Drug and Biologic Coverage Policy

Effective Date **11/1/2021**
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Coverage Policy Number **4026**

Omalizumab

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Related Coverage Resources

Benralizumab, Mepolizumab and Reslizumab - (1608)
Dupilumab – (1810)

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Coverage Policy

Omalizumab (Xolair®) is considered medically necessary when ONE of the following criteria is met:

I. Treatment of moderate to severe, persistent allergen-related asthma when ALL of the following criteria are met:

- Individual is 6 years of age or older
- Positive skin test or in vitro reactivity to a perennial aeroallergen
- Inadequately controlled with (or not a candidate for) a moderate dose of inhaled corticosteroids (ICS) plus ONE of the following: long-acting beta-agonists, inhaled long-acting muscarinic antagonist, leukotriene receptor antagonist, OR theophylline for at least 3 months
- Continued use of an ICS plus ONE of the following: long-acting beta agonist, inhaled long-acting muscarinic antagonist, leukotriene receptor antagonist OR theophylline with add-on omalizumab (Xolair)
- Laboratory data reflecting baseline IgE levels greater than 30
  Note: "Baseline" is defined as prior to receiving any Xolair or anti-interleukin 4/13 therapy (i.e., Dupixent® [dupilumab subcutaneous injection]).
- Prescribed by or in consultation with an allergist, immunologist, or pulmonologist

II. Treatment of chronic idiopathic urticaria (CIU) when ALL of the following criteria are met:

- Individual is 12 years of age or older
- Symptoms for greater than 6 weeks
- Failure or inadequate response, contraindication per FDA label, documented intolerance, or not a candidate for a second generation H1 antihistamines (for example, cetirizine, desloratadine, fexofenadine used individually or in combination with each other), including a trial at four times the standard FDA-approved dose for at least 4 weeks
- Prescribed by, or in consultation with, an allergist, immunologist, or dermatologist

III. Treatment of rhinosinusitis with nasal polyposis as add on maintenance treatment when ALL of the following criteria are met:

- Individual is 18 years of age or older
- Laboratory data reflecting baseline IgE levels greater than 30
  Note: "Baseline" is defined as prior to receiving any Xolair or anti-interleukin 4/13 therapy (i.e., Dupixent® [dupilumab subcutaneous injection]).
- Individual has evidence of nasal polyposis by direct examination, endoscopy, or sinus CT scan
- Individual is experiencing significant rhinosinusitis symptoms such as nasal obstruction, rhinorrhea, or reduction/loss of smell according to the prescriber
- Individual meets **BOTH** of the following:
  - Individual has received at least 8 weeks of therapy with an intranasal corticosteroid
  - Individual will continue intranasal corticosteroid therapy unless contraindicated per FDA label
- Individual meets ONE of the following:
  - Individual has received treatment with a systemic corticosteroid within the previous two years or has a contraindication per FDA label to systemic corticosteroid therapy
  - Individual has had prior surgery for nasal polyps
- Prescribed by, or in consultation with, an allergist, immunologist, or otolaryngologist (ear, nose, and throat [ENT])

Xolair will not be approved in combination with other monoclonal antibodies (for example: benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair]).

For allergen-related asthma or chronic idiopathic urticaria, initial authorization is up to 12 months.

For rhinosinusitis with nasal polyposis, initial authorization is up to 6 months.

Reauthorization of Xolair is considered medically necessary for allergen-related asthma when ALL of the following criteria are met:

- Pretreatment clinical condition met the initial criteria
- Documented evidence of continued beneficial clinical response to Xolair
- Continued use of an ICS AND another controller therapy such as a long-acting beta agonist, inhaled long-acting muscarinic antagonist, leukotriene receptor antagonist or theophylline with add-on omalizumab (Xolair)

Reauthorization of Xolair is considered medically necessary for chronic idiopathic urticaria, when ALL of the following are met:

