PRIOR AUTHORIZATION POLICY

POLICY: Immunologicals – Xolair Prior Authorization Policy
- Xolair® (omalizumab subcutaneous injection – Genentech/Novartis)

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INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xolair, an anti-immunoglobulin (Ig)E monoclonal antibody, is indicated for the following uses:[1]

- **Asthma,** in patients ≥ 6 years of age with moderate to severe persistent disease who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids (ICSs). Xolair has been shown to decrease the incidence of asthma exacerbations in these patients. Limitations of Use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus. It is also not indicated for the treatment of other allergic conditions.
- **Chronic rhinosinusitis with nasal polyps** (CRSwNP), as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids.

- **Chronic spontaneous urticaria**, in patients ≥ 12 years of age who remain symptomatic despite H_1 antihistamine treatment. Limitation of Use: Xolair is not indicated for the treatment of other forms of urticaria.
- **IgE-mediated food allergy**, in patients ≥ 1 year of age, 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. Limitation of Use: Xolair is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

Dosing of Xolair for the treatment of asthma or nasal polyps is based on body weight and the serum total IgE level measured before the start of treatment.[1] Dosing for these indications is only provided for patients with a pretreatment serum IgE level ≥ 30 IU/mL. Dosing of Xolair in patients with chronic idiopathic urticaria is not dependent on serum IgE level or body weight.

Clinical Efficacy

Timing of efficacy assessments varied by indication across the numerous pivotal studies in which Xolair demonstrated benefit. In the majority of the asthma trials, efficacy with Xolair was assessed as early as 16 weeks.[1-11] In chronic spontaneous urticaria, one of the studies included a 12-week double-blind treatment period, while the other was longer with 24 weeks of double-blind treatment.[12,13] Across both studies evaluating Xolair in CRSwNP, efficacy was evaluated at Week 24.[14] Patients continued treatment with intranasal corticosteroids throughout the study. In the pivotal study of Xolair for food allergy, patients were required to have a positive skin prick test response to a food and to have a positive IgE test (blood test) to food.[15] Patients were provided with an epinephrine auto-injector throughout the study.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2025) proposes a step-wise approach to asthma treatment.[16] Xolair is listed as an option for add-on therapy in patients ≥ 6 years of age with severe allergic asthma. Severe asthma is defined as asthma that is uncontrolled despite adherence to optimized high-dose ICS/long-acting $beta_2$-agonist (LABA) therapy or that worsens when high-dose treatment is decreased. Allergy-driven symptoms and childhood-onset asthma may predict a good asthma response to Xolair.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.[17,18] Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20;

2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;
3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: forced expiratory volume in 1 second (FEV_1) < 80% predicted after appropriate bronchodilator withholding.

Chronic Rhinosinusitis with Nasal Polyps Guidelines

The Joint Task Force on Practice Parameters (JTFPP) published a focused guideline update for the medical management of CRSwNP (2023), which updated recommendations regarding intranasal corticosteroids and biologic therapies.[20] Intranasal corticosteroids are recommended for the treatment of CRSwNP. Use of biologics (e.g., Xolair) are also recommended. However, in patients who derived a sufficient benefit from other therapies such as intranasal corticosteroids, surgery, or aspirin therapy after desensitization, biologics may not be preferred. Conversely, biologics may be preferred over other medical treatment options in patients who continue to have a high burden of disease despite receiving at least 4 weeks of treatment with an intranasal corticosteroid.

The diagnosis of CRSwNP was not addressed in this focused guideline update. Previous guidelines have noted that the presence of two or more signs and symptoms of chronic rhinosinusitis (e.g., rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge) that persist for an extended period of time makes the diagnosis of chronic rhinosinusitis likely.[21-24] However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Oral corticosteroids and surgical intervention were not specifically addressed in this update. Prior guidelines recommend short courses of oral corticosteroid as needed and consideration of surgical removal as an adjunct to medical therapy in patients with CRSwNP that is not responsive or is poorly responsive to medical therapy.[21,22,24]

