# Background

Xolair is a recombinant humanized immunoglobulin G (IgG)1κ monoclonal antibody which selectively binds to human immunoglobulin E (IgE), thus inhibiting IgE from binding to the surface of mast cells and basophils (at the high-affinity IgE receptor [FcεRI]), and resulting in a decrease of mediators released in the allergic response. Xolair treatment also reduces the number of FcεRI receptors on basophils in atopic patients. Xolair is indicated for use in patients aged ≥ 6 years with moderate to severe persistent asthma and who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair decreases the incidence of asthma exacerbations in these patients. Safety and efficacy of Xolair in pediatric patients with asthma aged < 6 years have not been established. Doses and dosing frequency in asthma are determined by serum total IgE level (which is measured before the start of therapy) and the patient’s body weight. Xolair is also indicated for the treatment of adults and adolescents (aged ≥ 12 years) with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment.

Dosing in patients with CIU does not depend on serum IgE (free or total) or on body weight. In CIU, Xolair binds to IgE and lowers free IgE levels; subsequently, FcεRI on cells down-regulate. How these effects of Xolair result in an improvement in CIU symptoms is not known. Xolair is not indicated for the following conditions:

- Treatment of other allergic conditions or other forms of urticaria
- Acute bronchospasm or status asthmaticus

# Required Review and Approvals

This policy involves the use of Xolair for SC injection. Prior authorization is recommended for prescription benefit coverage of Xolair. 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, initial and continuing approval requires Xolair to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration listed below.

# Indications/Criteria

Coverage of Xolair is recommended in those who meet one of the following criteria:
FDA-Approved Indications

1. Asthma in Patients with Moderate to Severe Persistent Disease.¹
   A) Initial Therapy. Approve for 4 months if the patient meets all of the following criteria (i, ii, iii, iv, v and vi):
      i. Patient is ≥ 6 years of age¹,²²-²⁴; AND
      ii. Xolair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
      iii. Baseline IgE level is ≥ 30 IU/mL¹-⁹,¹¹,²²-²⁴; AND
      iv. The patient has a baseline positive skin test or in vitro testing (i.e., a blood test for allergen-specific IgE antibodies such as an enzyme-linked immunosorbant assay [e.g., ImmunoCAP™, ELISA] or the radioallergosorbent test [RAST]) for one or more perennial aeroallergens (e.g., house dust mite [Dermatophagoides farinae, D. pteronyssinus], animal dander [dog, cat], cockroach, feathers, mold spores)¹, AND/OR for one or more seasonal aeroallergens (grass, pollen, weeds); AND
      v. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
         a) An inhaled corticosteroid (ICS) [e.g. Flovent® HFA {fluticasone inhalation aerosol}, Flovent® Diskus® {fluticasone inhalation powder}, Arnuity™ Ellipta® {fluticasone furoate inhalation powder}, Asmanex® Twinhaler® {mometasone inhalation powder}, Asmanex® HFA {mometasone inhalation aerosol}, Aerocraft™ {flunisolide HFA inhalation aerosol}, Alvesco® {ciclesonide inhalation aerosol}, Pulmicort Flexhaler® {budesonide inhalation powder}, QVAR® {beclomethasone HFA inhalation aerosol}]; AND
         b) At least ONE of the following (1, 2, 3 or 4):
            (1) Inhaled long-acting beta-agonist (LABA) [e.g., Serevent® Diskus® {salmeterol xinafoate inhalation powder}]; OR NOTE: Use of a combination inhaler containing both an ICS and a LABA would fulfill the requirement for both criteria a and b (e.g., Advair® Diskus/HFA [fluticasone propionate and salmeterol inhalation powder/aerosol], Symbicort® [budesonide and formoterol fumarate inhalation aerosol], Breo® Ellipta® [fluticasone furoate and vilanterol inhalation powder], and Dulera® [mometasone furoate and formoterol fumarate inhalation aerosol]).
            (2) Inhaled long-acting muscarinic antagonist (LAMA) [e.g., Spiriva® Respimat® {tiotropium bromide inhalation spray}]; OR
            (3) Leukotriene receptor antagonist (LTRA) [e.g. montelukast tablets/granules {Singulair®, generics}, Accolate® {zafirlukast tablets}]; OR
            (4) Theophylline (Theo-24, Uniphyl, TheoChron ER, generics); AND
vi. Patient’s asthma continues to be uncontrolled as defined by ONE of the following (a, b, c, d, or e)
   a) The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
   b) The patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) 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) The patient’s asthma worsens upon tapering of oral corticosteroid therapy.