- Pretreatment clinical condition met the initial criteria
- Documented evidence of continued beneficial clinical response to Xolair (for example, reduced exacerbations)
- Continued concomitant therapy with a second generation H1 antihistamine

Reauthorization of Xolair is considered medically necessary for rhinosinusitis with nasal polyposis, when ALL of the following are met:

- Pretreatment clinical condition met the initial criteria

- Documented evidence of continued beneficial clinical response to Xolair (for example, reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, and/or improved sense of smell)
- Continued concomitant therapy with a intranasal corticosteroid

Reauthorization for up to 12 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Omalizumab (Xolair®) is considered experimental, investigational, or unproven for ANY other use including the following:
- Non-allergic asthma
- Seasonal allergic rhinitis (SAR)
- Perennial allergic rhinitis (PAR)
- Food allergy
- Atopic dermatitis
- Chronic Rhinosinusitis without nasal polyps
- Eosinophilic Gastroenteritis (EG), Eosinophilic Esophagitis (EE), or Eosinophilic Colitis
- Latex Allergy in Health Care Workers with Occupational Latex Allergy

Note: Receipt of sample product does not satisfy any criteria requirements for coverage

FDA Approved Indications

FDA Approved Indication

Asthma

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

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.
- Xolair is not indicated for treatment of other allergic conditions.

Nasal Polyps

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

Chronic Idiopathic Urticaria (CIU)

Xolair is also indicated for the treatment of adults and adolescents 12 years of age and above with chronic idiopathic urticaria who remain symptomatic despite H1 antihistamine treatment.

Limitation of Use:
- Xolair is not indicated for treatment of other forms of urticaria.

Recommended Dosing

FDA Recommended Dosing

Overview of Dosage Determination

Asthma and Nasal Polyps
Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL) measured before the start of treatment, and by body weight (kg). For patients with both asthma and nasal polyps, dosing determination should be based on the primary diagnosis for which Xolair is being prescribed. Adjust doses for significant changes in body weight during treatment (see Tables 1 and 2 for treatment of asthma and Table 3 for treatment of nasal polyps).

Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during Xolair treatment cannot be used as a guide for dose determination.

- Interruptions lasting less than one year: Dose based on serum IgE levels obtained at the initial dose determination.
- Interruptions lasting one year or more: Re-test total serum IgE levels for dose determination using Table 1 or 2, based on the patient's age.

Chronic Idiopathic Urticaria Dosing Xolair in chronic idiopathic urticaria patients is not dependent on serum IgE (free or total) level or body weight.

Recommended Dosage for Asthma
The recommended dosage for treatment of asthma is Xolair 75 mg to 375 mg by subcutaneous injection every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment and by body weight (kg).

Adult and adolescent patients 12 years of age and older: Refer to Table 1 in the Prescribing Information for Subcutaneous Xolair Doses Every 2 or 4 Weeks for Patients 12 Years of Age and Older with Asthma

Pediatric patients 6 to <12 years of age: Refer to Table 2 in the Prescribing Information for Subcutaneous Xolair Doses Every 2 or 4 Weeks for Pediatric Patients with Asthma Who Begin Xolair Between the Ages of 6 to <12 Years

Recommended Dosage for Nasal Polyps
Administer Xolair 75 mg to 600 mg by subcutaneous injection every 2 or 4 weeks based on serum total IgE level (IU/mL) measure before the start of treatment and by body weight (kg).

Refer to Table 3 in the Prescribing Information for Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Adult Patients with Nasal Polyps

Chronic Idiopathic Urticaria
Administer Xolair 150 or 300 mg by subcutaneous injection every 4 weeks. Dosing of Xolair in CIU patients is not dependent on serum IgE (free or total) level or body weight. The appropriate duration of therapy for CIU has not been evaluated. Periodically reassess the need for continued therapy.