Chronic Spontaneous Urticaria Guidelines

Guidelines for the definition, classification, diagnosis, and management of urticaria have been published by the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/Asia Pacific Association of Allergy, Asthma and Clinical Immunology (2022).[19] The American Academy of Dermatology was involved in the development of these guidelines and endorses their recommendations. Chronic spontaneous urticaria is defined as the appearance of wheals, angioedema, or both for > 6 weeks due to known or unknown causes. Signs and symptoms may be present daily/almost daily or have an intermittent recurrent course. Second generation H_1-antihistamines taken regularly are the recommended first-line treatment for all types of urticaria following elimination of possible underlying causes. If standard doses do not eliminate urticaria signs and symptoms, the dose of the antihistamine should be increased up to 4-fold. If symptoms persist following 2 to 4 weeks of antihistamine therapy, the addition of Xolair may be considered. For patients with refractory chronic urticaria, the addition of Xolair may be considered. Short courses of rescue systemic corticosteroids are

recommended for treatment of patients with acute exacerbations of chronic urticaria. However, guidelines recommend against the long-term use of systemic steroids.

Food Allergy Guidelines

Consensus-based guidance on the use and implementation of Xolair as food allergy treatment from the American Academy of Allergy, Asthma, and Immunology Adverse Reactions to Foods Committee (2025) note that Xolair is a potential treatment option which can be offered to patients with one or more IgE-mediated food allergies.[25] All candidates for Xolair therapy for food allergy should have a total IgE level that allows for Xolair dosing (i.e., > 30 to < 1,850 IU/mL). It is also recommended that patients have evidence of sensitization determined via either (or both) a positive food-specific skin prick test or measurement of a serum-specific IgE level to a food that would indicate a high likelihood of having an IgE-mediated reaction within the context of the patient's history. Both skin testing and specific IgE testing are not required as long as sensitization can be documented to one or more foods.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xolair. All approvals are provided for the duration noted below. In cases where approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xolair, as well as the monitoring required for adverse events and long-term efficacy, approval requires Xolair to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Xolair® (omalizumab subcutaneous injection - Genentech/Novartis) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Asthma.** Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient has a baseline immunoglobulin E (IgE) level ≥ 30 IU/mL; AND
       Note: "Baseline" is defined as prior to receiving any treatment with Xolair or another monoclonal antibody therapy that may lower IgE levels (e.g., Dupixent [dupilumab subcutaneous injection], Tezspire [tezepelumab-ekko subcutaneous injection]).
     - **iii.** Patient has a baseline positive skin test or *in vitro* test (i.e., a blood test) for allergen-specific immunoglobulin E (IgE) for one or more perennial aeroallergens and/or for one or more seasonal aeroallergens; AND
       Note: "Baseline" is defined as prior to receiving any Xolair or another monoclonal antibody therapy that may interfere with allergen testing (e.g.,

Dupixent and Tezspire). Examples of perennial aeroallergens are house dust mite, animal dander, cockroach, feathers, and mold spores. Examples of seasonal aeroallergens are grass, pollen, and weeds.

iv. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
- **a)** An inhaled corticosteroid; AND
- **b)** At least one additional asthma controller or asthma maintenance medication; AND

  Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting beta$_2$-agonists, inhaled long-acting muscarinic antagonists, and monoclonal antibody therapies for asthma (e.g., Xolair, Cinqair [reslizumab intravenous infusion], Dupixent, Fasenra [benralizumab subcutaneous injection], Nucala [mepolizumab subcutaneous injection], and Tezspire. Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfil the requirement for both criteria a and b.

v. Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, or e):

Note: "Baseline" is defined as prior to receiving Xolair or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Cinqair, Dupixent, Fasenra, Nucala, Tezspire, and Xolair.
- **a)** Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
- **b)** Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR
- **c)** Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR
- **d)** Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR
- **e)** Patient has asthma that worsens upon tapering of oral corticosteroid therapy; AND

vi. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; OR

B) Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has already received at least 4 months of therapy with Xolair; AND

Note: A patient who has received < 4 months of therapy or who is restarting therapy with Xolair should be considered under criterion 1A (Asthma, Initial Therapy).

ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND

iii. Patient has responded to therapy as determined by the prescriber.

Note: Examples of a response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department, urgent care, or medical clinic visits due to asthma;

decreased reliever/rescue medication use; and improved lung function parameters.