B) Patients Continuing Xolair Therapy. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):
   i. Patient is ≥ 6 years of age; AND
   ii. Xolair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
   iii. The patient has responded to therapy (e.g., decreased asthma symptoms or exacerbations; decreased hospitalizations, emergency room, urgent care, or physician visits due to asthma; decreased reliever/rescue medication use; increased lung function parameters {forced expiratory volume in 1 second (FEV₁), peak expiratory flow (PEF)}), as determined by the prescribing physician.

Xolair is indicated for use in patients aged ≥ 6 years 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 is not indicated for acute bronchospasm or status asthmaticus. Doses and dosing frequency are determined by serum total IgE level (which is measured before the start of therapy) and the patient’s body weight. Based on the prescribing information for Xolair, an IgE level of ≥ 30 IU/mL is required to calculate a dose. In addition, most of the clinical studies used a baseline IgE level of ≥ 30 IU/mL for inclusion. Serum total IgE levels increase during Xolair therapy due to formation of Xolair:IgE complexes and remain elevated for up to one year after Xolair is stopped. The 2014 ERS/ATS guidelines for the definition, evaluation, and treatment of severe asthma suggest a trial of Xolair may be considered when a patient’s total serum IgE level is ≥ 30 IU/mL and < 700 IU/mL (in addition to other qualifiers). The 2016 GINA guidelines also reference this IgE level requirement for a trial of Xolair therapy. The GINA guidelines and the 2007 NAEPP guidelines indicate that inhaled corticosteroids plus a LABA are the recommended controller medications for asthma patients prior to the potential addition of Xolair. The ERS/ATS guidelines reference the GINA guidelines for these therapy recommendations. The following agents are noted as alternatives to LABA therapy according to the GINA guidelines: sustained-release theophylline, tiotropium, or a LTRA (e.g., montelukast). However, tiotropium is not indicated in patients < 12 years of age.
age at this time, and therefore is not recommended in guidelines. If a patient is uncontrolled despite optimal therapy with the previously listed agents, the GINA guidelines support referral to a specialized physician for further investigation and consideration of additional therapies, such as Xolair.

In regard to assessing current clinical control (preferably over 4 weeks), the GINA guidelines state that uncontrolled asthma is demonstrated by at least three of the following: daytime symptoms more than twice per week, any limitation of activities, any nocturnal symptoms/awakening, or the need for reliever/rescue treatment more than twice per week. The NAEPP guidelines recommend patient referral to an asthma specialist for consultation or co-management if the patient is having difficulty achieving or maintaining control of asthma, if immunotherapy or Xolair are considered, or if the patient has had an exacerbation requiring hospitalization. Following initiation of Xolair therapy, the ERS/ATS guidelines also recommend a physician assessment of treatment response, taking into consideration asthma control, exacerbations, unscheduled healthcare utilization, and patient quality of life. These guidelines note that if a patient has not responded within 4 months of initiating treatment, further Xolair therapy is unlikely to be beneficial. The ERS/ATS guidelines define uncontrolled asthma in patients ≥ 6 years of age, as asthma that meets one of the following four criteria: poor symptom control; frequent severe exacerbations (two or more requiring systemic corticosteroids per year); serious exacerbations (one hospitalization in the previous year); or airflow limitation (FEV₁ < 80% of predicted in the setting of reduced FEV₁/FVC). Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids (high-dose ICSs or systemic corticosteroids). In the professional opinion of specialist physicians reviewing the data, we have adopted the seasonal aeroallergens listed in the criteria above (Criterion 1, A, iv).

2. Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria). A) Initial Therapy. Approve for 4 months if the patient meets all of the following criteria (i, ii, iii, and iv):
   i. Patient is ≥ 12 years of age; AND
   ii. Xolair is prescribed by, or in consultation with, an allergist, immunologist, or dermatologist; AND
   iii. Patient has urticaria for > 6 weeks, with symptoms present > 3 days per week despite daily non-sedating H₁ antihistamine therapy (e.g., cetirizine, desloratadine, fexofenadine, levocetirizine, loratadine) with doses that have been titrated up to a maximum of four times the standard FDA-approved dose; AND
   iv. Patient has tried therapy with a leukotriene modifier (e.g., montelukast) with a daily non-sedating H₁ antihistamine; AND

B) Patients Continuing Xolair Therapy. Approve for 1 year if the patient meets the following criteria (i, ii, and iii):
i. Patient is ≥ 12 years of age; AND

ii. Xolair is prescribed by, or in consultation with, an allergist, immunologist, or dermatologist; AND

iii. The patient has responded to therapy (e.g., decreased severity of itching, decreased number and/or size of hives) as determined by the prescribing physician.

Xolair is indicated for the treatment of adults and adolescents aged ≥ 12 years with CIU who remain symptomatic despite H₁ antihistamine treatment.¹ Dosing in patients with CIU does not depend on serum IgE (free or total) or on body weight. Xolair is not indicated for other forms of urticaria. In studies and guidelines, patients with chronic urticaria are generally defined as those having symptoms (e.g., pruritus and hives) for > 3 days per week for > 6 consecutive weeks despite treatment with an H₁ antihistamine.¹⁶⁻¹⁹ Guidelines recommend non-sedating (second-generation) H₁ antihistamines at standard daily doses as first-line therapy for CIU.¹⁹⁻²¹ In patients who do not respond adequately to standard doses of non-sedating H₁ antihistamines, the dosage should be increased up to four times the standard dose. Adding a second non-sedating antihistamine, an H₂ antagonist, a LTRA, or a 1ˢᵗ generation antihistamine to be taken at bedtime may be considered for patients with refractory CIU despite non-sedating H₁ antihistamine therapy. If the patient still has poorly controlled symptoms, treatment with hydroxyzine or doxepin may be considered as part of step-up therapy. Patients with refractory chronic urticaria despite treatment with the previously listed therapies for 1 to 4 weeks may consider alternative therapies, such as Xolair or cyclosporine. For any drug therapy, it is recommended to temporarily discontinue the drug to check for spontaneous remission.²⁰ Adequate controlled clinical studies have not been conducted in patients less than 12 years of age with CIU.¹ In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

Other Uses with Supportive Evidence

3. Allergic Rhinitis, Seasonal or Perennial.

A) Initial Therapy. Approve for 4 months if the patient meets all of the following criteria (i, ii, iii, iv, v, and vi):

i. Patient is ≥ 12 years of age; AND

ii. Xolair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND

iii. Baseline IgE level is ≥ 30 IU/mL; AND

iv. Patient has seasonal or perennial allergic rhinitis as demonstrated by baseline positive skin testing (e.g., grass, tree, or weed pollen, mold spores, house dust mite, animal dander, cockroach) AND/OR baseline positive in vitro testing (i.e., a blood test for allergen-specific IgE antibodies) for one or more relevant allergens
(e.g., grass, tree, or weed pollen; mold spores; house dust mite; animal dander; cockroach); AND

