mepolizumab (Nucala®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO046

Description

Omalizumab (Xolair) is a subcutaneously administered monoclonal antibody that binds to IgE causing the IgE receptors to downregulate and limit the degree of release of the mediators of allergic response.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Provider Administered Agents*,++			
Product name	**Indication***	**Dosage form**	**Quantity limit**
omalizumab (Xolair)	Chronic idiopathic urticaria (CIU)	150 mg*	2 vials/28 days (1.2ml/28 days)
		150 mg/1 mL prefilled syringe/autoinjector	1/28 (1ml/28 days)
		300 mg/2 mL prefilled syringe/autoinjector	1/28 (2ml/28 days)
	Allergic asthma**	150 mg vial*	2 vials/28 days (1.2ml/28 days)
		75 mg/0.5 mL prefilled syringe/autoinjector	2/28 (1ml/28 days)
		150 mg/1 mL prefilled syringe/autoinjector	2/28 (2ml/28 days)
		300 mg/2 mL prefilled syringe/autoinjector	2/28 (4ml/28 days)
	Chronic rhinosinusitis with nasal polyposis (CRSwNP)**	150 mg vial*	8 vials/28 days (9.6ml/28 days)
		75 mg/0.5 mL prefilled syringe/autoinjector	2/28 (1ml/28 days)
		150 mg/1 mL prefilled syringe/autoinjector	2/28 (2ml/28 days)
		300 mg/2 mL prefilled syringe/autoinjector	4/28 (8ml/28 days)
	IgE-mediated Food Allergy	150 mg vial*	8 vials/28 days (9.6ml/28 days)
		75 mg/0.5 mL prefilled syringe/autoinjector	2/28 (1ml/28 days)

		150 mg/1 mL prefilled syringe/autoinjector	2/28 (2ml/28 days)
		300 mg/2 mL prefilled syringe/autoinjector	4/28 (8ml/28 days)
	Systemic mastocytosis	150 mg/1.2mL vial*	2 vials/28 days (1.2 ml/28 days)
		150 mg/1 mL prefilled syringe/autoinjector	1/28 (1ml/28 days)
		300 mg/2 mL prefilled syringe/autoinjector	1/28 (2ml/28 days)

**Medical drug that requires administration by a healthcare professional and is not available for self-administration by the member, considered one of the excluded classes under the prescription benefit.*

***Certain groups have opted into the pharmacy benefit optimization (PBO) program in which case selected infused specialty medications will only be covered under the pharmacy benefit, and claims submitted under the medical benefit will be denied as provider liability. For more details, please reference: https://www.modahealth.com/medical/injectables/*

*** Quantity limit can vary by IgE level and body weight. Higher quantities may be appropriate or allowed in specific scenarios depending on IgE and weight. Reviewing clinician should refer to the dosing listed in Appendix at the end of this policy.*

Initial Evaluation

I. **Omalizumab (Xolair)** may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, immunology, or ENT (ear, nose, throat); **AND**
   B. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, dupilumab, mepolizumab, reslizumab, etc.); **AND**
   C. A diagnosis of one of the following:
      1. **Moderate to severe persistent allergic asthma; AND**
         i. Member is six years of age or older; **AND**
         ii. Member has a positive skin test or in vitro reactivity to a perennial aeroallergen; **AND**
         iii. Member must weigh between 20 kg (44 lbs.) and 150 kg (330 lbs.); **AND**
         iv. Member has a serum total IgE level, measured before the start of treatment, of either:
            a. ≥ 30 IU/mL and ≤ 700 IU/mL in members age ≥ 12 years; **OR**
            b. ≥ 30 IU/mL and ≤ 1300 IU/mL in members age 6 to <12 years; **AND**
         v. Member has **MODERATE** asthma as defined by one of the following:
            a. Daily symptoms
            b. Nighttime awakenings > 1x/week but not nightly
            c. SABA (e.g. albuterol, levalbuterol) use for symptom control occurs daily

d. Some limitation to normal activities
e. Lung function (percent predicted FEV1) >60%, but <80%
f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to mild asthma; **OR**

vi. Member has **SEVERE** asthma as defined by <u>one</u> of the following:
a. Symptoms throughout the day
b. Nighttime awakenings, often 7x/week
c. SABA (e.g. albuterol, levalbuterol) use for symptom control occurs several times per day
d. Extremely limited normal activities
e. Lung function (percent predicted FEV1) <60%
f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma; **AND**

vii. Member is currently being treated with:
a. A medium- to high-dose, or maximally tolerated inhaled corticosteroid (ICS) [e.g., budesonide, fluticasone, mometasone]; **AND**
i. One additional asthma controller medication (e.g., long-acting beta-2 agonist [LABA] {e.g., Serevent Diskus}, long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat}, leukotriene receptor antagonist [e.g., Singular], or theophylline); **OR**
b. A maximally tolerated ICS/LABA combination product (e.g., Advair, Airduo, Breo, Dulera, Symbicort); **OR**