2. Chronic Rhinosinusitis with Nasal Polyps. Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi, vii, and viii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has chronic rhinosinusitis with nasal polyps as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND

iii. Patient has had the diagnosis of chronic rhinosinusitis with nasal polyps for at least 6 months; AND

iv. Patient has experienced two or more of the following symptoms for at least 8 weeks: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND

v. Patient has a baseline immunoglobulin E (IgE) level ≥ 30 IU/mL; AND
Note: "Baseline" is defined as prior to receiving any treatment with Xolair or another monoclonal antibody therapy that may lower IgE levels (e.g., Dupixent [dupilumab subcutaneous injection], Tezspire [tezepelumab-ekko subcutaneous injection]).

vi. Patient meets BOTH of the following (a and b):

a) Patient has received at least 4 weeks of therapy with an intranasal corticosteroid; AND

b) Patient will continue to receive therapy with an intranasal corticosteroid concomitantly with Xolair; AND

vii. Patient meets ONE of the following (a, b, or c):

a) Patient has received at least one course of treatment with a systemic corticosteroid within the previous year; OR
Note: One course of a systemic corticosteroid is ≥ 3 consecutive days of treatment or one long-acting injectable dose.

b) Patient has a contraindication to systemic corticosteroid therapy; OR

c) Patient has had prior surgery for nasal polyps; AND

viii. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose, and throat [ENT] physician specialist); OR

B) Patient is currently receiving Xolair. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has already received at least 6 months of therapy with Xolair; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 2A (Nasal Polyps, Initial Therapy).

ii. Patient continues to receive therapy with an intranasal corticosteroid; AND

iii. Patient has responded to Xolair therapy as determined by the prescriber.
Note: Examples of a response to Xolair therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, and/or improved sense of smell.

3. **Chronic Spontaneous Urticaria.** Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient has/had urticaria for ≥ 6 weeks (prior to treatment with Xolair); AND
     - **iii.** According to the prescriber, the patient has tried high-dose oral second-generation H_1 antihistamine therapy; AND
       Note: High-dose oral second-generation H_1 antihistamine therapy is the highest dose tolerated by the patient and can be up to four times the FDA-approved dose. Examples of second-generation H_1 antihistamines are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.
     - **iv.** The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist; OR
   - **B)** Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has already received at least 6 months of therapy with Xolair; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 3A (Chronic Spontaneous Urticaria, Initial Therapy).
     - **ii.** Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, or c):
       - **a)** Decreased itch severity; OR
       - **b)** Decreased number of hives; OR
       - **c)** Decreased size of hives.

4. **Immunoglobulin (Ig)E-Mediated Food Allergy**. Approve Xolair for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   - **A)** Patient is ≥ 1 year of age; AND
   - **B)** Patient has a baseline immunoglobulin (Ig)E level ≥ 30 IU/mL; AND
     Note: "Baseline" is defined as prior to receiving any treatment with Xolair or another monoclonal antibody therapy that may lower IgE levels (e.g., Dupixent [dupilumab subcutaneous injection], Tezspire [tezepelumab-ekko subcutaneous injection]).
   - **C)** Patient meets ONE of the following(i or ii):
     - **i.** Patient has a positive skin prick test response to one or more foods; OR
     - **ii.** Patient has a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods; AND
   - **D)** According to the prescriber, the patient has a history of an allergic reaction to a food that met each of the following (i, ii, and iii):
     - **i.** Patient demonstrated signs and symptoms of a significant systemic allergic reaction; AND
       Note: Signs and symptoms of a significant systemic allergic reaction include hives, swelling, wheezing, hypotension, and gastrointestinal symptoms.
     - **ii.** This reaction occurred within a short period of time following a known ingestion of the food; AND

iii. The prescriber deemed this reaction significant enough to require a prescription for an epinephrine self-administered injectable or nasal product; AND
Note: Examples of epinephrine self-administered injectable and nasal products include EpiPen, EpiPen Jr., Auvi-Q, generic epinephrine auto-injectors, and Neffy.

