled analysis of two double-blind, placebo controlled studies (Milgrom 2001 and Lanier 2009). Children on optimized asthma care were randomized (2:1) to omalizumab (75-375 mg every 2 or 4 weeks) or placebo. Adverse events (AEs) were more frequently reported in the placebo (91.7%) than omalizumab (89.7%) group. The most common AEs were nasopharyngitis, upper respiratory tract infection and headache. Suspected treatment-related AEs included headache, erythema and urticaria; none of which were reported by ≥ 2% of patients receiving omalizumab. Serious adverse effects were reported by 3.4% and 6.6% of patients receiving omalizumab and placebo, respectively; the most common were appendicitis, pneumonia, and bronchitis; no deaths were reported.

Allergic Asthma With IgE Levels > 700 IU/ml

A retrospective study evaluated the response of asthmatic patients treated with omalizumab with IgE levels greater than 700 IU/mL. Emergency department (ED) visits, hospitalizations, change in forced expiratory volume in 1 second (FEV1), corticosteroid bursts, and Asthma Control Test (ACT) scores were recorded for a period of 6 months before and after treatment with omalizumab in patients with elevated IgE levels or treatment length of ≥ 6 months. Twenty-six patients with an IgE level > 700 IU/mL (group 1) were matched by age, sex, and severity of asthma to patients with an IgE of 30 to 700 IU/mL (group 2). The mean numbers of ED visits before and after treatment was 0.96 vs 0.23 (p = 0.008) in group 1 and 0.65 vs 0.15 (p = 0.02) in group 2. Both groups had an improvement in asthma control based on the mean ACT score before and after treatment [15.6 vs 18.9 (p = 0.02) and 15.4 vs 19 (p = 0.006), respectively]. Additionally, there was a significant reduction in the frequency of systemic corticosteroid use during the 6 months before and after treatment [2.58

vs 0.96 ($p < 0.001$) and 2.62 vs 1.23 ($p < 0.001$) systemic steroid treatments, respectively]. Researchers concluded that omalizumab was just as effective in reducing ED visits, controlling asthma symptoms, and reducing the need for systemic corticosteroids in patients with IgE levels > 700 IU/mL compared with patients with levels within 30 to 700 IU/mL.

A multicenter, randomized, double-blind, parallel-group, placebo-controlled study evaluated use of high dose omalizumab in adult patients with IgE levels > 700 IU/ml. Fifty asthmatic patients (pre-bronchodilator forced expiratory volume in 1 second (FEV1) ≥ 65% predicted; had been asthma exacerbation-free for ≥ 4 weeks; and skin reactivity to a specific allergen within 2 years before screening) with an age range of 18 to 65 years and a body weight range of 40 to 150 kg were divided into two groups according to IgE levels (group 1: 30-300 IU/ml and group 2: 700-2000 IU/ml) and randomized 2:1 to receive either omalizumab or placebo every 2 or 4 weeks. Allergen bronchoprovocation (ABP) testing was performed at baseline, week 8 and week 16. The primary efficacy endpoint measured was the early-phase allergic response (EAR; defined as the maximum percentage drop in forced expiratory volume in 1 second during the first 30 minute after ABP). Secondary outcome evaluated with the late-phase allergic response (LAR; defined as maximum percentage drop in FEV1 over 3-8 hours after ABP). Additional outcomes assessed included serum free IgE (as a pharmacodynamic endpoint) and the exhaled fractional concentration of nitric oxide (FENO; as an exploratory endpoint). At week 8, EAR was 23.1% for placebo and treatment with omalizumab reduced it to 9.3% in in group 1 ($p = 0.018$ vs placebo) and 5.6% in group 2 ($p < 0.001$ vs placebo). Additionally, at week 16, reported EAR was 20%, 11.8% ($p = 0.087$) and 5.1% ($p < 0.001$), respectively. LAR analysis was not performed due to the small number of patients studied. Serum free IgE levels decreased in groups 1 and 2 and remained < 50 ng/ml in all patients during weeks 6-16. Treatment with omalizumab suppressed FENO increases after ABP in both groups. Authors conclude that the outcomes of this study demonstrated that the protective effects of omalizumab against allergen-induced bronchoconstriction in patients with allergic asthma and baseline IgE up to 2000 IU/ml.