2. Chronic idiopathic urticaria/chronic spontaneous urticaria (CIU/CSU); **AND**

i. Member is 12 years of age or older; **AND**
ii. Underlying cause of the member's condition is <u>NOT</u> considered to be any other allergic condition(s) or other form(s) of urticaria; **AND**
iii. Member is avoiding triggers (e.g., NSAIDs, etc.); **AND**
iv. A baseline score from an objective clinical evaluation tool has been provided, such as: urticaria activity score (UAS7), angioedema activity score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), or Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL); **AND**
v. Member had an inadequate response to a minimum (1) month trial on previous therapy of a second-generation H1-antihistamine product*; **AND**
vi. Member had an inadequate response to a minimum (1) month trial on previous therapy of at least **<u>one</u>** of the following:
a. Updosing/dose advancement (up to 4-fold) of a second generation

H1-antihistamine*

b. Add-on therapy with a leukotriene antagonist (e.g., montelukast, zafirlukast, etc.)
c. Add-on therapy with another H1-antihistamine*
d. Add-on therapy with a H2-antagonist (e.g. ranitidine, etc.)
e. Add-on therapy with cyclosporine; **OR**

3. Systemic mastocytosis; AND

i. Member is 18 years of age or older; **AND**
ii. Used for the prevention of **one** of the following:
   a. Chronic mast-cell-mediator-related cardiovascular (e.g., pre-syncope, tachycardia, etc.) or pulmonary (e.g., wheezing, throat-swelling, etc.) symptoms insufficiently controlled by conventional therapy (e.g., H1 or H2 blockers or corticosteroids); **OR**
   b. Unprovoked anaphylaxis; **OR**
   c. Hymenoptera or food-induced anaphylaxis in members with a negative test for specific IgE antibodies or a negative skin test; **OR**
iii. Used to improve tolerance while on immunotherapy (i.e., venom immunotherapy [VIT]); **OR**

4. Chronic rhinosinusitis with nasal polyposis (CRSwNP); AND

i. Member is 18 years of age or older; **AND**
ii. Member must weigh between 30 kg (66 lbs.) and 150 kg (330 lbs.); **AND**
iii. Member has a serum total IgE level ≥ 30 IU/mL and ≤ 1500 IU/mL measured before the start of treatment; **AND**
iv. Provider attests that the member has ALL of the following:
   a. Diagnosis of bilateral sinonasal polyposis as evidenced by an endoscopy or computed tomography (CT); **AND**
   b. Member has impaired Health-Related Quality of Life due to ongoing nasal congestion, blockage, or obstruction with moderate to severe symptom severity; **AND**
   c. Member has at least **one** of the following symptoms:
      i. Nasal discharge
      ii. Facial pain or pressure
      iii. Reduction or loss of smell; **AND**
v. Provider attestation or clinical documentation that member has current persistent symptomatic nasal polyps despite maximal treatment with an intranasal corticosteroid, unless ineffective, not tolerated, or contraindicated; **AND**
vi. Background intranasal corticosteroid will be continued with the use of omalizumab (Xolair), unless contraindicated; **OR**

5. Food Allergies; AND

i. Member is one year of age or older; **AND**
ii. Member has a serum total IgE level ≥ 30 IU/mL and ≤ 1850 IU/mL measured before the start of treatment; **AND**
iii. Member weight is provided; **AND**
iv. Omalizumab (Xolair) not be used in combination with oral immunotherapy (e.g., peanut allergen powder-dnfp (Palforzia) or other peanut desensitization therapy); **AND**
v. Member has a diagnosis of IgE-mediated food allergy, as demonstrated by:
    a. At least one IgE-mediated food allergy (i.e., peanut, milk, egg, wheat, or tree nuts, etc); **AND**
    b. Confirmation of food allergy by at least one of the following:
        i. Positive skin prick test or serologic evidence of IgE-mediated antibody to a potent extract of the allergen; **OR**
        ii. Reacted to an oral food challenge; **AND**
    c. Provider attestation of all of the following:
        i. Member has a history of Type 1 reaction (e.g., hives, rash, stomach cramps, vomiting, etc.) or anaphylaxis from ingestion of one or more food allergens; **AND**
        ii. Member will continue to practice food avoidance to reduce risk of anaphylaxis while on omalizumab (Xolair); **AND**
        iii. Member has an active prescription for epinephrine.