E) Patient has been prescribed an epinephrine self-administered injectable or nasal product; AND
Note: Examples of epinephrine self-administered injectable and nasal products include EpiPen, EpiPen Jr., Auvi-Q, generic epinephrine auto-injectors, and Neffy.

F) According to the prescriber, Xolair will be used in conjunction with a food allergen-avoidant diet; AND

G) The medication is prescribed by or in consultation with an allergist or immunologist.

CONDITIONS NOT COVERED

Xolair® (omalizumab subcutaneous injection - Genentech/Novartis) is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Atopic Dermatitis.** One single-center, double-blind, placebo-controlled trial, Atopic Dermatitis Anti-IgE Pediatric Trial (ADAPT) evaluated the efficacy of Xolair in patients 4 to 19 years of age with severe atopic dermatitis (n = 62).[26] After 24 weeks of therapy, the difference in the objective Scoring Atopic Dermatitis [SCORAD] index with Xolair vs. placebo was -6.9 (P = 0.01). This was statistically significant; however, the clinical significance is unknown. Quality of life measurements were also improved with Xolair. Smaller studies have not shown benefit and case studies have yielded mixed results.[26-28] Additional larger, well-designed clinical trials are needed to determine if Xolair has a role in the treatment of atopic dermatitis. Atopic dermatitis guidelines from the American Academy Dermatology (2023) note that there are insufficient data to make a recommendation regarding the use of Xolair.[29]

2. **Concurrent use of Xolair with another Monoclonal Antibody Therapy.** The efficacy and safety of Xolair used in combination with other monoclonal antibody therapies have not been established. There are very limited case reports describing the combined use of Nucala and Xolair for severe asthma as well as off-label indications.[30-35] One limited case series also reported the use of Xolair and Dupixent in patients with asthma or chronic idiopathic urticaria.[36] Further investigation is warranted.
Note: Monoclonal antibody therapies are Adbry® (tralokinumab-ldrm subcutaneous injection), Cinqair® (reslizumab intravenous infusion), Dupixent® (dupilumab subcutaneous injection), Ebglyss™ (lebrikizumab-lbkz SC injection), Fasenra® (benralizumab subcutaneous injection), Nemluvio® (nemolizumab-ilto

SC injection), Nucala® (mepolizumab subcutaneous injection), or Teszpire® (tezepelumab-ekko subcutaneous injection).

3. **Eosinophilic Gastroenteritis, Eosinophilic Esophagitis, or Eosinophilic Colitis.** There are limited and conflicting data from very small studies and case series on the use of Xolair for the treatment of eosinophilic gastrointestinal conditions.[37] Guidelines for the diagnosis and management of eosinophilic esophagitis from the American College of Gastroenterology (2025) recommend against the use of Xolair in patients with this condition.

4. **Latex Allergy in Health Care Workers with Occupational Latex Allergy.** A small European study assessed the effects of Xolair treatment in health care workers (n = 18) with occupational latex allergy.[38] Xolair use in these patients resulted in a reduction in mean conjunctival challenge test scores as compared with placebo-treated patients after 16-weeks of therapy. Also, three patients who did not respond to Xolair treatment during the double-blind phase responded during the 16-week open-label phase. Thus, the overall ocular response rate for all patients in the open-label phase was 93.8% (n = 15/16). Also 11 of 15 patients in the open-label phase had a negative response to a latex glove challenge test (4 patients had a mild response). Well-controlled trials are needed.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xolair® subcutaneous injection [prescribing information]. South San Francisco, CA and East Hanover, NJ: Genentech and Novartis; February 2024.
2. 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):184-190.
3. Finn A, Gross G, van Bavel J, et al. Omalizumab improves asthma-related quality of life in patients with severe allergic asthma. *J Allergy Clin Immunol.* 2003;111(2):278-284.
4. Lanier BQ, Corren J, Lumry W, et al. Omalizumab is effective in the long-term control of severe allergic asthma. *Ann Allergy Asthma Immunol.* 2003;91:154-159.
5. Bousquet J, Wenzel S, Holgate S, et al. Predicting response to omalizumab, an anti-IgE antibody, in patients with allergic asthma. *Chest.* 2004;125(4):1378-1386.
6. 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;18:254-261.
7. Buhl R, Solèr M, Matz J, et al. Omalizumab provides long-term control in patients with moderate-to-severe allergic asthma. *Eur Respir J.* 2002;20:73-78.
8. Buhl R, Hanf G, Solèr M, et al. The anti-IgE antibody omalizumab improves asthma-related quality of life in patients with allergic asthma. *Eur Respir J.* 2002;20:1088-1094.
9. Holgate S, Chuchalin A, Herbert J, et al. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. *Clin Exp Allergy.* 2004;34:632-638.
10. Kulus M, Hebert J, Garcia E, et al. Omalizumab in children with inadequately controlled severe allergic (IgE-mediated) asthma. *Curr Med Res Opin.* 2010;26:1285-1293.
11. Milgrom H, Berger W, Nayak A, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). *Pediatrics.* 2001;108(2).
12. 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;135:67-75.