Researchers conducted a post-marketing observational surveillance trial to evaluate the efficacy and tolerability of omalizumab in a real-life setting in Spain, particularly in those patients with immunoglobulin E (IgE) levels out of range. Patients were recruited if they had a diagnosis of uncontrolled severe, persistent, allergic asthma while on high-dose inhaled corticosteroids (ICSs) plus long-acting β2-agonist (LABA); had an age ≥ 12 years; and had received at least one dose of omalizumab between May 2006 and November 2009, Main efficacy outcomes evaluated included asthma exacerbation rate (AER), asthma control test (ACT), and global evaluation of treatment effectiveness (GETE). Of the 266 patients enrolled, 7 patients had IgE levels < 30 IU/ml and 46 patients has IgE levels > 700 IU/ml. Average AER reported for all groups showed a reduction from 3.6 in previous year to 0.67 at 4 months ($p < 0.05$) and to 1.04 at 2 years ($p < 0.05$). Average ACT increased from 14.3 at baseline to 18.4 at 4 months ($p < 0.05$) and to 20.3 $p < 0.05$) at 2 years. After 4 months, 74.6% of patients had reached a good or excellent rate on the GETE scale ($p < 0.05$) and this rate continued to increase to 81.6% at 2 years. Similarly, in the IgE > 700 IU/ml group, researchers reported an increased ACT from 13.6 at baseline to 20.9 at the 2-year visit ($p < 0.05$) and a decrease in exacerbations from 3.58 at baseline to 0.72 at the 2-year visit ($p < 0.05$). At follow-up, maintenance treatment with oral steroids was reduced from 89 patients to 19 patients ($p < 0.05$). Omalizumab was discontinued because of lack of efficacy in 28/266 (10.5%) patients and 30 patients (11.4%) reported adverse events (none were severe). Researchers conclude that this observational study confirms that omalizumab is efficacious and well tolerated in patients with uncontrolled severe asthma, including those patients with IgE levels > 700 IU/ml.

Chronic Urticaria

Omalizumab is indicated for treatment of chronic idiopathic urticaria in adults and adolescents (12 years of age and above) who remain symptomatic despite H1 antihistamine treatment.

Saini et al conducted a 40-week, randomized, double-blind, placebo-controlled trial (ASTERIA I) to evaluate the efficacy and safety of subcutaneous omalizumab as add-on therapy for 24 weeks in patients (n = 319) with chronic idiopathic urticaria/spontaneous urticaria (CIU/CSU) who remained symptomatic despite H_1 antihistamine treatment. Eligible patients aged 12–75 years with CIU/CSU who remained symptomatic despite treatment with approved doses of H_1 antihistamines were randomized (1:1:1:1) in a double-blind manner to subcutaneous omalizumab 75 mg (n = 78), 150 mg (n = 80), or 300 mg (n = 81) or placebo (n = 80) every 4 weeks for 24 weeks followed by 16 weeks of follow-up. The primary outcome measured was change from baseline in weekly itch severity score (ISS) at week 12. Secondary outcomes evaluated at week 12, included changes from baseline in UAS7 and weekly number of hives score; time to MID response (≥ 5-point decrease) in weekly ISS; the proportion of patients with UAS7 ≤ 6; the proportion of weekly ISS MID responders; changes from baseline in weekly size of largest hive score and overall DLQI score; the proportion of angioedema-free days during weeks 4 to 12; and the proportion of patients with complete response (UAS7 = 0). Compared with placebo mean weekly ISS was reduced from baseline to week 12 by an additional 2.96 points (95% confidence interval (CI): −4.71 to −1.21; $p = 0.0010$), 2.95 points (95% CI: −4.72 to −1.18; $p = 0.0012$), and 5.80 points (95% CI: −7.49 to −4.10; $p < 0.0001$) in the omalizumab 75-mg, 150-mg, and 300-mg groups, respectively. The omalizumab 300-mg group met all nine secondary end points, including a significant decrease in the duration of time to reach minimally important difference response (≥ 5-