Dosage (12 years of age and older) for Second Generation Antihistamines
Allegra (fexofenadine): Tablets: 180 mg once daily or 60 mg twice daily
Claritin (loratadine): 10 mg once daily
Zyrtec (cetirizine): 5 to 10 mg once daily

Table 1. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Patients 12 Years of Age and Older with Asthma

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight			
		30–60 kg	>60–70 kg	>70–90 kg	>90–150 kg
		Dose (mg)			
≥30–100	Every 4 weeks	150	150	150	300
>100–200		300	300	300	225
>200–300		300	225	225	300
>300–400	Every 2 weeks	225	225	300	
>400–500		300	300	375	
>500–600		300	375		
>600–700		375			

Insufficient Data to Recommend a Dose

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Table 2. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Pediatric Patients with Asthma Who Begin XOLAIR Between the Ages of 6 to <12 Years

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)									
30-100	Every 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300		
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375				
>600-700		300	225	225	300	375					
>700-800	Every 2 weeks	225	225	300	375						
>800-900		225	225	300	375						
>900-1000		225	300	375							
>1000-1100		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

Insufficient Data to Recommend a Dose

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Table 3. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Adult Patients with Nasal Polyps

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Bodyweight							
		>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	> 125-150 kg
		Dose (mg)							
30 - 100	Every 4 Weeks	75	150	150	150	150	150	300	300
>100 - 200		150	300	300	300	300	300	450	600
>200 - 300		225	300	300	450	450	450	600	375
>300 - 400		300	450	450	450	600	600	450	525
>400 - 500		450	450	600	600	375	375	525	600
>500 - 600		450	600	600	375	450	450	600	
>600 - 700		450	600	375	450	450	525		
>700 - 800	Every 2 Weeks	300	375	450	450	525	600		
>800 - 900		300	375	450	525	600			
>900 - 1000		375	450	525	600				
>1000 - 1100		375	450	600					
>1100 - 1200		450	525	600	Insufficient Data to Recommend a Dose				
>1200 - 1300		450	525						
>1300 - 1500		525	600						

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Drug Availability

Injection: Xolair injection is a clear to slightly opalescent and colorless to pale brownish-yellow solution available as:

- 75 mg/0.5 mL in a single-dose prefilled syringe with blue needle shield
- 150 mg/mL in a single-dose prefilled syringe with purple needle shield

For injection: 150 mg white lyophilized powder in a single-dose vial for reconstitution.

General Background

Pharmacology

Omalizumab is a monoclonal antibody that interferes with allergic response by binding to immunoglobulin E (IgE). Omalizumab binds to the receptor-binding portion of IgE, eliminating IgE's ability to bind to receptors on mast cells, basophils, B cells, macrophages, and platelets. Because omalizumab only binds to freely circulating IgE, it lacks the ability to induce inflammatory responses by crosslinking cell-bound IgE molecules. Free IgE levels decrease dramatically during omalizumab treatment. Total IgE levels increase during omalizumab treatment, and may persist for up to a year after discontinuation.

Professional Societies/Organizations

Asthma Guidelines

Global Initiative for Asthma (GINA)

The Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention (2018) proposes a step-wise approach to asthma treatment. (GINA, 2018) For patients with persistent symptoms or exacerbations despite therapy with a medium- to high-dose ICS/long-acting beta$_2$-agonist (LABA) combination with or without an additional controller, GINA recommends referral of the patient to a specialist with expertise in the management of severe asthma. Xolair is listed as a treatment option for add-on therapy in patients ≥ 6 years of age with moderate to severe allergic asthma. However, it is also noted that Xolair should only be considered when all other causes of uncontrolled asthma have been addressed.

European Respiratory Society (ERS)/American Thoracic Society (ATS)

The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014) for the definition, evaluation, and treatment of severe asthma suggest a trial of Xolair in both adults and children with severe allergic asthma. (Chung, 2014) If a trial of Xolair is considered, patients (adults and children ≥ 6 years of age) should have confirmed IgE-dependent allergic asthma that is uncontrolled despite optimal pharmacological and non-pharmacological management and appropriate allergen avoidance and their total serum IgE level should be ≥ 30 IU/mL and < 700 IU/mL. It is also noted that further administration of Xolair is unlikely to be beneficial if a patient does not respond to therapy within the first 4 months of treatment. The ERS/ATS guidelines also provide a definition of severe asthma. 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. Uncontrolled asthma is defined as asthma that meets one of the following four criteria: poor symptom control; frequent severe exacerbations; serious exacerbations; or airflow limitation. Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids.