v. Patient has tried therapy with at least one drug from TWO of the following groups of drugs at the same time (a, b, c, or d):
   a) Oral second-generation/less-sedating antihistamines (e.g., cetirizine, desloratadine, fexofenadine, levocetirizine, or loratadine) [Rx or OTC]; OR
   b) Intranasal antihistamines (e.g., azelastine nasal spray [Astelin®, generics], Astepro® [azelastine nasal spray, generics] or Patanase® [olopatadine nasal spray]); OR
   c) Intranasal corticosteroids (e.g., fluticasone); OR
   d) Montelukast; AND

vi. Patient meets one of the following (a, b, or c):
   a) Patient has had immunotherapy, is receiving immunotherapy, or will be receiving immunotherapy; OR
   b) There is no immunotherapy available for the allergen identified as causing clinically significant allergy; OR
   c) The patient has contraindications to immunotherapy (e.g., patients receiving beta blockers or patients with medical conditions that reduce their ability to survive a systemic allergic reaction [e.g., markedly compromised lung function, poorly controlled asthma, unstable angina, recent myocardial infarction or significant dysrhythmia, uncontrolled hypertension, failure of a major organ system such as renal failure]).

B) Patients Continuing Xolair Therapy. Approve for 1 year if the patient meets all of the following criteria (i, ii, and iii):
   i. Patient is ≥ 12 years of age; AND
   ii. Xolair is prescribed by, or in consultation with, an allergist, immunologist, or pulmonologist; AND
   iii. The patient has responded to therapy (e.g., decreased symptoms of sneezing; itchy nose; watery, red, or itchy eyes; itchy throat; nasal congestion) as determined by the prescribing physician.

Several controlled clinical studies have been performed assessing the efficacy of Xolair in treating patients with seasonal or perennial allergic rhinitis. Adequate controlled clinical studies have included patients ≥ 12 years of age. Dosing and frequency are determined by serum total IgE level (which is measured before the start of therapy) and the patient’s body weight. Based on the prescribing information for Xolair, an IgE level of ≥ 30 IU/mL is required to calculate a dose. In addition, most of the clinical studies used a baseline IgE level of ≥ 30 IU/mL for inclusion. The 2015 American Academy of Otolaryngology (AAO) Clinical Practice Guidelines on Allergic Rhinitis recommends intranasal steroids as an initial choice for the treatment of allergic rhinitis due to their proven efficacy,
superiority over other therapies and good safety record. Oral second-generation antihistamines may also be an appropriate first-line therapy, especially if the patient has primary complaints of sneezing and itching. Other therapeutic options include intranasal antihistamines and oral LTRAs; however, the guidelines do not recommend LTRAs as primary therapy. It is noted that combination pharmacologic therapy may be necessary in patients who have an inadequate response to monotherapy. The AAO guidelines state that clinicians should offer immunotherapy for patients who do not have an acceptable response to other pharmacologic therapy options, but do not mention the use of Xolair in this setting. A 2008 practice parameter for management of rhinitis notes that determination of specific IgE by skin testing or in vitro testing is indicated to provide evidence of an allergic basis for the patient’s symptoms, confirm suspected causes of the patient’s symptoms, or assess the sensitivity to a specific allergen for avoidance measures and/or allergen immunotherapy. In one double-blind, placebo-controlled study involving 159 patients, the use of Xolair for 9 weeks prior to rush immunotherapy (RIT) resulted in a lower rate of any systemic or other adverse reaction on the day of RIT, including a statistically significant reduction in the incidence of anaphylaxis (5.6% for Xolair plus RIT vs. 25.6% for placebo plus RIT; P = 0.026). Well-controlled clinical studies have demonstrated that allergen immunotherapy is beneficial in allergic rhinitis caused by: pollens, dust mites, animal allergens, fungi, and cockroaches. Immunotherapy usually is given for at least 3 to 5 years and longer in some patients. The major risk in patients with allergic rhinitis receiving immunotherapy is anaphylaxis. A recent meta-analysis reported that in nine studies including patients with allergic rhinitis, Xolair significantly reduced daily nasal symptom scores; rescue medication use was also decreased (in studies that evaluated medication use as an endpoint). In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