point decrease) in weekly ISS ($p < 0.0001$) and higher percentages of patients with well-controlled symptoms (urticaria activity score over 7 days (UAS7) ≤ 6: 51.9% vs. 11.3% $p < 0.0001$) and complete response (UAS7 = 0: 35.8% vs. 8.8% $p < 0.0001$) versus placebo. During the 24-week treatment period, the proportions of patients who experienced one or more treatment-emergent adverse events (AEs) ranged from 57 to 69% in the omalizumab groups versus 51% in the placebo group. Additionally, 2 (2.9%), 3 (3.4%), 0, and 4 (5.0%) patients in the omalizumab 75-mg, 150-mg, 300-mg, and placebo groups, respectively, experienced a serious adverse event. Omalizumab 300 mg administered every 4 weeks reduced weekly ISS and other symptom scores versus placebo in CIU/CSU patients who remained symptomatic despite treatment with approved doses of H_1 antihistamines. Additionally, the results of this study showed a sustained treatment effect of omalizumab 300 mg for up to 24 weeks on CIU/CSU symptom scores in patients with H1 antihistamine–refractory CIU/CSU. The safety profile for omalizumab over 24 weeks of treatment in patients with CIU/CSU receiving approved doses of H1 antihistamines was consistent with the established safety profile in allergic asthma and with previous observations in CIU/CSU.

Nasal Polyps

Omalizumab is indicated for nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.

The safety and efficacy of omalizumab was evaluated in two, randomized, multicenter, double-blind, placebo-controlled clinical trials that enrolled patients with nasal polyps with inadequate response to nasal corticosteroids (Nasal Polyps Trial 1, n = 138; Nasal Polyps Trial 2, n = 127). Patients received omalizumab or placebo subcutaneously every 2 or 4 weeks, for 24 weeks followed by a 4-week follow-up period. All patients received background nasal mometasone therapy during both the treatment period and during a 5-week run-in period. Prior to randomization, patients were required to have evidence of bilateral polyps as determined by a nasal polyp score (NPS) ≥ 5 with NPS ≥ 2 in each nostril, despite use of nasal mometasone during the run-in period. NPS was measured via endoscopy and scored (range 0-4 per nostril: 0 = no polyps; 1 = small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2 = polyps reaching below the lower border of the middle turbinate; 3 = large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4 = large polyps causing complete obstruction of the inferior nasal cavity) for a total NPS (range 0-8). Patients were furthermore required to have a weekly average of nasal congestion score (NCS) > 1 prior to randomization, despite use of nasal mometasone. Nasal congestion was measured by a daily assessment on a 0 to 3-point severity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). Prior sino-nasal surgery or prior systemic corticosteroid usage were not required for inclusion in the trials and sinus CT scans were not performed to evaluate for sinus opacification.

The co-primary endpoints in Trials 1 and 2 were NPS and average daily NCS at Week 24. In both trials, patients who received omalizumab had a statistically significant greater improvement from baseline at Week 24 in NPS and weekly average NCS, than patients who received placebo. The greater improvements in NPS and NCS in the omalizumab group compared to the placebo group were observed as early as the first assessment at Week 4 in both studies.