Urticaria Guidelines

European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA[2]LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO)

Urticaria guidelines from the European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA[2]LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) [2018] also stress the importance of identification and elimination of underlying causes and trigger avoidance followed by pharmacologic treatment to reduce release of mast cell mediators (e.g. histamine) and/or decrease the effect of these mast cell mediators at target organs. (Zuberbier, 2018) Continuous therapy with antihistamines (second generation H_1-antagonists) is recommended as first-line treatment. If symptoms persist following 2 to 4 weeks of initial therapy, the dose of the second generation H_1-antagonist should be increased to up to 4-fold. If symptoms persist an additional 2 to 4 weeks despite the higher dosing, the addition of Xolair may be considered. Cyclosporine is referenced as an add-on therapy to Xolair if there is inadequate control or symptoms are intolerable within 6 months. Short courses of oral corticosteroids may also be considered if needed to control exacerbations. However, long-term use of systemic corticosteroids is not recommended.

American Academy of Allergy, Asthma, & Immunology (AAAAI); the American College of Allergy, Asthma, & Immunology (ACAAI); and the Joint Council of Allergy, Asthma, & Immunology (JCAAI)

In 2014, the American Academy of Allergy, Asthma, & Immunology (AAAAI); the American College of Allergy, Asthma, & Immunology (ACAAI); and the Joint Council of Allergy, Asthma, & Immunology (JCAAI) published a Joint Task Force Practice Parameter on the diagnosis and management of acute and chronic urticaria. (Joint Task Force, 2014) This parameter recommends a four-step approach to treatment of chronic urticaria. Initially, trigger avoidance is indicated along with a second generation antihistamine (Step 1). Step 2 includes increasing

the dose of the antihistamine; a 2- to 4-fold increase in the FDA-approved dose of the second-generation antihistamine may be effective to achieve symptom control in some patients. Additionally, adding a second non-sedating antihistamine, an H_2 antagonist, a leukotriene receptor antagonist (LTRA), or a first generation antihistamine to be taken at bedtime may also be beneficial. If the patient's urticarial remains poorly controlled, hydroxyzine or doxepin may be considered as part of Step 3 therapy. Patients with refractory chronic urticaria (Step 4) may consider other alternative therapies, such as Xolair and cyclosporine.

Nasal Polyp Guidelines
A 2014 Joint Practice Parameter on the Diagnosis and Management of Rhinosinusitis and a 2008 (evidence update in 2017) Joint Practice Parameter for the Management of Rhinitis recommend nasal corticosteroids be used in patients with chronic rhinosinusitis with nasal polyps, as they decrease nasal polyp size, prevent regrowth of nasal polyps following surgical removal, and improve nasal symptoms. (Peters, 2014, Joint Task Force on Practice Parameters, 2008, Dykewicz, 2017) 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 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. A 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology (AAO) makes similar recommendations, stating that clinicians should recommend saline nasal irrigation, topical nasal corticosteroids, or both for symptom relief in patients with chronic rhinosinusitis (with or without nasal polyps). (Rosenfield, 2015) The AAO guidelines do not address Xolair.

Experimental, Investigational, Unproven Uses

Xolair has been evaluated for use in seasonal allergic rhinitis (Casale, 2001; Kamin, 2009), perennial allergic rhinitis (Chervinsky, 2003), and solar urticaria (Aubin, 2016). At this time, however, there is insufficient published data in terms of safety and efficacy to support the use of Xolair for these indications. Xolair has not been found efficacious in cow's milk allergy. (Wood, 2016) There is insufficient evidence in the peer-reviewed published scientific literature to support safety and efficacy of omalizumab for food allergies.