II. Omalizumab (Xolair) is considered investigational when used for all other conditions, including but not limited to:
    A. Management of Immune Checkpoint Inhibitor related toxicity
    B. Eosinophilic esophagitis
    C. Interstitial cystitis
    D. Painful bladder syndrome
    E. Eosinophilic bronchitis
    F. Multi-food oral immunotherapy
    G. Bullous pemphigoid
    H. Solar urticaria
    I. Cholinergic urticaria
    J. Seasonal allergic rhinitis
    K. Emergency treatment of any allergic reaction, including anaphylaxis
    L. Non-IgE-mediated food allergy, other food reactions (e.g., celiac disease)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, dupilumab, mepolizumab, reslizumab, etc.); **AND**

IV. A diagnosis of one of the following:

i. Moderate to severe persistent allergic asthma; AND

1. Member must weigh between 20 kg (44 lbs.) and 150 kg (330 lbs.); **AND**

2. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations, FEV1, reduced systemic corticosteroid requirements, reduced hospitalizations); **OR**

ii. **Chronic idiopathic urticaria/chronic spontaneous urticaria (CIU/CSU)**; **AND**

1. Member has exhibited improvement or stability of disease symptoms from baseline using objective clinical evaluation tools (e.g., urticaria activity score [UAS7], angioedema activity score [AAS], Dermatology Life Quality Index [DLQI], Angioedema Quality of Life [AE-QoL], or Chronic Urticaria Quality of Life Questionnaire [CU-Q2oL]); **AND**

2. Submitted current UAS7, AAS, DLQI, AE-QoL, or Cu-Q2oL was recorded within the past **30** days; **OR**

iii. **Systemic mastocytosis**; **AND**

1. Member has exhibited improvement or stability of disease symptoms compared to baseline (e.g., decreased frequency of exacerbations); **OR**

iv. Chronic rhinosinusitis with nasal polyposis (CRSwNP); AND

1. Member must weigh between 30 kg (66 lbs.) and 150 kg (330 lbs.); **AND**

2. Member has exhibited improvement or stability of disease symptoms (e.g., improvement in nasal congestion/obstruction severity, reduction in nasal polyps); **AND**

3. Background intranasal corticosteroid (e.g., beclomethasone [Qnasl], budesonide [Rhinocort], ciclesonide [Omnaris; Zetonna], flunisolide, fluticasone [Flonase], mometasone [Nasonex], triamcinolone [Nasacort]) will be continued with the use of omalizumab (Xolair), unless contraindicated.

4. **IgE-mediated Food Allergies**; **AND**

i. Provider attestation that omalizumab (Xolair) continues to reduce allergic reactions to more than one type of food after accidental exposure and treatment provides clinical benefit to the member; **AND**

ii. Treatment will not be used in combination with oral immunotherapy (e.g., peanut allergen powder-dnfp (Palforzia) or other peanut desensitization therapy); **AND**
iii. Member continues to practice food avoidance to reduce risk of anaphylaxis; **AND**
iv. Member has an active prescription for epinephrine

Supporting Evidence

I. There is a lack of evidence supporting treatment with dual use of biologic therapies and a potential for increased risk of side effects.
II. Omalizumab (Xolair) is FDA approved for 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 (ICS), as add-on maintenance treatment for patients 18 years of age with chronic rhinosinusitis with nasal polyps (CRSwNP), as chronic spontaneous urticaria in patients 12 years of age and older who remain symptomatic despite H1 antihistamine treatment, and for immunoglobin E (IgE)-mediated food allergy in adult and pediatric patients 1 year of age and older for the reduction of allergic reactions (Type I) that may occur with accidental exposure to one or more foods.
    - Omalizumab (Xolair) is not FDA approved for use in the setting of systemic mastocytosis; however, it is compendia recommended.

III. Omalizumab (Xolair) prefilled syringes and autoinjectors have been FDA approved for self-administration for the treatment of asthma in patients 6 years and older, chronic spontaneous urticaria (CSU) in patients 12 years and older, nasal polyps in patients aged 18 years and older, and IgE-mediated food allergies in patients aged 1 year and older. According to the package insert, therapy should be initiated in a healthcare setting. Once therapy has been safely established, the healthcare provider may determine whether self-administration of omalizumab (Xolair) is appropriate, based on careful assessment of risk for anaphylaxis and risk reduction strategies. Patient-specific factors considered when selecting patients for self-administration include the following criteria:

- Patient should have no prior history of anaphylaxis, including to XOLAIR or other agents, such as latex, foods, drugs, biologics, etc.
- Patient should receive at least 3 doses of XOLAIR under the guidance of a healthcare provider with no hypersensitivity reactions
- Patient or caregiver is able to recognize symptoms of anaphylaxis
- Patient or caregiver is able to treat anaphylaxis appropriately
- Patient or caregiver is able to perform subcutaneous injections with XOLAIR prefilled syringe or autoinjector with proper technique according to the prescribed dosing regimen and Instructions for Use

