omalizumab (Xolair®)

Medicare Advantage Medical Policy #MA-242
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Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Blue Advantage does not cover investigational or experimental services, including any drug, device, procedure, or service provided under the investigational arm of a clinical trial or study unless mandated by the Centers for Medicare and Medicaid Services. Coverage is limited to routine services for Category A IDE studies and to devices and related services for Category B IDE studies when not supplied by the trial sponsor. Approved IDE studies are posted on www.cms.gov/medicare/coverage/evidence.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Asthma

Based on review of available data, the Health Plan may consider omalizumab (Xolair®)‡ for the management of moderate to severe persistent asthma to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) will be considered for the treatment of moderate persistent or severe persistent asthma when ALL of the following criteria are met:

Initial:

- Patient has a diagnosis of moderate persistent or severe persistent asthma; AND
- Patient is 6 years of age or older; AND
- Patient has a positive skin test or in vitro reactivity to a perennial aeroallergen; AND
- Xolair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma (e.g., reslizumab [Cinqair®]‡, mepolizumab [Nucala®]‡, benralizumab [Fasenra®]‡, dupilumab [Dupixent®]‡, tezepelumab-ekko [Tezspire™]‡); AND
- Patient has received at least 3 consecutive months of combination therapy with BOTH of the following:
    - An inhaled corticosteroid (ICS) (e.g. fluticasone products [Arnuity™ Ellipta®, Armonair™ Respiclick®]‡, mometasone products [Asmanex® Twisthaler®, Asmanex® HFA]‡, flunisolide products [Aersopan™]‡, ciclesonide products [Alvesco®]‡, budesonide products [Pulmicort Flexhaler®]‡, beclomethasone products [QVAR®]‡); AND
    - At least ONE of the following:
        - ❖ Inhaled long-acting beta-agonist (LABA) (e.g., salmeterol products [Serevent® Diskus]‡, olodaterol products [Striverdi® Respimat®], indacaterol products [Arcapta™ Neohaler™]); 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. fluticasone propionate and salmeterol inhalation powder/aerosol [Advair® Diskus/HFA, fluticasone/salmeterol generics, Wixela™ Inhub, AirDuo™ Respiclick]‡, budesonide and formoterol fumarate inhalation aerosol [Symbicort®]‡, fluticasone furoate and vilanterol inhalation powder [Breo® Ellipta®]‡, mometasone furoate and formoterol fumarate inhalation aerosol [Dulera®]‡).

- ❖ Inhaled long-acting muscarinic antagonist (LAMA) (e.g. tiotropium bromide inhalation spray [Spiriva® Respimat®, Stiolto® Respimat]‡, aclidinium products [Tudorza® Pressair®]‡, glycopyrrolate products [Seebri™ Neohaler, Bevespi™ Aerosphere, Utibron™ Neohaler], umeclidinium products [Incruse® Ellipta, Anoro® Ellipta]); OR
- ❖ Leukotriene receptor antagonist (LTRA) (e.g. montelukast tablets/granules [Singulair®, generics], zafirlukast tablets [Accolate®])‡; OR
- ❖ Theophylline (Theo-24, Uniphyl, TheoChron ER, generics); AND

- Patient has the following serum IgE levels based on their age:
  - o Patients 12 years of age or older: greater than or equal to 30 IU/mL to 700 IU/mL; OR
  - o Patients 6 to less than 12 years of age: greater than or equal to 30 IU/mL to 1300 IU/mL; AND
- Xolair is ordered by a pulmonologist, allergist, or appropriate specialist; AND
- Patient's asthma continues to be uncontrolled as defined by ONE of the following:
  - o Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
  - o Patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) visit in the previous year; OR
  - o Patient has a forced expiratory volume in 1 second (FEV_1) less than 80% predicted; OR
  - o Patient has an FEV_1/forced vital capacity (FVC) less than 0.80; OR
  - o Patient's asthma worsens upon tapering of oral corticosteroid therapy.