13. Maurer M, Rosen K, Hsieh HJ, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med.* 2013;368:924-935.
14. 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.
15. Wood RA, Togias A, Sicherer SH, et al. Omalizumab for the treatment of multiple food allergies. *N Engl J Med*. 2024;390(10):889-899..
16. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2025. Available at: http://www.ginasthma.org. Accessed on: July 22, 2025.
17. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43:343-373.
18. Holguin F, Cardet JC, Chung KF, *et al*. Management of severe asthma: a European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J.* 2020;55:1900588.
19. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA2LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2022;73:734-766.
20. Rank MA, Chu DK, Bognanni A, et al. 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.
21. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. *Ann Allergy Asthma Immunol.* 2014:347-385.
22. Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: an evidenced-based focused 2017 guideline update. *Ann Allergy Asthma Immunol.* 2017;119(6):489-511.
23. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Rhinitis 2020: a practice parameter update. *J Allergy Clin Immunol.* 2020;146:721-767.
24. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2S):S1-S39.
25. Anagnostou A, Bird JA, Chinthraja S, et al. The use and implementation of omalizumab as food allergy treatment: Consensus-based guidance and Work Group Report of the Adverse Reactions to Foods Committee of the American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2025;155(1):62-69.
26. Chan S, Cornelius V, Cro S, et al. Treatment effect of omalizumab on severe pediatric atopic dermatitis: the ADAPT randomized clinical trial. *JAMA Pediatr*. 2019;174(1):29-37.
27. Holm JG, Agner T, Sand C, et al. Omalizumab for atopic dermatitis: case series and a systematic review of the literature. *Int J Dermatol.* 2017;56(1):18-26.
28. Wang HH, Li YC, Huang YC, et al. Efficacy of omalizumab in patients with atopic dermatitis: a systematic review and meta-analysis. *J Allergy Clin Immunol*. 2016;138(6):1719-1722.
29. Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2024;90(2):E43-E56.
30. Baccelli A, Kocwin M, Parazzini EM, et al. Long-term outcomes of combination biologic therapy in uncontrolled severe asthma: a case study. *J Asthma*. 2023;60(5):1050-1053.
31. Altman MC, Lenington J, Bronson S, et al. Combination omalizumab and mepolizumab therapy for refractory allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol Pract*. 2017;5(4):1137-1139.
32. Han D, Lee JK. Severe asthma with eosinophilic gastroenteritis effectively managed by mepolizumab and omalizumab. *Ann Allergy Asthma Immunol*. 2018;121(6):742-743.
33. Dedaj R, Unsel L. Case study: a combination of mepolizumab and omalizumab injections for severe asthma. *J Asthma*. 2019;56(5):473-474.
34. Matsumoto T, Sakurai Y, Tashima N, et al. Dual biologics for severe asthma and atopic dermatitis: synopsis of two cases and literature review. *Respirol Case Rep*. 2023;12(1):e01266.
35. Sezgin ME, Colak M, Caglayan O, et al. Efficacy and mepolizumab and omalizumab combination therapy in uncontrolled asthma. *J Asthma*. 2024;61(2):173-175.
36. Gisondi P, Maurelli M, Costanzo A, et al. The combination of dupilumab with other monoclonal antibodies. *Dermatol Ther (Heidelb)*. 2023;13(1):7-12.
37. Dellon ES, Muir AB, Katzka DA, et al. ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. *Am J Gastroenterol*. 2025;120(1):31-59.
38. Leynadier F, Doudou O, Gaouar H, et al. Effect of omalizumab in health care workers with occupational latex allergy [letter]. *J Allergy Clin Immunol.* 2004;113(2):360-361.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Conditions Not Covered:** Criteria were updated to clarify that use of Xolair with another monoclonal antibody therapy is specific to Cinqair, Fasenra, Nucala, Dupixent, Tezspire, and Adbry.	03/22/2023