IV. Omalizumab (Xolair) autoinjectors at all doses are not intended for use in pediatric patients under 12 years of age.

V. Moderate to severe persistent allergic asthma

- For patients 12 years of age and older, omalizumab (Xolair) was studied in 3 randomized, double-blind, placebo-controlled, multicenter trials. The patients enrolled in these trials were 12 to 76 years of age, with moderate to severe persistent asthma for at least one year, and a positive skin test reaction to a perennial aeroallergen. All patients were required to have a baseline IgE level between 30 and 700 IU/mL and body weight ≤150 kg. Patients with IgE levels less than 30 IU/mL, greater than 700 IU/mL, or a weight greater than 150 kg have not been studied and efficacy has not been demonstrated in a randomized controlled clinical trial.
    i. Trials 1 and 2: All patients were symptomatic and were treated with ICS/SABA. The primary endpoint was mean number asthma exacerbations per patient during steroid stable phase versus steroid reduction phase in comparison to placebo. In the stable steroid phase, the mean number of exacerbations per patient was 0.2 in the active arm compared to 0.3 in the placebo arm, p-value=0.005 (Trial 1) and 0.1 in the active arm compared to 0.4 in the placebo arm, p-value<0.001 (Trial 2). In the steroid reduction phase, the mean number of exacerbations per patient was 0.2 in the active arm compared to 0.4 in the placebo arm, p-value=0.004 (Trial 1) and 0.2 in the active arm compared to 0.3 in the placebo arm, p-value<0.001 (Trial 2).
    ii. Trial 3: Long-acting beta2-agonists were allowed. Patients received at least 1000 mcg/day fluticasone propionate and a subset also received oral corticosteroids (OCS). The primary endpoint was percentage of patients with at least 1 exacerbation during steroid stable phase versus steroid reduction phase in comparison to placebo. In the stable steroid phase, the treatment difference in percentage of patients with at least one exacerbation was 0.9 (95% CI -9.7, 13.7) in the ICS only arm compared to 9.8 (95% CI -10.5, 31.4) in the OCS/ICS arm. In the steroid reduction phase, the treatment difference in percentage of patients with at least one exacerbation was -4.4 (95% CI -17.6, 7.4) in the ICS only arm compared to -0.2 (95% CI -22.4, 20.1) in the OCS/ICS arm.
- For patients 6 to <12 years of age, omalizumab (Xolair) was studied in one double-blind, placebo controlled, multi-center trial. All patients were required to have a baseline IgE level between 30 and 1300 IU/mL and body weight between 20 to 150 kg. The primary endpoint was the rate of asthma exacerbations during the 24-week, fixed steroid treatment phase, which was 0.45 in the active arm compared to 0.64 in the placebo arm (RR 0.69, 95% CI 0.53, 0.9).

- The Global Initiative for Asthma (GINA) 2020 update recommends the addition of respiratory biologics, with respect to their allergic biomarkers, after inadequate asthma control despite good adherence and inhaler technique on maximized Step 4 (medium dose ICS-LABA) or Step 5 (high dose ICS-LABA) therapy. Other controller options for Step 4 include high dose ICS-LABA or add-on tiotropium, or add-on LTRA. Other controller options for Step 5 include add-on anti-IL5, or add-on low dose OCS, though guidelines note to consider side effects.
- Dose adjustments should be considered for drastic changes in body weight. Dosing should not be adjust based off IgE levels unless therapy has been interrupted for greater than one year. A minimum of three to six months of treatment is suggested to reach maximum efficacy.

VI. **Chronic idiopathic urticaria/chronic spontaneous urticaria (CIU/CSU)**

- Omalizumab (Xolair) was studied in two placebo-controlled, multiple-dose clinical trials. Patients received omalizumab (Xolair) 75 mg, 150 mg, or 300 mg or placebo by subcutaneous injection every 4 weeks in addition to their baseline level of H1 antihistamine therapy for 24 or 12 weeks, followed by a 16-week washout observation period. Per the prescribing label, the 75-mg dose did not demonstrate consistent evidence of efficacy and is not approved for use in CIU. Clinical trials required a UAS7 score of greater than or equal to 16 with weekly reassessments to objectively measure treatment benefit. The primary endpoints were mean weekly itch severity score and weekly hive count.