Continuation:
Coverage continuation for omalizumab (Xolair) will be considered for the treatment of moderate persistent or severe persistent asthma when ALL of the following criteria are met:

I. Patient received an initial authorization from the plan OR has provided documentation of authorization for an active course of treatment from previous health plan; AND
II. Xolair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g., reslizumab (Cinqair), mepolizumab (Nucala), benralizumab (Fasenra), dupilumab (Dupixent)], tezepelumab-ekko [Tezspire]); AND
III. Patient continues to receive the medications required in criterion V. in the "Initial Criteria"; AND

IV. Patient has responded to Xolair therapy as determined by the prescribing physician [e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy.]

Chronic Spontaneous Urticaria

Based on review of available data, the Health Plan may consider omalizumab (Xolair) for the treatment of chronic spontaneous urticaria to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) for the treatment of chronic spontaneous urticaria will be considered when ALL of the following criteria are met:

Initial:

I. Patient has a diagnosis of Chronic Spontaneous Urticaria (defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger); AND
II. Patient is 12 years of age or older; AND
III. Xolair is dosed 150 mg or 300 mg every 4 weeks; AND
IV. Patient remains symptomatic despite at least 6 weeks of treatment with standard therapeutic doses of H1 antihistamine (e.g., cetirizine 10 mg, levocetirizine 5 mg, fexofenadine 180 mg)
V. Patient has tried and failed (e.g., intolerance or inadequate response) one of the following step-up measures unless there is clinical evidence or patient history that suggests these measures will be ineffective or cause an adverse reaction to the patient:
    - Addition of a different second-generation H1 antihistamine
    - Addition of an H2 antagonist
    - Addition of a first-generation H1 antihistamine at bedtime
    - Addition of a leukotriene receptor antagonist.

Continuation:

Coverage continuation for omalizumab (Xolair) will be considered for the treatment of chronic spontaneous urticaria when the following criteria are met:

I. Patient received an initial authorization from the plan OR has provided documentation of authorization for an active course of treatment from previous health plan; AND
II. Xolair is dosed 150 mg or 300 mg every 4 weeks; AND
III. Patient has responded to Xolair therapy as determined by the prescribing physician (e.g., reduction in exacerbations, itch severity, hives).

Chronic Rhinosinusitis with Nasal Polyps

Based on review of available data, the Health Plan may consider omalizumab (Xolair) for the treatment of chronic rhinosinusitis with nasal polyps to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) will be considered for the treatment of chronic rhinosinusitis with nasal polyps when ALL of the following criteria are met:

Initial:

I. Patient has a diagnosis of inadequately controlled chronic rhinosinusitis with nasal polyps; AND
II. Patient is 18 years of age or older; AND
III. Patient has recurrent polyposis after at least ONE surgical resection (unless resection is contraindicated); AND
IV. Patient's nasal polyposis has been confirmed as grade 3 or higher with nasal endoscopy; AND
V. Patient's polyposis recurrence occurred within 6 months of at least one high dose oral steroid taper after the most recent resection unless there is clinical evidence or patient history that suggests the use of a high dose oral steroid taper will be ineffective or cause an adverse effect to the patient; AND
VI. Patient has tried and failed (e.g., intolerance or inadequate response) BOTH fluticasone 50 mcg (generic OR over the counter) AND GENERIC mometasone after at least 30 days with EACH product unless there is clinical evidence or patient history that suggests the use of these nasal sprays will be ineffective or cause an adverse effect to the patient; AND
VII. Patient has tried and failed (e.g., intolerance or inadequate response) Xhance®‡ (fluticasone 93 mcg) after at least 30 days of therapy unless there is clinical evidence or patient history that suggests the use of Xhance (fluticasone 93 mcg) will be ineffective or cause an adverse effect to the patient; AND
VIII. Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC montelukast after at least 30 days of therapy unless there is clinical evidence or patient history that suggests the use of GENERIC montelukast will be ineffective or cause an adverse effect to the patient; AND
IX. Patient will continue to use an intra-nasal corticosteroid (e.g., fluticasone, mometasone, Xhance) in combination with Xolair (if the intra-nasal corticosteroid was tolerated); AND
X. Patient will NOT use Xolair in combination with other biologics used to treat nasal polyps (e.g., Dupixent); AND
XI. Patient has an IgE level of greater than or equal to 30 IU/mL to 1500 IU/mL.