Omalizumab had statistically significant improvements on sense of smell score compared to placebo. Sense of smell was measured by a daily assessment on a 0 to 3-point severity scale (0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms). The LS mean difference for change from baseline at Week 24 in sense of smell score in omalizumab compared to placebo was -0.3 (95% CI: -0.6, -0.1) in Trial 1 and -0.5 (95% CI: -0.7, -0.2) in Trial 2. Omalizumab had statistically significant improvements on post-nasal drip compared to placebo. The LS mean difference for change from baseline at Week 24 in post-nasal drip score in omalizumab compared to placebo was -0.6 (95% CI: -0.8, -0.3) in Trial 1 and -0.5 (95% CI: - 0.8, -0.3) in Trial 2. Omalizumab had statistically significant improvements on runny nose compared to placebo. The LS mean difference for change from baseline at Week 24 in runny nose score in omalizumab compared to placebo was -0.4 (95% CI: -0.7, -0.2) in Trial 1 and -0.6 (95% CI: - 0.9, -0.4) in Trial 2. In a pre-specified pooled analysis of systemic corticosteroid use during the 24-week treatment period, there was no significant reduction in systemic corticosteroid use between the treatment arms. The proportion of patients taking systemic corticosteroid in omalizumab was 2.3% compared to 6.2% in placebo. The odds-ratio of systemic corticosteroid use with omalizumab compared to placebo was 0.4 (95% CI: 0.1, 1.5). There were no sino-nasal surgeries reported, in either placebo or omalizumab arms, in either trial.

IgE-Mediated Food Allergy

The use of Xolair in the treatment of IgE-mediated food allergy was studied in 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). Patients were randomized to Xolair or placebo for 16 to 20 weeks. The efficacy analysis included 165 pediatric patients. The primary endpoint was 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 (refer to table below).

Food, Challenge Dose	Response Rate		Treatment Difference (95% CI)
	Xolair	Placebo	
Peanut, ≥ 600 mg	68%	5%	63% (50, 73)
Peanut, ≥ 1000 mg	65%	0%	65% (56, 74)
Cashew, ≥ 1000 mg	42%	3%	39% (20, 53)
Milk, ≥ 1000 mg	66%	11%	55% (29, 73)
Egg, ≥ 1000 mg	67%	0%	67% (49, 80)

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.

Unproven

Seasonal Allergic Rhinitis

Researchers conducted a systemic review and meta-analysis of the efficacy and safety of omalizumab in poorly controlled allergic rhinitis in randomized controlled trials dating through 2013. Eleven studies that assessed 2870 randomized patients were included. A statistically significant reduction in the daily nasal symptom severity score [standardized mean difference -0.67 (95% CI, -1.3 to -0.31); p < .0001; I(2), 92%] and a statistically significant reduction in daily nasal rescue medication score [-0.22 (95% CI, -0.39 to -0.05); p = 0.01; I(2), 58%] were observed. There was not a statistically significant difference in the occurrence of any adverse event [relative risk 1.06 (95% CI, 0.94-1.19); I(2), 55%].The meta-analysis showed that, in seasonal and perennial allergic rhinoconjunctivitis, treatment with omalizumab provided an improvement of the daily nasal symptom severity score (DNSSS) and a reduction of antiallergic medication use compared with placebo. The rhinosinusitis-related quality of life (rQoL) appeared to be improved in the limited randomized evidence available. The observed safety profile indicated an adequate tolerability and a comparable overall AEs pattern, The potential benefits of omalizumab need to be considered in the context of costs of therapy and rare AEs. Larger clinical trials and economic studies are needed to address issues of rare events occurrence and cost-effectiveness, respectively.

Several studies have evaluated the use of omalizumab therapy in children, adolescents, and adults with seasonal allergic rhinitis. Though results appear to be promising, additional trials are warranted to establish long-term efficacy and safety, as well as appropriate dosage and timing.

Perennial Allergic Rhinitis

Corren et al. assessed 19 patients (ages 18-65 years) with perennial allergic rhinitis in a 26 week open-label study of intravenous (IV) omalizumab 0.015-0.03mg/kg/IgE (IU/mL) every 2 weeks. Serum free IgE concentrations decreased by up to 99%. Nasal allergen challenge symptom scores (e.g., sneezing, rhinorrhea) decreased significantly.