**Conditions Not Recommended for Approval**

Xolair has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Atopic Dermatitis (AD).** Several case series have reported inconsistent results with the use of Xolair in adult and pediatric patients with AD. Three of these case series directly assessed the use of Xolair for treating AD, while a fourth study evaluated Xolair for managing persistent asthma in patients with concomitant AD. A fifth case series report assessed the use of Xolair for treating AD in patients with persistent asthma. One small study (n = 10) was conducted in patients with AD and a history of allergic asthma with elevated IgE levels. In total, seven patients had ≥ 25% reduction in objective AD scores; three patients had no clinically relevant reduction. Another small study (n = 9) was
conducted in patients with severe AD refractory to at least two systemic agents. Of the nine patients, three patients also had asthma; all patients had elevated IgE levels. In total, two patients experienced good control of AD, while four patients achieved only a slight improvement in the AD lesions. Another small study (n = 8) evaluated Xolair in patients 4 to 22 years of age with severe refractory AD. Significant reductions in the serum level of cytokines implicated in the pathogenesis of AD were observed in patients receiving Xolair. Improvements in clinical outcomes (as measured by Scoring Atopic Dermatitis [SCORAD]) were observed with Xolair therapy; however, these were not significantly different from the improvements observed with placebo. An open-label pilot study (n = 10) evaluated Xolair in adult patients with severe AD and elevated IgE levels whose AD was refractory to two or more conventional systemic treatment options. All patients underwent immunoglobulin apheresis (immunoadsorption) to reduce IgE levels as much as possible and then began Xolair 450 mg SC administered every 2 weeks for 24 weeks. IgE levels fell during immunoadsorption and continued to decrease with Xolair therapy. Throughout the study, clinical improvements (measured by SCORAD as well as a subjective visual analog scale) were observed. However, the small study size, open-label design, and additional therapy received (immunoadsorption) make the efficacy of Xolair in this study difficult to interpret. Additional well-controlled clinical trials are needed to determine if Xolair has a role in the treatment of AD.

2. **Chronic Rhinosinusitis.** A small study assessed the effects of Xolair in patients (n = 14) with chronic rhinosinusitis. The majority of patients had severe and refractory disease and presented with nasal polyposis; all had undergone endoscopic sinus surgery. After 4 months Xolair-treated patients showed reduced sinus inflammation (as determined by computed tomography [CT] imaging) while placebo-treated patients showed no change in inflammation; however, the net difference between groups was not statistically significant. The 2015 Clinical Practice Guideline: Adult Sinusitis from the American Academy of Otolaryngology (AAO) does not mention Xolair or anti-IgE therapy in its recommendations.

3. **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. 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. 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. 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. 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. 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.

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. 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. 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). 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.\textsuperscript{57-58,63-64} In one Phase I study (n = 11) patients were given Xolair for 9 weeks prior to rapid desensitization treatment.\textsuperscript{57} 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).\textsuperscript{58} 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.\textsuperscript{59} 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.\textsuperscript{60} Allergen avoidance and use of antihistamines are recommended for treatment of food-induced allergic reactions. The 2014 updated food allergy practice parameter from the AAAAI, ACAAI, and JCAAI Joint Task Force 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.\textsuperscript{43} 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.

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

SPECIAL CONSIDERATIONS
None

LIMITATIONS/EXCLUSIONS
Please refer to a product line’s certificate of coverage for benefit limitations and exclusions for these services:

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<td>Xolair® subcutaneous injection [prescribing information]. South San Francisco, CA and East Hanover, NJ: Genentech, Inc. and Novartis Pharmaceuticals Corporation; July 2016.</td>
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34. 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.
### References


### OTHER REFERENCES UTILIZED


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