Continuation:

Coverage continuation for omalizumab (Xolair) will be considered for the treatment of inadequately controlled nasal polyps when ALL of the following criteria are met:

I. Patient has received an initial authorization from the plan OR has provided documentation of authorization for an active course of treatment from previous health plan; AND
II. Patient will continue to use an intra-nasal corticosteroid (e.g., fluticasone, mometasone, Xhance) in combination with Xolair (if the intra-nasal corticosteroid was tolerated); AND

III. Patient will NOT use Xolair in combination with other biologics used to treat nasal polyps (e.g., Dupixent); AND
IV. Patient has responded to requested therapy as determined by the prescribing physician (e.g., decrease in nasal polyps, decreased congestion/obstruction, etc.).

IgE-Mediated Food Allergy

Based on review of available data, the Health Plan may consider omalizumab (Xolair) for the treatment of IgE-mediated food allergy to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of omalizumab (Xolair) will be considered for the treatment of IgE-mediated food allergy when ALL of the following criteria are met:

I. Patient is 1 year of age or older; AND
II. Patient has a baseline immunoglobulin IgE level greater than or equal to 30 IU/mL; AND
III. Patient has a history of an allergic reaction to one or more foods; AND
IV. Patient has demonstrated signs and symptoms of a significant systemic allergic reaction (e.g., hives, swelling, wheezing, hypotension, and gastrointestinal symptoms); AND
V. Patient's allergic reaction occurred within a short period of time following a known ingestion of the food; AND
VI. Patient's allergic reaction was significant enough to require a prescription for an epinephrine auto-injector; AND
VII. Patient has a positive skin prick test response to one or more foods; AND
VIII. Patient has a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods; AND
IX. Xolair will be used in conjunction with a food allergen-avoidant diet.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of omalizumab (Xolair) when any of the following patient selection criteria for the requested diagnosis are NOT met to be **not medically necessary:****

I. Asthma
    - Patient has used one of the following in combination with an inhaled corticosteroid prior to requesting Xolair: 1) inhaled long-acting beta agonist; 2) inhaled long-acting muscarinic antagonist; 3) leukotriene receptor antagonist; 4) theophylline
    - Patient has been on the listed pre-requisite asthma medications (criteria V.) for at least 3 months
    - Xolair is ordered by a pulmonologist, allergist, or appropriate specialist
    - For re-authorization requests: Patient has responded to requested therapy as determined by the prescribing physician (e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, ED/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy).

- For re-authorization requests: Patient continues to receive the medications required in criterion V. in the "Initial Criteria"

II. Chronic Spontaneous Urticaria
- Patient remains symptomatic despite at least 6 weeks of treatment with standard therapeutic doses of H1 antihistamine (e.g., cetirizine 10 mg, levocetirizine 5 mg, fexofenadine 180 mg)
- Patient has tried and failed (e.g., intolerance or inadequate response) one of the following step-up measures unless there is clinical evidence or patient history that suggests these measures will be ineffective or cause an adverse reaction to the patient:
  - Addition of a different second-generation H1 antihistamine
  - Addition of an H2 antagonist
  - Addition of a first-generation H1 antihistamine at bedtime
  - Addition of a leukotriene receptor antagonist.
- For re-authorization requests: Patient has responded to Xolair therapy as determined by the prescribing physician (e.g., reduction in exacerbations, itch severity, hives).

III. Chronic Rhinosinusitis with Nasal Polyps
- Patient has recurrent polyposis after at least ONE surgical resection (unless resection is contraindicated)
- Patient's nasal polyposis has been confirmed as grade 3 or higher with nasal endoscopy
- Patient's polyposis recurrence occurred within 6 months of at least one high dose oral steroid taper after the most recent resection
- Patient has tried and failed (e.g., intolerance or inadequate response) BOTH fluticasone 50 mcg (generic OR over the counter) AND GENERIC mometasone after at least 30 days with EACH product
- Patient has tried and failed (e.g., intolerance or inadequate response) Xhance (fluticasone 93 mcg) after at least 30 days of therapy
- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC montelukast after at least 30 days of therapy
- For re-authorization requests: Patient has responded to requested therapy as determined by the prescribing physician (e.g., decrease in nasal polyps, decreased congestion/obstruction, etc.).

