



PRIOR AUTHORIZATION POLICY

POLICY: Immunologicals – Xolair Prior Authorization Policy

- Xolair® (omalizumab subcutaneous injection – Genentech/Novartis)

REVIEW DATE: 03/22/2023

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xolair, an anti-immunoglobulin E (IgE) 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 idiopathic urticaria**, in patients ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment. Limitation of Use: Xolair is not indicated for the treatment of other forms of urticaria.
- **Nasal polyps**, as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids.

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 idiopathic 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 nasal polyps, efficacy was evaluated at Week 24.¹⁴ Patients continued treatment with intranasal corticosteroids throughout the study.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2022) proposes a step-wise approach to asthma treatment.¹⁵ Xolair is listed as an option for add-on therapy in patients ≥ 6 years of age with difficult-to-treat, severe eosinophilic asthma (i.e., asthma that cannot be managed by therapy with medium- to high-dose ICS/formoterol [as both maintenance and reliever therapy] or medium- to high-dose ICS/long-acting beta₂-agonist [LABA] combination therapy with an as needed short-acting beta₂-agonist reliever, with or without an additional controller). Higher blood eosinophil levels, elevated fractional exhaled nitric oxide, 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.^{16,17} 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 (FEV₁) $< 80\%$ predicted after appropriate bronchodilator withholding.

Chronic Urticaria Guidelines

A Practice Parameter on the Diagnosis and Management of Acute and Chronic Urticaria (2014) from the Joint Task Force on Practice Parameters (JTFPP) and guideline from the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/World Allergy Organization (2018) define chronic urticaria as urticaria that has been continuously or intermittently present for at least 6 weeks.^{18,19} Continuous therapy with antihistamines (second generation H₁-antagonists) is generally recommended as first-line pharmacologic treatment for urticaria following trigger avoidance. If

symptoms persist following 2 to 4 weeks of initial therapy, the dose of the second generation H1-antagonist should be increased to up to 4-fold. For patients with refractory chronic urticaria, the addition of Xolair may be considered.

Nasal Polyp Guidelines

A 2014 Practice Parameter on the Diagnosis and Management of Rhinosinusitis (2014) and a Practice Parameter for the Management of Rhinitis from the JTFPP (2020), and a 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology (AAO), make similar recommendations regarding the diagnosis and management of chronic rhinosinusitis with nasal polyposis (CRSwNP).^{20,22-24} 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 CRS likely. However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography scan. Nasal corticosteroids are recommended for the management of CRSwNP, as they decrease nasal polyp size, prevent regrowth of nasal polyps following surgical removal, and improve nasal symptoms. Short courses of oral corticosteroids are also recommended. Endoscopic surgical intervention may be considered as an adjunct to medical therapy in patients with chronic rhinosinusitis that is not responsive or is poorly responsive to medical therapy. The JTFPP parameter lists Xolair as a therapy that may be considered for the treatment of nasal polyps based on the limited data available at the time of publication. The AAO guidelines do not address Xolair.

The European Forum for Research and Education in Allergy expert board on uncontrolled severe CRSwNP and biologics (2021) recommends that these agents, including Xolair, only be used for severe uncontrolled CRSwNP when Type 2 inflammation is present.⁴⁹ Severe CRSwNP is defined as bilateral CRSwNP with a nasal polyp score ≥ 4 and persistent symptoms (e.g., loss of smell/taste, nasal obstruction, secretion or postnasal drip, facial pain or pressure) with the need for add-on treatment to supplement intranasal corticosteroids. Severe CRSwNP is considered to be uncontrolled if the patient has received continuous treatment with an intranasal corticosteroid and has needed at least one course of systemic corticosteroids in the previous 2 years (or has a medical contraindication or intolerance) and/or has a previous sinonasal surgery.

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 conditions (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets the following criteria (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 beta₂-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor 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 (FEV₁) < 80% predicted; OR
 - d) Patient has an FEV₁/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.
- B) Patient is Currently Receiving Xolair.** Approve Xolair for 1 year if the patient meets the following criteria (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 Idiopathic Urticaria (Chronic Spontaneous Urticaria). Approve Xolair for the duration noted if the patient meets one of the following conditions (A or B):

- A) Initial Therapy.** Approve for 4 months if the patient meets the following criteria (i, ii, and iii):
- i. Patient is ≥ 12 years of age; AND
 - ii. Patient has/had urticaria for > 6 weeks (prior to treatment with Xolair), with symptoms present > 3 days per week despite daily non-sedating H₁ antihistamine therapy with doses that have been titrated up to a maximum of four times the standard FDA-approved dose; AND
Note: Examples of non-sedating H₁ antihistamine therapy are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.
 - iii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.
- B) Patient is Currently Receiving Xolair.** Approve Xolair for 1 year if the patient meets the following criteria (i and ii):
- 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 2A (Chronic Idiopathic Urticaria, Initial Therapy).
 - ii. Patient has responded to therapy as determined by the prescriber.