In another study, 40 patients with perennial allergic rhinitis receiving open-label omalizumab 0.015-0.030 mg/kg/IgE (IU/mL) IV every 2 weeks for 28 weeks showed up to 99% decrease in serum free IgE and decreased reaction to wheal-and-flare skin tests at day 98. However, upon decreased dosage to 0.0015-0.005mg/kg/IgE (IU/mL) for another 18 weeks, serum free IgE and skin test reactivity increased significantly and returned to baseline upon discontinuation.

Chervinsky et al. studied the efficacy, safety, and tolerability of omalizumab in the short-term treatment of patients 12 to 70 years of age with perennial allergic rhinitis with moderate to severe symptoms in a randomized, double-blind trial. The patients completed 16 weeks of either placebo (n = 145) or at least 0.016 mg/kg/IgE (IU/mL) subcutaneous omalizumab every four weeks (n = 144). Patients maintained a diary of their daily symptoms including nasal severity scores throughout the study period, which was based on a 4-point scale (0 = no symptoms to 3 = severe symptoms). Patients in the omalizumab group had a 69% reduction in the average daily nasal severity score from baseline compared to 49% of the placebo treated patients (p = 0.001). Symptoms were controlled, which was defined as a score of less than 0.75 on a 4 point scale, in 28% (40/143) of patients in the omalizumab group compared to 10% (14/145) of patients in the placebo

group. In both study groups, antihistamine use was low, however omalizumab significantly decreased antihistamine use per month more than placebo (omalizumab; 4.5 to 1.5 days per month, placebo: 3.6 to 2.7 days per month, p = 0.005). Three patients in each group dropped out due to intolerance of study medication or placebo, but no severe safety concerns were noted throughout the study. In this study, there was a large placebo effect making the true effect of omalizumab difficult to determine. Additional and larger studies are needed in this population.

Atopic Dermatitis

Heil et al. investigated the effects of omalizumab or placebo on the expression of IgE and its receptors on cells and on serum components of patients with atopic dermatitis (AD). Additional evaluation included whether omalizumab would revert preexisting lesions in patients with long lasting and ongoing AD. Twenty patients were randomized 2:1 in a placebo-controlled, double blind study for 16 weeks. Male and female patients (ages 12-60 years) with a clinical diagnosis of AD and a serum IgE between 30 and 1300 IU/ml were included. Patients in the omalizumab treatment had reduced serum levels of free IgE and decreased surface-bound IgE. However, omalizumab treatment did not significantly alter several measures of clinical disease activity (i.e., atopy patch test results in single patients). Researchers conclude that a therapeutic benefit of omalizumab treatment, if present at all, would be seen in patients with acute rather than chronic forms of AD.

Acute Bronchospasm or Status Asthmaticus

The US Food and Drug Administration (FDA) has required the manufacturer of omalizumab to state in its labeling that Xolair cannot be used to treat acute bronchospasm or status asthmaticus.

Professional Societies

Allergic Asthma

The Global Initiative for Asthma (GINA, 2024) defines uncontrolled, difficult-to-treat, and severe asthma as follows:

- Uncontrolled asthma is asthma with poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma) and/or frequent exacerbations (≥ 2/year) requiring OCS, or serious exacerbations (≥ 1/year) requiring hospitalization.
- Difficult-to-treat asthma is asthma that is uncontrolled despite prescribing of medium- or high-dose ICS with a second controller (usually a LABA) or maintenance OCS, or that requires high-dose treatment to maintain good symptom control and reduce the risk of exacerbations.
- Severe asthma is asthma that is uncontrolled despite adherence with maximal optimized high-dose ICS-LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased. Asthma is not classified as severe if it markedly improves when contributory factors such as inhaler technique and adherence are addressed.