IV. IgE-Mediated Food Allergy
- Patient's allergic reaction was significant enough to require a prescription for an epinephrine auto-injector

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of omalizumab (Xolair) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Based on review of available data, the Health Plan considers the use of omalizumab (Xolair) for any non-FDA approved indication to be **investigational.***

Background/Overview

Xolair is a recombinant DNA-derived humanized $IgG1_k$ monoclonal antibody that selectively binds to human immunoglobulin E (IgE). Xolair is approved for the treatment of: 1) moderate to severe persistent asthma in patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids; 2) chronic spontaneous urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H_1 antihistamine treatment; 3) chronic rhinosinusitis with nasal polyps in adult patients with an inadequate response to nasal corticosteroids, as an add on maintenance treatment; and 4) the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adults and pediatric patients aged 1 year and older with IgE-mediated food allergy. When prescribed for IgE-mediated food allergy, Xolair is to be used in conjunction with food allergen avoidance. Xolair is administered subcutaneously once or twice a month for the asthma, nasal polyps, and IgE-mediated food allergy indications and the dose is based on total serum IgE concentrations and body weight prior to therapy. Chronic spontaneous urticaria dosing is once monthly and is not weight or serum IgE level dependent.

Asthma

Asthma is a respiratory disorder characterized by increased responsiveness of the trachea and bronchi to various stimuli resulting in the narrowing of the airways, along with mucous secretion. Symptoms vary in severity and intensity and include wheezing, cough and dyspnea. Attacks can be triggered by exercise, allergens, irritants and viral infections. Based on symptoms, the four levels of asthma severity are:

- Mild intermittent (comes and goes)—you have episodes of asthma symptoms twice a week or less, and you are bothered by symptoms at night twice a month or less; between episodes, however, you have no symptoms and your lung function is normal.
- Mild persistent asthma—you have asthma symptoms more than twice a week, but no more than once in a single day. You are bothered by symptoms at night more than twice a month. You may have asthma attacks that affect your activity.

- Moderate persistent asthma—you have asthma symptoms every day, and you are bothered by nighttime symptoms more than once a week. Asthma attacks may affect your activity.
- Severe persistent asthma—you have symptoms throughout the day on most days, and you are bothered by nighttime symptoms often. In severe asthma, your physical activity is likely to be limited.

Chronic Spontaneous Urticaria
Chronic spontaneous urticaria (CSU) is defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger. Typical treatments for CSU include antihistamines, leukotriene modifiers, and immunomodulatory agents.

Chronic Rhinosinusitis with Nasal Polyps
Chronic rhinosinusitis is an inflammatory condition involving the nasal sinuses and the lining of the nasal passages. Chronic rhinosinusitis often involves nasal drainage, nasal obstruction, facial pain and/or pressure and decreased sense of smell. Chronic rhinosinusitis with nasal polyposis is characterized by the presence of bilateral nasal polyps in the middle meatus. As imagined, these polyps lead to worsening nasal congestion, pressure, drainage, etc. Treatments for chronic rhinosinusitis with nasal polyposis includes various treatment modalities including, but not limited to, intranasal saline, intranasal steroids, oral steroids, surgery, non-sedating antihistamines, anti-leukotriene agents, and for those who have failed these more traditional therapies, biologics such as Xolair or Dupixent.