Note: Examples of a response to Xolair therapy are decreased severity of itching, decreased number and/or size of hives.

3. Nasal Polyps. Approve Xolair for the duration noted if the patient meets one of the following conditions (A or B):

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

- i.** Patient is ≥ 18 years of age; AND
- ii.** Patient has chronic rhinosinusitis with nasal polyposis as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND
- iii.** Patient has experienced two or more of the following symptoms for at least 6 months: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND
- iv.** 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]).
- v.** Patient meets BOTH of the following (a and b):
 - a)** Patient has received at least 3 months of therapy with an intranasal corticosteroid; AND
 - b)** Patient will continue to receive therapy with an intranasal corticosteroid concomitantly with Xolair; AND
- vi.** Patient meets ONE of the following (a, b, or c):
 - a)** Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR
 - b)** Patient has a contraindication to systemic corticosteroid therapy; OR
 - c)** Patient has had prior surgery for nasal polyps; AND
- vii.** The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] physician specialist).

B) Patient is currently receiving Xolair. Approve for 1 year if the patient meets the following criteria (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 3A (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.

CONDITIONS NOT COVERED

- **Xolair® (omalizumab subcutaneous injection (Genentech/Novartis)**

is(are) considered experimental, investigational or unproven 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).²⁵ 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.²⁵⁻²⁷ 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 (2014) note that data are limited to determine if Xolair is efficacious.²⁸ These guidelines do not make a recommendation regarding Xolair use in this patient population. European consensus guidelines for the treatment of atopic dermatitis (2018) also note the mixed data and state that they cannot recommend Xolair for the treatment of atopic dermatitis.²⁹
- 2. Concurrent use of Xolair with another Monoclonal Antibody Therapy (i.e., Cinqair, Fasenra, Dupixent, Nucala, Tezspire, or Adbry).** 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.^{21,30-32} Further investigation is warranted.
- 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.³³⁻³⁶ Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association and the Joint Task Force on Allergy-Immunology Practice Parameters (2020) recommend against the use of Xolair in patients with this condition.³⁷
- 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. Peanut and Other Food Allergies. Limited data are available regarding the use of Xolair to facilitate desensitization to food allergens. A Phase II multicenter clinical trial was initiated using Xolair in patients with peanut allergy; however, it was discontinued prematurely due to concerns regarding the safety of the oral peanut challenges in some patients.³⁹ Insufficient data were obtained to reach any conclusions about the efficacy of Xolair. Data are also available from a Phase II study using Xolair as pretreatment in patients receiving multi-food oral immunotherapy, as well as a small pilot study examining the use of Xolair to facilitate rapid oral desensitization in high-risk peanut-allergic patients.^{40,51} There are also minimal data (a Phase I study and a case series) on the use of Xolair to facilitate desensitization in patients with severe cow's milk allergy.⁴¹⁻⁴⁴ Additionally, a Phase I study and a Phase II study have evaluated the use of Xolair to facilitate desensitization in patients with multiple food allergies.^{45,46} Guidelines for the diagnosis and management of food allergy in the US from the National Institute of Allergy and Infectious Diseases (2010; 2017 addendum) indicate there are currently no medications recommended to prevent IgE-mediated or non-IgE-mediated food-induced allergic reactions from occurring in an individual with existing food allergies.⁴⁷ The Practice Parameter on Food Allergy from the JTFPP (2014) also states that immunotherapies (such as the oral immunotherapy desensitization described above) show promise for the treatment of food allergy; however, there is currently inadequate evidence that the therapeutic benefit outweighs the risk.⁴⁸ Trials of these have been uncontrolled, small studies, which are subject to selection bias and uncertain safety profiles. However, treatment with anti-IgE monoclonal antibodies might increase the threshold for doses needed to stimulate an allergic reaction and potentially may enhance the safety profile for patients. A food allergy management guideline from the Global Allergy and Asthma European Network (2022) specifically states that no recommendation can be made for or against the use of Xolair for the treatment of food allergy due to insufficient evidence.⁵⁰ Additional well-controlled trials are needed.