	XOLAIR 75mg	XOLAIR 150mg	XOLAIR 300mg	Placebo
n	77	80	81	80
Weekly Itch Severity Score				
Mean Baseline Score (SD)	14.5 (3.6)	14.1 (3.8)	14.2 (3.3)	14.4 (3.5)
Mean Change Week 12 (SD)	−6.46 (6.14)	−6.66 (6.28)	−9.40 (5.73)	−3.63 (5.22)
Difference in LS means vs. placebo	−2.96	−2.95	−5.80	
95% CI for difference	−4.71, −1.21	−4.72, −1.18	−7.49, −4.10	-
Weekly Hive Count Score †				
Mean Baseline Score (SD)	17.2 (4.2)	16.2 (4.6)	17.1 (3.8)	16.7 (4.4)
Mean Change Week 12 (SD)	−7.36 (7.52)	−7.78 (7.08)	−11.35 (7.25)	−4.37 (6.60)
Difference in LS means vs. placebo	−2.75	−3.44	−6.93	
95% CI for difference	−4.95, −0.54	−5.57, −1.32	−9.10, −4.76	-

- Per the EAACI/GA²LEN/EDF/WAO guidelines for the definition, classification, diagnosis, and management of urticaria the recommended starting dose of Omalizumab (Xolair) for CIU is 300 mg every 4 weeks.
- Per clinical trials of patients with CIU taking Omalizumab (Xolair), 36% of patients treated with 300 mg reported no itch or hives at week 12 compared to 15% treated with 150 mg, 12% with 75mg, and 9% with placebo.

- There is limited data regarding the continuation of Omalizumab (Xolair) and the need for dose reductions. Preliminary studies discuss the potential for dose reductions or increased dosing intervals, although there is currently no consensus on the best method.

VII. Systemic mastocytosis

- Omalizumab (Xolair) is recommended per NCCN guidelines for Systemic Mastocytosis for the treatment of mast-cell-mediator-related cardiovascular or pulmonary symptoms after prior trial of an H1 blocker, H2 blocker, and corticosteroids. Use of omalizumab (Xolair) for the management of Systemic Mastocytosis is supported by case studies and prospective reviews, though no clinical trials have been completed. Omalizumab (Xolair) has been found to prevent mast-cell-mediator-related cardiovascular or pulmonary symptoms despite use of conventional therapies and has been shown to improve tolerance while on immunotherapy.

VIII. **Chronic rhinosinusitis with nasal polyposis (CRSwNP)**

- Omalizumab (Xolair) was studied as an add-on therapy with background intranasal corticosteroid in adult patients with CRSwNP with inadequate response to intranasal corticosteroids. Omalizumab (Xolair) was evaluated in two identical phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter trials. Trials enrolled patients aged 18 through 75 years with persistent bilateral nasal polyps, nasal congestion, impaired HRQoL, and weight 30-150 kg and serum IgE level 30- 1500 IU/mL. The primary endpoints were change from baseline to week 24 in endoscopic nasal polyp score (NPS) and mean daily nasal congestion score (NCS). Key secondary endpoints were change from baseline at week 24 in Sino-Nasal Outcome Test-22 (SNOT-22) score, University of Pennsylvania Smell Identification Test (UPSIT) score, and Asthma Quality of Life Questionnaire (AQLQ).

	POLYP 1			POLYP 2		
	PBO N=66	**OMA N=72**	**Treatment Difference (95% CI), p-value**	**PBO N=65**	**OMA N=62**	**Treatment Difference (95% CI), p-value**
Primary Endpoint						
NPS (range, 0-8)	0.06 (0.16)	-1.08 (0.16)	-1.14 (-1.59 to -0.69) p<0.0001	-0.31 (0.16)	-0.9 (0.19)	-0.59 (-1.05 to 0.12) p<0.14
NCS (range, 0-3)	-0.35 (0.11)	-0.89 (0.1)	-0.55 (-0.84 to -0.25) p<0.0004	-0.20 (0.11)	-0.70 (0.11)	-0.50 (-0.80 to -0.19) p<0.0017
Secondary Endpoint						
SNOT-22 score (range, 0-110)	-8.58 (2.08)	-24.70 (2.01)	-16.12 (-21.86 to -10.38) p<0.0001	-6.55 (2.19)	-21.59 (2.25)	-15.04 (-21.26 to -8.82) p<0.0001
UPSIT score (range, 0-40)	0.63 (0.90)	4.44 (0.84)	3.81 (1.38-6.24) p<0.0024	0.44 (0.81)	4.31 (0.83)	3.86 (1.57-6.15) p<0.0011

AQLQ score, OR of MCID (≥0.5-point improvement)	OR 3.71 (95% CI 1-13.71, p=0.0492)	OR 4.04 (95% CI 1.07-15.25, p=0.0396)

MCID: minimal clinically important difference

- The American Academy of Allergy, Asthma, and Immunology (AAAAI), American College of Allergy, Asthma, and Immunology (ACAAI), and Joint Council of Allergy, Asthma, and Immunology (JCAAI) 2014 guidelines recommend short-term treatment with oral steroids in patients with CRSwNP "because it decreases nasal polyp size and symptoms". Additionally, guidelines recommend both intranasal corticosteroids and omalizumab for treatment of CRSwNP.