Atopic Dermatitis (AD)
There have been several case series/reports and two small randomized, double-blind, placebo-controlled pilot studies evaluating the efficacy and safety of Xolair for the treatment of patients with AD. (Holm, 2017, Wang, 2016) Efficacy data have been mixed. One systematic review and meta-analysis reported that of the studies reviewed (n = 103 patients total), 43% of patients achieved an excellent clinical response with Xolair, while 27.2% of patients had satisfying results and another 30.1% had no clinical change or worsening of their disease. However, these data are difficult to interpret due to the very small sample sizes in each case series/report and the non-controlled, non-randomized design of the majority of the available studies. Additional larger, well-designed clinical trials are needed to determine if Xolair has a role in the treatment of AD. AD guidelines from the American Academy Dermatology (AAD) [2014] note that data are limited to determine if Xolair is efficacious in the treatment of AD. (Sidbury, 2014) These guidelines do not make a recommendation regarding Xolair use in this patient population. European consensus guidelines for the treatment of AD (2018) from multiple European dermatology associations, including the European Dermatology Forum (EDF), the European Academy of Dermatology and Venereology (EADV), and the European Academy of Allergy and Clinical Immunology (EAACI) also note the mixed data and state that they cannot recommend Xolair for the treatment of AD. (Wollenberrg, 2018) There is currently one randomized, double-blind, placebo controlled study evaluating Xolair for the treatment of pediatric AD (Atopic Dermatitis Anti-IgE Paediatric Trial [ADAPT]). (Chan, 2017) This trial is ongoing and results are not yet available.

Concurrent use of Xolair with an Anti-Interleukin (IL) Monoclonal Antibody. The efficacy and safety of Xolair used in combination with IL antagonist monoclonal antibodies (e.g., Cinqair® [reslizumab injection for intravenous use], Fasenra™ [benralizumab injection for subcutaneous use], Nucala® [mepolizumab injection for subcutaneous use], Dupixent® [dupilumab subcutaneous injection]) have not been established. There very limited case reports describing the combination use of Nucala and Xolair for severe asthma as well as off-label indications. (Altman, 2017, Han, 2018, Dedaj,2018) Further investigation is warranted.

Eosinophilic Gastroenteritis (EG), Eosinophilic Esophagitis (EE), or Eosinophilic Colitis

There are limited and conflicting data on the use of Xolair for the treatment of eosinophilic gastrointestinal conditions. In a case series evaluating patients with eosinophil-associated gastrointestinal disorders, Xolair was effective in decreasing absolute eosinophil count, allergen skin test wheal and erythema responses, and symptom scores. (Foroughi, 2007) Subsequently, a small (n = 15), open-label, single-arm, unblinded study (published) evaluated Xolair for the treatment of patients 12 to 75 years of age with EE. (Clayton 2014) Following 12 weeks of Xolair therapy (dose calculated in mg/kg per IU IgE units/mL), tissue IgE levels were significantly reduced in 13 of the 15 patients, with full remission (defined as histologic and clinical improvement) present in 33% of patients. Conversely, a prospective, randomized, double-blind, placebo-controlled trial (n = 30) also examined the effects of Xolair in patients 12 to 60 years of age with EE who were either refractory to or relapsed after a trial of topical corticosteroids. (Clayton, 2014, Fang, 2011) Patients received either Xolair or placebo every 2 to 4 weeks for 16 weeks (dose of Xolair based on weight and serum IgE level). Xolair therapy was not found to improve the symptoms of EE (dysphagia scores) or eosinophil counts in biopsy samples when compared with placebo. An additional case series including two patients with multiple food allergies and EE reported an improvement in patient symptoms with Xolair therapy, but did not find an improvement in esophageal endoscopy and histology in short-term follow-up. (Dellon, 2013) The 2013 American College of Gastroenterology guidelines for the diagnosis and management of esophageal eosinophilia and EE do not recommend Xolair therapy for these conditions; the guidelines note that Xolair was ineffective in a case series involving two patients (referenced above). It is recognized that corticosteroids (systemic or topical administered by swallowing a formulation for inhalation) are the standard treatment for management of both EG and EE. (Furata, 2007, Mendez-Sanchez, 2007) Adequate controlled clinical studies have not been conducted in patients less than 12 years of age with EG, EE, or eosinophilic colitis. A 2014 updated food allergy practice parameter from the AAAAI, ACAAI, and JCAAI Joint Task Force also addresses EE and EG, but does not address Xolair as a treatment for these conditions. (Joint task force on Practice Parameter, 2014)