IgE-Mediated Food Allergy
Food allergies are often categorized by IgE-mediated or non IgE-mediated processes. IgE-mediated food allergic reactions typically occur very rapidly after ingestion, often within minutes to up to 2 hours from ingestion of food. While most patients may only react to one or two specific foods or food groups, an increasing number of patients are reacting to several foods and/or food groups. Signs and symptoms of IgE-mediated food allergies can involve several organ systems including the skin, respiratory tract, gastrointestinal tract, and cardiovascular system. Reactions are believed to be caused by mediator release from tissue mast cells and circulating basophils, and these can range from mild such as nasal pruritus or sneezing to more severe reactions such as anaphylaxis and anaphylactic shock. Diagnosis of IgE-mediated food allergies are often based on a combination of the following: clinical history, physical examination, prick/puncture skin testing, in vitro testing, and food challenges. Prick/puncture skin testing is commonly used and should only be performed by an allergy specialist. It is also highly sensitive, but moderately specific. In vitro testing is used to identify food specific IgE antibodies in the serum. Though in vitro testing may report a high food specific IgE level, this does not always correlate to a severe reaction. Patients can also have a positive food specific IgE level for a food to which they are tolerant. Treatment for acute reactions depend upon the type and severity of the reaction. The most recommended strategy for long term management of IgE-mediated food allergy is avoidance of the culprit food allergens. Xolair is the first FDA approved medication to reduce allergic reactions to one or more types of food after accidental exposure.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xolair is approved to treat patients 6 years of age and above 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. In 2014, Xolair gained an indication for the treatment of chronic idiopathic urticaria in patients 12 years of age or older who remain symptomatic despite H_1 antihistamine treatment. In mid-2016, the indication for asthma was expanded to those 6 years of age and older. In late 2020, Xolair gained an additional indication for the treatment of nasal polyps in adult patients with an inadequate response to nasal corticosteroids, as an add on maintenance treatment. It should be noted that in July 2021, the package insert was updated to reflect a change in indication from "chronic idiopathic urticaria" to "chronic spontaneous urticaria." Xolair received FDA approval for the reduction of allergic reactions (Type I) that may occur with accidental exposure to one or more foods in adult and pediatric patients aged 1 year and older with IgE-mediated food allergy in February of 2024.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Asthma

The initial asthma indication was based on data from three multicenter, randomized, double blind, placebo-controlled studies in over 1,400 patients 12 years of age or older with symptomatic moderate to severe persistent asthma for at least 1 year and a positive skin test reaction to a perennial aeroallergen. In 2 of the 3 studies, treatment with Xolair was associated with lower incidence of asthma exacerbations compared with placebo; the incidence of asthma exacerbations was similar between Xolair and placebo in study 3. No reduction in the incidence of asthma exacerbations was observed in patients with a baseline forced expiratory volume in 1 second exceeding 80% or in patients who required oral corticosteroids as maintenance therapy in any of the studies.

The expansion of age for those 6 years to less than 12 years for the asthma indication was based on a randomized, double-blind, placebo controlled, multi-center trial studying pediatric patients aged 6 to less than 12 years of age with moderate to severe asthma. This study was conducted over 52 weeks and was conducted on children who were inadequately controlled despite the use of inhaled corticosteroids with or without controller asthma medications. During the first 24 weeks, the steroid doses remained constant from baseline. The initial 24 week period was then followed with a 28 week period in which the inhaled corticosteroid adjustment was allowed. The primary endpoint was the rate of asthma exacerbations during the 24 week steroid treatment phase. At 24 weeks, the Xolair group had a statistically significantly lower rate of asthma exacerbations (0.45 vs. 0.64) with an

estimated rate ratio of 0.69 (95% CI: 0.53, 0.90). The Xolair group also had a lower rate of asthma exacerbations compared to placebo over the full 52 week double blind treatment period (0.78 vs. 1.36; rate ratio 0.57; 95% CI: 0.45, 0.72). Other efficacy variables such as nocturnal symptom scores, beta agonist use, and measures of airflow (FEV_1) were not statistically significantly different in Xolair treated patients compared to placebo. Another trial lasting 28 weeks demonstrated similar results.

Chronic Spontaneous Urticaria
The safety and efficacy of Xolair for the treatment of CSU was assessed in two placebo-controlled, multiple-dose clinical studies of 24 weeks' duration and 12 weeks' duration. Patients received Xolair 75, 150, or 300 mg or placebo by subcutaneous injection every 4 weeks in addition to their baseline level of H_1 antihistamine therapy for 24 or 12 weeks, followed by a 16-week washout observation period. In both CSU Studies 1 and 2, patients who received Xolair 150 mg or 300 mg had greater decreases from baseline in weekly itch severity scores and weekly hive count scores than placebo at week 12. The 75 mg dose did not demonstrate consistent evidence of efficacy and is not approved for use.