IX. IgE-mediated Food Allergies

- Omalizumab (Xolair) is the first FDA-approved medication to reduce the health impact of allergic reactions to more than one type of food after accidental exposure. Goals of treatment include increasing tolerance to small amounts of food allergens and reducing the chances of having a severe anaphylactic reaction upon accidental ingestion. There is currently no cure for food allergy; management requires the patient strictly avoid any exposure to known allergens, along with prompt administration of epinephrine to treat anaphylaxis if accidental exposures occur. Therefore, the use of omalizumab (Xolair) is reserved for members with medical history of severe food allergy reactions that cannot be managed despite food avoidance to control allergic symptoms and conventional therapies such as antihistamines (e.g., reaction causes anaphylaxis, requires epinephrine use, allergy that can be triggered by smell).
- Coverage requires a confirmed food allergy diagnosis consisting of a clinical history of allergy along with confirmatory values with a positive skin prick test and elevated serum IgE levels or food challenge, as per guideline recommendations.
- The efficacy and safety of omalizumab (Xolair) was evaluated in 168 pediatric patients in a phase 3, randomized, placebo-controlled trial (OUtMATCH). The study enrolled patients 1 - 55 years of age who were allergic to peanut and at least two other foods, including milk, egg, wheat, cashew, hazelnut, or walnut. Patients were randomized 2:1 to receive Xolair or placebo SC based on serum total IgE level and body weight, for 16 to 20 weeks. The study excluded patients with severe anaphylaxis and high baseline IgE levels (>1500mg). The primary endpoint evaluated the percentage of patients who were able to consume a single dose of ≥600 mg of peanut protein (~2.5 peanuts or ½ teaspoon of regular peanut butter) without moderate to severe allergic symptoms. Omalizumab (Xolair) treatment led to a statistically higher response rate compared to placebo (68% omalizumab vs. 5% placebo; treatment difference, 63% [95% CI, 50% to 73%]). However, 17% of subjects receiving omalizumab (Xolair) had no significant change in the amount of peanut protein tolerated (could not tolerate 100 mg or more of peanut protein).

The incidence of adverse events was similar between groups and no new safety signals were identified.

- Omalizumab (Xolair) does not modulate any food response and patients must still practice food avoidance. There is unknown clinical significance and meaningfulness of improving tolerance of a single dose of 600 mg peanut protein. Furthermore, tolerance of 600 mg of peanut protein did not result in improvements in quality of life and reductions in reactions to accidental exposure to peanuts in the clinical trial.
- Restricted to treating peanut allergy, peanut allergen powder-dnfp (Palforzia) is an oral immunotherapy product approved in patients 4–17 years of age for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. Safety and efficacy of combination treatment has not been evaluated and is therefore considered experimental and investigational. Furthermore, patients taking Palforzia were excluded from participating in the clinical trial evaluating omalizumab (Xolair).

Investigational or Not Medically Necessary Uses

I. Omalizumab (Xolair) has not been adequately studied for the following conditions and does not have established safety and efficacy in these populations:
   A. Management of Immune Checkpoint Inhibitor related toxicity
      i. Though use is supported by NCCN guidelines for Management of Immunotherapy-related toxicities, there are no clinical trials demonstrating clinical efficacy or safety of the use of omalizumab (Xolair) in the treatment of Immune Checkpoint Inhibitor related toxicity.
   B. Emergency treatment of any allergic reaction, including anaphylaxis
   C. Non-IgE-mediated food allergy, other food reactions (e.g., celiac disease)
      i. Non-IgE mediated food allergies present as more subacute and/or chronic symptoms that are typically isolated to the GI tract and/or skin. Of note, celiac disease is caused by a non–IgE-mediated immune reaction to a food protein (gluten) and having a diagnosis alone is not considered a food allergy.
   D. Ongoing clinical trials for the following conditions without outcomes demonstrating efficacy of treatment:
      i. Eosinophilic esophagitis
      ii. Interstitial cystitis
      iii. Painful bladder syndrome
      iv. Eosinophilic bronchitis
      v. Multi-food oral immunotherapy
      vi. Bullous pemphigoid
      vii. Solar urticaria

viii. Cholinergic urticaria
ix. Seasonal allergic rhinitis

Appendix

I. Table 1: Indication and dosing

Indication	Dose
Allergic Asthma	75 to 375 mg administered subcutaneously every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See tables below.
Chronic idiopathic urticaria	150 or 300 mg administered subcutaneously every 4 weeks. Dosing is not dependent on serum IgE (free or total) level or body weight.
Chronic rhinosinusitis with nasal polyposis	75 to 600 mg SC administered subcutaneously every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See tables below.
IgE-mediated Food Allergies	75 to 600 mg SC administered subcutaneously every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See tables below.
All other indications	150 or 300 mg administered subcutaneously by a health care provider every 4 weeks. Dosing is not dependent on serum IgE (free or total) level or body weight.