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. (Levnadier, 2004) 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.

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. (Sampson, 2011) Insufficient data were obtained to reach any conclusions about the efficacy of Xolair. Another pilot study also used Xolair to facilitate rapid oral desensitization in high-risk peanut-allergic patients (8 to 16 years of age). (Schneider, 2013) In total, 13 patients were pretreated with Xolair for 12 weeks prior to rush oral desensitization, followed by an escalation phase where patients were administered increasing amounts of peanut flour daily. At 20 weeks following the rush desensitization, Xolair was discontinued, but the peanut flour dosing continued. For the primary outcome, all 13 patients reached the maximum rush desensitization dose on Day 1; 12 of the 13 patients (92%) reached the 4,000 mg maintenance dose (secondary outcome). At Week 32, 11 patients tolerated a double-blind, placebo-controlled food challenge.

There are also minimal data on the use of Xolair in patients with severe cow's milk allergy. (Nadeau, 2011, Nilsson, 2014, Takahashi 2015, Begin 2014) In one Phase I study (n = 11) patients were given Xolair for 9 weeks prior to rapid desensitization treatment. (Nadeau, 2011) In total, 9 of the 11 patients were able to tolerate desensitization to a daily maintenance dose of 2,000 mg of milk within a 7 to 11 week period. Another case-series describes five pediatric patients treated with Xolair for 4 months until they had a negative basophil allergen threshold sensitivity test (CD-sens). (Nilsson, 2014) Once the CD-sense test was negative, the patients were administered a milk challenge. Following Xolair therapy, all five patients ultimately had a negative milk challenge. Another Phase I study also evaluated the safety and tolerability of Xolair in patients with multiple food allergies undergoing a rush immunotherapy protocol to multiple foods. (Begin, 2014) In this study (n = 25), Xolair was administered for 8 weeks prior to and 8 weeks following the initiation of rush oral immunotherapy using up to

five different food allergens. The goal maintenance dose was 4,000 mg protein per allergen. All patients were able to reach the goal dose by 9 months, with the median time to reach the maintenance dose of 18 weeks. One randomized, double-blind, placebo-controlled study evaluated Xolair combined with oral immunotherapy for the treatment of cow's milk allergy in pediatric and adult patients. Following 4 months of therapy with either Xolair or placebo, open-label milk oral immunotherapy was initiated and escalated to a maintenance dose from Week 22 to Week 40. After Week 40, patients received daily oral immunotherapy through Month 28. At Month 28, Xolair therapy was discontinued and patients passing an oral food challenge continued oral immunotherapy for an additional 8 weeks. A rechallenge was initiated at Month 21 to assess sustained unresponsiveness. Small, non-significant improvements in the proportion of patients passing the oral food challenge (at Month 28) and the sustained unresponsiveness challenge at Month 32 were observed with Xolair vs. placebo.

Guidelines for the diagnosis and management of food allergy in the US (published in 2010) 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. (Boyce, 2010) Allergen avoidance and use of antihistamines are recommended for treatment of food-induced allergic reactions. The updated food allergy practice parameter from the AAAAI, ACAAI, and JCAAI Joint Task Force (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. (Joint Task Force on Practice Parameters, 2014) 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. Additional well-controlled trials are needed.