The Global Initiative for Asthma (GINA, 2024) recommends add-on biologic therapy for treatment of adults, adolescents, and children with uncontrolled severe asthma despite optimized maximal therapy as follows:

- Add-on anti-immunoglobulin E (anti-IgE) treatment (omalizumab) for patients aged ≥ 6 years) with severe allergic asthma (Evidence A)
- Add-on anti-interleukin 5/5R treatment (subcutaneous mepolizumab for patients aged ≥ 6 years; intravenous reslizumab for ages ≥ 18 years; subcutaneous benralizumab for ages ≥ 12 years) with severe eosinophilic asthma (Evidence A)
- Add-on anti-interleukin-4R α treatment (subcutaneous dupilumab) for patients aged ≥ 6 years with severe eosinophilic/Type 2 asthma, or for adults or adolescents requiring treatment with maintenance OCS. (Evidence A)
- Add-on anti-thymic stromal lymphopoietin (anti-TSLP) treatment (subcutaneous tezepelumab for patients aged ≥ 12 years with severe asthma (Evidence A)

The first European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines on severe asthma were published in 2014. Severe asthma was defined as that which requires treatment with high-dose ICSs plus a second controller (or systemic corticosteroids) to prevent progression to uncontrolled disease status or continuing uncontrolled disease status despite this therapy. Emphasis was placed on the necessity to confirm the diagnosis of asthma and exclude other conditions that may mimic asthma. In addition, the guidelines recognized that severe asthma is a heterogeneous condition consisting of phenotypes such as severe eosinophilic asthma, and specific recommendations were made on the use of sputum eosinophil count and exhaled nitric oxide fraction (F_{ENO}) to guide therapy. Recommendations were also made for the use of methotrexate, macrolide antibiotics, antifungal agents, bronchial thermoplasty and the anti-IgE antibody omalizumab in severe asthma.

In 2020, the European Respiratory Society (ERS)/American Thoracic Society (ATS) published updated guidelines for the management of asthma. Six specific and important questions were formulated using the PICO (Patient population, Intervention, Comparison and Outcome) format. The GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach was used to assess the strength of evidence and develop recommendations. These recommendations are summarized below:

- An anti-interleukin (IL)-5 and anti-IL-5 receptor α for severe uncontrolled adult eosinophilic asthma phenotypes
- A blood eosinophil cut-point ≥ 150 μL^{-1} to guide anti-IL-5 initiation in adult patients with severe asthma
- Specific eosinophil (≥ 260 μL^{-1}) and exhaled nitric oxide fraction (≥ 19.5 ppb) cut-offs to identify adolescents or adults with the greatest likelihood of response to anti-IgE therapy
- Inhaled tiotropium for adolescents and adults with severe uncontrolled asthma despite Global Initiative for Asthma (GINA) step 4-5 or National Asthma Education and Prevention Program (NAEPP) step 5 therapies
- A trial of chronic macrolide therapy to reduce asthma exacerbations in persistently symptomatic or uncontrolled patients on GINA step 5 or NAEPP step 5 therapies, irrespective of asthma phenotype
- Anti-IL-4/13 for adult patients with severe eosinophilic asthma and for those with severe corticosteroid-dependent asthma regardless of blood eosinophil levels

Nasal Polyps

In 2023, the Joint Task Force on Practice Parameters (JTFPP) published GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. The guideline panel used the Grading of Recommendations Assessment, Development and Evaluation approach to inform and develop recommendations. The task force recommended the use of biologics rather than no biologics (conditional recommendation based on moderate certainty of evidence) in the following patients:

- For patients using inhaled corticosteroid (INCS) for at least 4 weeks and who continue to have high disease burden, biologics may be preferred over other medical treatment choices.
- For patients who have higher disease severity at presentation, biologics may be preferred over other medical treatment choices.
- There is variability in efficacy among the biologics and this may influence the overall choice. Dupilumab and omalizumab are the most beneficial for most patient-important outcomes when comparing with other biologics.
- Patients with comorbid diseases that led to a dual indication for biologic treatment (e.g., asthma) may be a reason to choose biologics in general and even specific biologics.