II. Table 1: Weight based dosing every 2 or 4 weeks in members ≥ 12 years of age and older with Asthma

	Omalizumab administered every 2 or 4 weeks (mg) in members ≥ 12 years with asthma				
Pre-treatment serum IgE (IU/mL)		**Body weight (kg)**			
	Dosing Frequency	**30 to 60**	**> 60 to 70**	**> 70 to 90**	**> 90 to 150**
≥ 30 to 100	Every 4 weeks	150	150	150	300
> 100 to 200		300	300	300	225
> 200 to 300		300	225	225	300
>300 to 400	Every 2 weeks	225	225	300	
>400 to 500		300	300	375	
>500 to 600		300	375	Insufficient Data to	

>600 to 700		375	recommend a dose

III. Table 2: Weight based dosing every 2 or 4 weeks for in members who begin Xolair between the ages of 6 to <12 years for Asthma

Omalizumab Doses Administered Every 2 or 4 Weeks (mg) for Pediatric Members with Asthma Who Begin Xolair Between the Ages of 6 to <12 Years											
Pre-treatment IgE (IU/mL)	Dosing Freq. (weeks)	Body Weight (kg)									
		20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
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					
>700-900	Every 2 weeks	225	225	300	375						
>900-1100		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

Insufficient data to recommend a dose

IV. Table 3. Weight based dosing every 2 or 4 weeks for adults with CRSwNP

Omalizumab Doses Administered Every 2 or 4 Weeks (mg) for adults with CRSwNP									
Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight							
		>30-40kg	>40-50kg	>50-60kg	>60-70kg	>70-80kg	>80-90kg	>90-125kg	> 125-150kg
		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					
>1200 - 1300		450	525						
>1300 - 1500		525	600						

Insufficient Data to Recommend a Dose

V. Table 4: Weight based dosing for adult and pediatric members with IgE-mediated Food Allergies

Omalizumab Doses Administered Every 2 or 4 Weeks (mg) for adult and pediatric members with IgE-Mediated Food Allergy														
Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight (kg)												
		≥10-12	>12-15	>15-20	>20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	> 125-150
		Dose (mg)												
30 - 100	Every 4 weeks	75	75	75	75	75	75	150	150	150	150	150	300	300
>100 -200		75	75	75	150	150	150	300	300	300	300	300	450	600
>200 - 300		75	75	150	150	150	225	300	300	450	450	450	600	375
>300 - 400		150	150	150	225	225	300	450	450	450	600	600	450	525
>400 - 500		150	150	225	225	300	450	450	600	600	375	375	525	600
>500 - 600		150	150	225	300	300	450	600	600	375	450	450	600	
>600 - 700		150	150	225	300	225	450	600	375	450	450	525		
>700 - 800	Every 2 weeks	150	150	150	225	225	300	375	450	450	525	600		
>800 - 900		150	150	150	225	225	300	375	450	525	600			
>900 - 1000		150	150	225	225	300	375	450	525	600				
>1000 - 1100		150	150	225	225	300	375	450	600					
>1100 - 1200		150	150	225	300	300	450	525	600					
>1200 - 1300		150	225	225	300	375	450	525						
>1300 - 1500		150	225	300	300	375	525	600						
>1500 - 1850			225	300	375	450	600							

Insufficient Data to Recommend a Dose

VI. Abbreviated list of H1 antihistamine products:

*H1 Antihistamine Products (not all inclusive)	
• fexofenadine • loratadine • desloratadine • cetirizine • levocetirizine • clemastine • diphenhydramine	• chlorpheniramine • hydroxyzine • cyproheptadine • brompheniramine • triprolidine • dexchlorpheniramine • carbinoxamine