Coding/ Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2357	Injection, omalizumab, 5 mg

References

1. Aubin F, Avenel-Audran M, Jeanmougin M, et al. Omalizumab in patients with severe and refractory solar urticarial. A phase II multicentric study. J Am Acad Dermatol. 2016 Mar;74(3):574-5.
2. 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.
3. 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.
4. Bernstein JA, Lang DM, Khan DA, et al of the Joint Task Force on Practice Parameters. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol 2014; 133 (5): 1270-7.
5. Bidder T, Sahota J, Rennie C, et al. Omalizumab treats chronic rhinosinusitis with nasal polyps and asthma together – a real life study. Rhinology. 2018;56(1):42-45.
6. 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.
7. 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.

8. Casale TB, Condemi J, LaForce C, et al. Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. JAMA. Dec 19 2001;286(23):2956-2967.
9. Chan S, Cornelius V, Chen T, et al. Atopic dermatitis anti-IgE paediatric trial (ADAPT): the role of anti-IgE in severe paediatric eczema: study protocol for a randomized controlled trial. Trials. 2017;18(1):136.
10. Chervinsky P, Casale T, Townley R, et al. Omalizumab, an anti-IgE antibody, in the treatment of adults and adolescents with perennial allergic rhinitis. Ann Allergy Asthma Immunol. Aug 2003;91(2):160-167.
11. 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
12. 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.
13. Dedaj R, Unsel L. Case study: a combination of mepolizumab and omalizumab injections for severe asthma. J Asthma. 2018 May 7. [Epub ahead of print].
14. 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 Gastroenteral. 2013;108(5):679-692.
15. 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.
16. 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.
17. 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.
18. Furata GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: A systemic review and consensus recommendations for diagnosis and treatment. Gastroenterology. 2007;133:1342-1363.
19. Genentech, Inc. Xolair (omalizumab) [product information]. South San Francisco, CA: Genentech, Inc. December 2015
20. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention (2018 update). 2018a; www.ginasthma.org. Accessed November 23, 2018.
21. Global Initiative for Asthma (GINA). Difficult-to-treat and severe asthma in adolescent and adult patients: diagnosis and management. 2018b; www.ginasthma.org. Accessed November 23, 2018.
22. Han D, Lee JK. Severe asthma with eosinophilic gastroenteritis effectively managed by mepolizumab and omalizumab. Ann Allergy Asthma Immunol. 2018;121(6):742-743.
23. 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.
24. International European Respiratory Society/American Thoracic Society. Guidelines on Definition, Evaluation, and Treatment of Severe Asthma (2014). Eur Respir J 2014; 43: 343-373.
25. 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.
26. 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 rhinitis: An updated practice parameter. J Allergy Clin Immunol. 2008;122(2):S1-S84.
27. Kamin W, et. al. Safety of anti-IgE treatment with omalizumab in children with seasonal allergic rhinitis undergoing specific immunotherapy simultaneously. Pediatr Allergy Immunol. 2010 Feb;21(1 Pt 2):e160-5. doi: 10.1111/j.1399-3038.2009.00900.x.
28. 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.
29. Mendez-Sanchez N, Chavez-Tapia N, Vazquez-Elizondo G, Uribe M. Eosinophilic gastroenteritis. Dig Dis Sci. 2007;52:2904-2911.
30. 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.

31. National Heart, Lung, and Blood Institute. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma (guideline on the Internet). NHLBI 2007. Available from http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines. Accessed February 6, 2016.
32. 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.
33. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. Ann Allergy Asthma Immunol. 2014:347-385.
34. Powell RJ, Leech SC, Till S, et al. BSACI guideline for the management of chronic urticaria and angioedema. Clin Exp Allergy. 2015;45(3):547-565.
35. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015;152(2S):S1-S39.
36. 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.
37. 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.
38. 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.
39. 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.
40. 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.
41. 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.
42. Wood RA, Kim JS, Linblad 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 Apr;137(4):1103-10.
43. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA/LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2018;73(7):1393-1414.doi: 10.1111/all.13397.