Chronic Urticaria

In 2014, the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology updated the practice parameter for the diagnosis and management of acute and chronic urticaria (CU). The practice parameter established a step-care approach to the treatment of chronic urticaria and angioedema. The task force recommended the following step-care treatment approach:

- Monotherapy with second-generation antihistamines: H1-antagonists are effective in the majority of patients with CU but might not achieve complete control in all patients.
- Dose advancement of H1-antihistamine therapy, combining first- and second-generation agents and adding an H2-antihistamine and/or an antileukotriene agent: Higher doses of second-generation antihistamines can provide greater efficacy when control is not achieved with conventional doses of these agents.
- Therapeutic trial of potent antihistamine (e.g., hydroxyzine or doxepin): First-generation antihistamines should be prescribed cautiously in the elderly or patients with occupations (e.g., machine operators, airline pilots, or alpine skiers) for which alertness is essential.
- Add an immunosuppressant or biologic agent: Omalizumab and cyclosporine have the greatest published experience documenting efficacy in patients with CU compared with all other alternative agents.

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 approved by the U.S. Food and Drug Administration (FDA) for use in adults and adolescents 6 years of age and older, who have moderate to severe persistent asthma and a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair is not indicated for acute bronchospasm or status asthmaticus. Xolair is also approved for chronic idiopathic urticaria in adults and adolescents (12 years of age and above) who remain symptomatic despite H_1 antihistamine treatment. It is not indicated for other allergic conditions or other forms of urticaria. Xolair is also indicated for 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. Xolair is also indicated in 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. Xolair is to be used in conjunction with food allergen avoidance when being used in the treatment of IgE-mediated food allergy. It is not indicated for the emergent treatment of allergic reactions including anaphylaxis conditions or other forms of urticaria. Because of the risk of anaphylaxis, healthcare providers administering Xolair should observe patients closely for an appropriate period of time and be prepared to manage anaphylaxis that can be life-threatening.[3]

References

1. 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 Dermatol. 2015 Jan;135(1):67-75.
2. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, 2024. Available at http://www.ginasthma.org. Accessed July 2, 2025.
3. Xolair® [package insert]. South San Francisco, CA: Genentech, Inc., February 2024.
4. National Institute for Health and Care Excellence (NICE). Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201). London (UK): National Institute for Health and Care Excellence (NICE); 2013 Apr. 64 p. (Technology appraisal guidance; no. 278).
5. Casale TB, Condemi J, LaForce C, et al. Omalizumab Seasonal Allergic Rhinitis Trial Group. Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. JAMA. 2001;286(23):2956-67.
6. Nayak A, Casale T, Miller SD, et al. Tolerability of retreatment with omalizumab, a recombinant humanized monoclonal anti-IgE antibody, during a second ragweed pollen season in patients with seasonal allergic rhinitis. Allergy Asthma Proc. 2003;24(5):323-9.
7. Rolinck-Werninghaus C, Hamelmann E, Keil T, et al. The co-seasonal application of anti-IgE after pre-seasonal specific immunotherapy decreases ocular and nasal symptom scores and rescue medication use in grass pollen allergic children. Allergy. 2004;59(9):973-979.
8. Kuehr J, Brauburger J, Zielen S, et al. Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis. J Allergy Clin Immunol. 2002;109(2):274-80.
9. Kopp MV Hamelmann E, Zielen S, et al. Combination of omalizumab and specific immunotherapy is superior to immunotherapy in patients with seasonal allergic rhino-conjunctivitis and co-morbid seasonal allergic asthma. Clin and Exp Allergy. 2009;39(2):271-9.
10. Casale TB, Busse WW, Kline JN, et al. Immune Tolerance Network Group. Omalizumab pretreatment decreases acute reactions after rush immunotherapy for ragweed-induced seasonal allergic rhinitis. J Allergy Clin Immunol. 2006;117(1):134-40.
11. Corren J, Diaz-Sanchez D, Saxon A, et al. Effects of omalizumab, a humanized monoclonal anti-IgE antibody, on nasal reactivity to allergen and local IgE synthesis. Ann Allergy Asthma Immunol. 2004;93(3):243-8.
12. Corren J, Shapiro G, Reimann J, et al. Allergen skin tests and free IgE levels during reduction and cessation of omalizumab therapy. J Allergy Clin Immunol. 2008;121(2):506-11.
13. Tsabouri S, Tseretopoulou X, Priftis K, et al. Omalizumab for the treatment of inadequately controlled allergic rhinitis: a systematic review and meta-analysis of randomized clinical trials. J Allergy Clin Immunol Pract. 2014 May-Jun;2(3):332-40.
14. Bernstein JA, Lang DM, Khan DA, et al. Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology. Practice parameter: The diagnosis and management of acute and chronic urticaria: 2014 update. J Allerg Clin Immunol. 2014; 133(5):1270-1277.
15. Milgrom H, Fowler-Taylor A, Vidaurre CF, et al. Safety and tolerability of omalizumab in children with allergic (IgE-mediated) asthma. Curr Med Res Opin. 2011 Jan;27(1):163-9.
16. Heil PM, Maurer D, Klein B, et al. Omalizumab therapy in atopic dermatitis: depletion of IgE does not improve the clinical course - a randomized, placebo-controlled and double blind pilot study. J Dtsch Dermatol Ges. 2010;8(12):990.