References

1. Xolair [package insert]. South San Francisco, CA; Genentech, Inc.; Updated February 2024. Accessed February 2024.
2. National Asthma Education and Prevention Program (NAEPP). Guidelines for the diagnosis and management of asthma. Expert Panel Report 3. Bethesda, MD: National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI);August 2007.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2020 Update. Available from: http://www.ginasthma.org. Accessed February 2021.
4. Baiardini I, Braido F, Bindslev-Jensen C, et al. Recommendations for assessing member- reported outcomes and health-related quality of life in members with urticaria: a GA(2)
5. National Comprehensive Cancer Network clinical practice guidelines, systemic mastocytosis. Version 1.2020. Updated May 21, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed February 1, 2021.
6. Broesby-Olsen S1, Vestergaard H2, Mortz CG,er al. Omalizumab prevents anaphylaxis and improves symptoms in systemic mastocytosis: Efficacy and safety observations. Allergy. 2018 Jan;73(1):230-238. doi: 10.1111/all.13237. Epub 2017 Jul 27.
7. National Comprehensive Cancer Network clinical practice guidelines, management of immunotherapy-related toxicities. Version 1.2020. Updated December 16, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed February 6, 2020.
8. Gevaert P, Omachi TA, Corren J et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. *J Allergy Clin Immunol* 2020;146(3):595-605. Available at: https://pubmed.ncbi.nlm.nih.gov/32524991/. Accessed January 27, 2021.
9. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter Update. *Ann Allergy Asthma Immunol* 2014 (113):347-385. Available at: http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/2014-October_Rhinosinusitis_Update.pdf. Accessed January 27, 2021.
10. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA2LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy. 2018;73(7):1393-1414.
11. UptoDate. Anti-IGgE Therapy, Updated November 18, 2021. Accessed June 3, 2022.
12. Wood RA, Togias A, Sicherer SH, et al. Omalizumab for the Treatment of Multiple Food Allergies. *N Engl J Med*. 2024;390(10):889-899. doi:10.1056/NEJMoa2312382
13. Asthma and Allergy Foundation of America. The allergic or atopic march. June 2022. Accessed March 7, 2024. https://aafa.org/allergies/prevent-allergies/allergic-march/
14. Bright DM, et al. Food allergies: Diagnosis, treatment, and prevention. *Am Fam Physician*. 2023;108(2):159-165.
15. Sampson HA, et al. Food allergy: a practice parameter update-2014. *J Allergy Clin Immunol.* 2014;134(5):1016-25.e43. doi:10.1016/j.jaci.2014.05.013

16. Santos AF, et al. EAACI guidelines on the diagnosis of IgE-mediated food allergy. *Allergy*. 2023;78(12):3057-3076. doi:10.1111/all.15902
17. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol.* 2010;126(6 Suppl):S1-S58. doi:10.1016/j.jaci.2010.10.007
18. Fleischer DM, et al. A consensus approach to the primary prevention of food allergy through nutrition: Guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology. *J Allergy Clin Immunol Pract*. 2021;9(1):22-43.e4. doi:10.1016/j.jaip.2020.11.002

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
dupilumab (Dupixent®) Policy	Asthma (moderate to severe)
	Atopic Dermatitis (moderate to severe)
	Chronic rhinosinusitis with nasal polyposis
	Eosinophilic esophagitis
	Prurigo nodularis
benralizumab (Fasenra Pen™) Policy	Asthma (severe)
mepolizumab (Nucala®)	Asthma (severe)
	Eosinophilic granulomatosis with polyangiitis
	Hypereosinophilic Syndrome
	Chronic Rhinosinusitis with Nasal Polyps
reslizumab (Cinqair®) Policy	Asthma (severe)
Tezepelumab (Tezspire®) Policy	Asthma (severe)
peanut allergen powder-dnfp (Palforzia™)	Peanut allergy

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed oral steroid requirement for CRSwNP.	03/2025
Updated food allergy indication to include any food allergen.	06/2024
Updated policy to include IgE-mediated food allergies indication. Updated quantity limits table. Updated CSU to CIU given name change as adapted by clinical practice guidelines. Updated E/I to remove urticaria given Xolair, and added emergency treatment of any allergic reaction, including anaphylaxis and non-IgE-mediated food allergy, other food reactions (e.g., celiac disease). Updated appendix with dosing tables, supporting evidence, references. Added related policies.	03/2024
Updated quantity limit for CIU and supporting evidence (dose recommendation)	06/2022
Update to supporting evidence (self-administration of Xolair)	05/2021
Updated policy to include chronic rhinosinusitis with nasal polyposis (CRSwNP) indication. Updated policy to include route of administration under Description, PBO program under Quantity Limits. For Initial Evaluation: added medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, immunology, or ENT (ear, nose, throat); asthma: removed moderate and severe asthma definition table in supporting evidence and built into criteria set, revised verbiage of	03/2021

previous combination therapy use and added ";OR a maximally tolerated ICS/LABA combination product". For Renewal Evaluation: asthma: revised to updated renewal verbiage and consolidated list of clinical improvement examples; CIU and systemic mastocytosis: revised to updated renewal verbiage. For supporting evidence: removed subjective verbiage and included more detailed information regarding each policy indication.	
Convert to Policy format. Removed Management of Immune Checkpoint Inhibitor related toxicity criteria to investigational rational given lack of clinical evidence to support. Removed toxicity assessment in renewal portion as this is managed by the provider.	02/2020
Previous reviews	10/2019, 10/2018, 06/2018, 03/2018, 12/2017, 09/2017, 06/2017, 03/2017, 12/2016, 09/2016, 07/2016, 07/2015, 09/2014, 04/2014, 02/2013, 06/2012
Policy created	01/2012