Selected Revision	**Chronic Rhinosinusitis with Nasal Polyps:** Approval condition updated from "Nasal Polyps" to "Chronic Rhinosinusitis with Nasal Polyps". Duration of the intranasal corticosteroid requirement was changed from 3 months to 4 weeks.	02/14/2024
Early Annual Revision	**Immunoglobulin (IgE)-Mediated Food Allergy:** New approval criteria for this indication were added. **Conditions Not Covered:** "Peanut and Other Food Allergies" was removed as a Condition Not Recommended for Approval.	03/06/2024 and 03/07/2024
Annual Revision	**Asthma:** Leukotriene receptor antagonists were removed as an example of additional asthma controller or asthma maintenance medications. **Immunoglobulin (IgE)-Mediated Food Allergy:** Criteria were updated to require the patient to have either a positive skin prick test response OR a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods. Previously, criteria required the patient to have both a positive skin prick test response and a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods.	03/05/2025
Early Annual Revision	**Chronic Spontaneous Urticaria (Chronic Idiopathic Urticaria):** Approval condition was updated to "Chronic Spontaneous Urticaria (Chronic Idiopathic Urticaria)". Previously, this approval condition was listed as "Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria). The approval duration for this condition was changed from 4 months to 6 months. Criteria for a patient currently receiving Xolair was updated to apply to a patient who has already received at least 6 months of therapy with Xolair. Previously, these criteria applied to a patient who had received at least 4 months of therapy with Xolair. Criteria for a patient currently receiving Xolair was also updated to require that the patient has experienced a beneficial clinical response, defined as either decreased itch severity, decreased number of hives, or decreased size of hives. Previously, these criteria required the patient to have responded to therapy as determined by the prescriber.	04/23/2025
Selected Revision	**Immunoglobulin (Ig)E-Mediated Food Allergy:** Throughout the criteria, references to "epinephrine auto-injectors" were updated to "epinephrine self-administered injectable or nasal products". Neffy was added as an example of an epinephrine self-administered injectable or nasal product.	08/06/2025
Selected Revision	**Chronic Spontaneous Urticaria:** This condition for approval was updated from "Chronic Spontaneous Urticaria (Chronic Idiopathic Urticaria)" to "Chronic Spontaneous Urticaria". Criteria were clarified to require that the patient has/had urticaria for ≥ 6 weeks (previously required > 6 weeks). The requirement that the patient have urticaria symptoms that have been present for > 3 days per week despite daily non-sedating H_1 antihistamine therapy with doses that have been titrated up to a maximum of four times the standard FDA-approved dose was removed. This was replaced with a requirement that the patient has tried high-dose oral second-generation H_1 antihistamine therapy, according to the prescriber. A "Note" was added to clarify that high-dose oral second-generation H_1 antihistamine therapy is the highest dose tolerated by the patient and can be up to four times the FDA-approved dose.	10/29/2025

Selected Revision	**Chronic Rhinosinusitis with Nasal Polyps:** Criteria were updated to require the patient has experienced symptoms for at least 8 weeks. Previously, criteria required the patient to have experienced symptoms for at least 6 months. A requirement that the patient has had the diagnosis of chronic rhinosinusitis with nasal polyps for at least 6 months was added. The requirement that the patient has received at least one course of treatment with a systemic corticosteroid was updated to require that the course of treatment has been within the previous year. Previously, criteria required that the course of treatment was for 5 days or more within the previous 2 years. A "Note" was added to clarify that one course of a systemic corticosteroid is ≥ 3 consecutive days of treatment or one long-acting injectable dose.	11/05/2025