17. Kulus M, Hébert J, Garcia E, et al. Omalizumab in children with inadequately controlled severe allergic (IgE-mediated) asthma. Curr Med Res Opin. 2010 Jun;26(6):1285-93.
18. Zielen S, Lieb A, De La Motte S, et al. Omalizumab Protects against Allergen-Induced Bronchoconstriction in Allergic (Immunoglobulin E-Mediated) Asthma. Int Arch Allergy Immunol. 2013;160(1):102-10.
19. Vennera M del C, Pérez De Llano L, Bardagí S, et al. Omalizumab therapy in severe asthma: experience from the Spanish registry--some new approaches. J Asthma. 2012 May;49(4):416-22.
20. Sorkness CA, Wildfire JJ, Calatroni A, et al. Reassessment of omalizumab-dosing strategies and pharmacodynamics in inner-city children and adolescents. J Allergy Clin Immunol Pract. 2013 Mar;1(2):163-71.
21. Deschildre A, Marguet C, Salleron J, et. al., Add-on omalizumab in children with severe allergic asthma: a 1-year real life survey. Eur Respir J. 2013 Nov;42(5):1224-33.
22. Maselli DJ, Singh H, Diaz J, Peters JI. Efficacy of omalizumab in asthmatic patients with IgE levels above 700 IU/mL: a retrospective study. Ann Allergy Asthma Immunol. 2013 Jun;110(6):457-61.
23. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014 May;133(5):1270-7.
24. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation, and treatment of severe asthma. Eur Respir J. 2014 Feb:43(2):343-73.
25. 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 2020146(3): 595-605.
26. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020 Jan 2;55(1):1900588. doi: 10.1183/13993003.00588-2019. PMID: 31558662.
27. 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.
28. Wood RA, Togias A, Sicherer SH, et al. Omalizumab for the Treatment of Multiple Food Allergies. n *Engl J Med*. Published online February 25, 2024. doi:10.1056/NEJMoa2312382.
29. Anvari S, Miller J, Yeh CY, Davis CM. IgE-Mediated Food Allergy. Clin Rev Allergy Immunol. 2019;57(2):244-260. doi:10.1007/s12016-018-8710-3.

Policy History/Revision Information

Date	Summary of Changes
10/01/2025	**Coverage Rationale** • Revised coverage criteria; replaced criterion requiring "the patient is not receiving any of [the listed therapies] in combination with Xolair" with "the patient is not receiving any of [the listed therapies] in combination with Xolair *for treatment of the same indication*" **Applicable Codes** • Updated list of applicable ICD-10 diagnosis codes to reflect annual edits: o Added Z91.0110, Z91.0111, Z91.0112, Z91.0120, Z91.0121, and Z91.0122 o Removed Z91.011 and Z91.012 **Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version IEXD0033.13

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare 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 benefit 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. UnitedHealthcare 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.

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