REFERENCES

1. Xolair® subcutaneous injection [prescribing information]. South San Francisco, CA and East Hanover, NJ: Genentech and Novartis; July 2021.
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. Soler 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, Soler 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, Soler 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. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2022. Available at: <http://www.ginasthma.org>. Accessed on: March 15, 2023.
16. 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.
17. 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.
18. Zuberbier T, Aberer W, Asero R, et al. EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy.* 2018;73:1393-1414.
19. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology; the American College of Allergy, Asthma and Immunology; and the Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol.* 2014;133(5):1270-1277.e66.
20. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. *Ann Allergy Asthma Immunol.* 2014:347-385.
21. Baccelli A, Kocwin M, Parazzini EM, et al. Long-term outcomes of combination biologic therapy in uncontrolled severe asthma: a case study. *J Asthma.* 2022 Sept 13. [Online ahead of print].
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. 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.
26. 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.
27. 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.
28. Sidbury R, et al. Guidelines of care for the management of atopic dermatitis Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol.* 2014;71(2): 327-349.
29. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for the treatment of atopic eczema (atopic dermatitis) in adults and children: part II. *J Eur Acad Dermatol Venereol.* 2018;32(6):850-878.
30. 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.
31. Han D, Lee JK. Severe asthma with eosinophilic gastroenteritis effectively managed by mepolizumab and omalizumab. *Ann Allergy Asthma Immunol.* 2018;121(6):742-743.
32. Dedaj R, Unsel L. Case study: a combination of mepolizumab and omalizumab injections for severe asthma. *J Asthma.* 2019;56(5):473-474.
33. Foroughi S, Foster B, Young Kim N, et al. Anti-IgE treatment of eosinophil-associated gastrointestinal disorders. *J Allergy Clin Immunol.* 2007;120(3):594-601.
34. Clayton F, Fang JC, Gleich GJ, et al. Eosinophilic esophagitis in adults is associated with IgG4 and not mediated by IgE. *Gastroenterology.* 2014;147:602-609.
35. Fang JC, Hilden K, Gleich GJ, et al. A pilot study of the treatment of eosinophilic esophagitis with omalizumab. *Gastroenterology.* 2011;140(5):S-235.

36. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis. *Am J Gastroenterol*. 2013;108(5):679-692.
37. Hirano I, Chan ES, Rank MA, et al. AGA Institute and Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786.
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.
39. Sampson HA, Leung DYM, Burks AW, et al. A phase II, randomized, double-blind, parallel-group, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy. *J Allergy Clin Immunol*. 2011;127:1309-1310.e1.
40. Schneider LC, Rachid R, LeBovidge J, et al. A pilot study of omalizumab to facilitate rapid oral desensitization in high-risk peanut-allergic patients. *J Allergy Clin Immunol*. 2013;132(6):1368-1374.
41. Nadeau KC, Schneider LC, Hoyte L, et al. Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy. *J Allergy Clin Immunol*. 2011;127(6):1622-1624.
42. Nilsson C, Nordvall L, Johansson SGO, et al. Successful management of severe cow's milk allergy with omalizumab treatment and CD-sens monitoring. *Asia Pac Allergy*. 2014;4:257-260.
43. Takahashi M, Taniuchi S, Soejima K, et al. Successful desensitization in a boy with severe cow's milk allergy by a combination therapy using omalizumab and rush oral immunotherapy. *Allergy Asthma Clin Immunol*. 2015;11(1):18.
44. Wood RA, Kim JS, Lindblad R, et al. A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy. *J Allergy Clin Immunol*. 2016;137(4):1103-1110.
45. Begin P, Domingues T, Wilson SP, et al. Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using omalizumab. *Allergy Asthma Clin Immunol*. 2014;10(1):7.
46. Andorf S, Purington N, Kumar D, et al. A phase 2 randomized controlled multisite study using omalizumab-facilitated rapid desensitization to test continued vs discontinued dosing in multifoed allergic individuals. *EClinicalMedicine*. 2019;7:27-38.
47. Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-sponsored expert panel report. *J Allergy Clin Immunol*. 2010;126:1105-1118.
48. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology; the American College of Allergy, Asthma and Immunology; and the Joint Council of Allergy, Asthma and Immunology. Food allergy: a practice parameter update – 2014. *J Allergy Clin Immunol*. 2014.
49. Bachert C, Han JK, Wagenmann, et al. EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: definitions and management. *J Allergy Clin Immunol*. 2021;147(1):29-36.
50. Muraro A, de Silva D, Halken S, et al. Managing food allergy: GA²LEN guideline 2022. *World Allergy Organ J*. 2022;15(9):100687.
51. Sindher SB, Kumar D, Cao S, et al. Phase 2, randomized multi oral immunotherapy with omalizumab 'real life' study. *Allergy*. 2022;77(6):1873-1884.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/16/2022
Selected Revision	Asthma: Notes were updated to include Tezspire as an example of a monoclonal antibody therapy that may lower immunoglobulin E (IgE) levels and interfere with allergen testing. Notes were also updated to include Xolair, Cinqair, Fasenra, Nucala, and Tezspire as examples of monoclonal antibody therapies for asthma. Criteria requiring the patient to have experienced one or more asthma exacerbation(s)	07/20/2022

	<p>requiring a hospitalization or an emergency department visit in the previous year, were updated to include an urgent care visit as well.</p> <p>Nasal Polyps: Notes were updated to include Tezspire as an example of a monoclonal antibody therapy that may lower immunoglobulin E (IgE) levels and interfere with allergen testing.</p> <p>Conditions Not Covered</p> <p>: Criteria were updated to recommend against use of Xolair with another monoclonal antibody therapy. Previously, criteria listed anti-interleukin monoclonal antibody therapies specifically.</p>	
Annual Revision	<p>Conditions Not Covered</p> <p>: Criteria were updated to clarify that use of Xolair with another monoclonal antibody therapy is specific to Cinqair, Fasenra, Nucala, Dupixent, Tezspire, and Adbry.</p>	03/22/2023

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