Chronic Rhinosinusitis with Nasal Polyps
The safety and efficacy of Xolair was evaluated in two multicenter, double blind, placebo-controlled clinical trials that enrolled patients with nasal polyps with inadequate response to nasal corticosteroids (Nasal Polyps Trial 1, n=138; Nasal Polyps Trial 2, n = 127). Patients received Xolair or placebo by subcutaneous injection every 2 or 4 weeks for 24 weeks followed by a 4-week follow-up period. All patients received background nasal mometasone therapy during both the treatment period and during a 5-week run-in period. Prior to randomization, patients were required to have evidence of bilateral polyps as determined by a nasal polyp score (NPS) ≥ 5 with NPS ≥ 2 in each nostril, despite use of nasal mometasone during the run-in period. NPS was measured via endoscopy and scored (range 0-4 per nostril: 0 = no polyps; 1 = small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2 = polyps reaching below the lower border of the middle turbinate; 3 = large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4 = large polyps causing complete obstruction of the inferior nasal cavity) for a total NPS (range 0-8). Patients were furthermore required to have a weekly average of nasal congestion score (NCS) > 1 prior to randomization, despite use of nasal mometasone. Nasal congestion was measured by a daily assessment on a 0 to 3 point severity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). The co-primary endpoints in Trials 1 and 2 were NPS and average daily NCS at week 24. The difference in least square means in placebo as compared to Xolair for the NPS was -1.1 and -0.6 in Trials 1 and 2, respectively. The difference in least square means in placebo as compared to Xolair for the NCS was -0.6 and -0.5 in Trials 1 and 2, respectively. In both trials, patients who received Xolair had a statistically significant greater improvement from baseline at week 24 in NPS and weekly average NCS, than patients who received placebo.

IgE-Mediated Food Allergy
The safety and efficacy of Xolair was evaluated in a multi-center, randomized, double-blind, placebo-controlled Food Allergy (FA) trial in 168 adult patients and pediatric patients 1 year of age to less than 56 years who were allergic to peanut and at least two other foods, including milk, egg, wheat, cashew, hazelnut, or walnut (i.e., studied foods). The FA trial enrolled patients who experienced dose-limiting symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) to a single dose of ≤ 100 mg of peanut protein and ≤ 300 mg protein for each of the other two foods (milk, egg, wheat, cashew, hazelnut, or walnut) during the screening double-blind placebo-controlled food challenge (DBPCFC). Patients with a history of severe anaphylaxis (defined as neurological compromise or requiring intubation) were excluded from the study. Patients were randomized 2:1 to receive a subcutaneous dosage of Xolair or placebo based on serum total IgE level (IU/mL), measured before the start of treatment, and by body weight for 16 to 20 weeks. After 16 to 20 weeks of treatment, each patient completed a DBPCFC consisting of placebo and each of their 3 studied foods. Following the DBPCFC, the first 60 patients that included 59 pediatric patients and one adult patient who completed the double-blind, placebo-controlled phase of the study could continue to receive Xolair in a 24 to 28 week open-label extension. The primary efficacy endpoint was the percentage of patients who were able to consume a single dose of ≥ 600 mg of peanut protein without dose-limiting symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) during DBPCFC. Xolair treatment led to a statistically higher response rate (68%) than placebo (5%) who achieved the primary endpoint. The secondary efficacy endpoints were the percentage of patients who were able to consume a single dose of ≥ 1000 mg of cashew, milk, or egg protein without dose-limiting symptoms during DBPCFC. The proportion of patients in the Xolair group who were able to meet secondary endpoints ranged from 42% to 67% compared to 0% to 11% of patients in the placebo group. Thus, the study met the secondary endpoints and demonstrated that Xolair treatment led to statistically higher response rates than placebo for all three foods.

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Policy History

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10/20/2026 UM Committee review and approval. New policy.
Next Scheduled Review Date: 10/2027

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2357, Q5154
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan's Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: All codes listed on the Medical Policy require prior authorization. This ensures appropriate utilization and alignment with current clinical guidelines.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Blue Advantage), Blue Advantage may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Blue Advantage health plan.

Medicare Advantage Members
Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-benehelp.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.