Medical Policy Bulletin

Title:
Omalizumab (Xolair®) and Related Biosimilars
Policy #:
MA08.025i

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

INITIAL THERAPY
Allergic Asthma

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered as an adjunctive treatment of moderate-to-severe persistent asthma in individuals who are at least 6 years of age when all of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual has a positive skin test or in vitro reactivity to a perennial aeroallergen.
- The individual has a baseline serum immunoglobulin E (IgE) level of between 30 IU/mL and 1500 IU/mL.
- High-dose inhaled corticosteroids (ICS) taken in combination with a long-acting beta-agonist (LABA) have been tried but failed to adequately control the individual's asthma symptoms.
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair]).
- Dosing and Frequency Requirements: See below

Chronic Urticaria

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered for the

treatment of chronic urticaria in individuals who are at least 12 years of age when all of the following criteria, including Dosing and Frequency Requirements listed below, are met:

- Documented failure, contraindication, or intolerance to a 4-week trial of one second-generation nonsedating H1 antihistamine at the maximum recommended doses (e.g., cetirizine [Zyrtec], fexofenadine [Allegra], loratadine [Claritin, Alavert], desloratadine [Clarinex], levocetirizine [Xyzal])
- Documented failure, contraindication, or intolerance to at least a 2-week trial of any of the following medications:
    - Leukotriene receptor antagonist (e.g., zafirlukast [Accolate], montelukast [Singulair], zileuton [Zyflo]) in addition to the nonsedating H1 antihistamine
    - Histamine H2-receptor antagonist (e.g., cimetidine [Tagamet], famotidine [Pepcid], nizatidine) in addition to the nonsedating H1 antihistamine
    - First-generation (sedating) H1 antihistamine (e.g., chlorpheniramine [Chlor-Trimeton], cyproheptadine, diphenhydramine [Benadryl]) in addition to the nonsedating H1 antihistamine
    - Systemic glucocorticosteroids administered as a short-term therapy (may treat for less than a 2-week trial) in addition to the nonsedating H1 antihistamine
    - Addition of, or substitution to, a different second-generation nonsedating H1 antihistamine
    - Cyclosporine, in addition to the nonsedating H1 antihistamine
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) and related biosimilars 150 or 300 mg by subcutaneous injection every 4 weeks. Dosing is not dependent on serum IgE levels or body weight.

IgE-Mediated Food Allergy

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered for the treatment of IgE-mediated food allergy (Type I) in individuals who are 1 year of age or older for the reduction of allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods when all of the following criteria, including Dosing and Frequency Requirements listed below and below are met:

- IgE mediated food allergy has been confirmed by at least one of the following:
    - Positive skin prick test (≥ 4 mm wheal greater than saline control)
    - Positive food specific serum IgE (≥ 6 IU/mL)
    - A positive physician controlled oral food challenge (e.g., moderate to severe skin, respiratory, or gastrointestinal [GI] symptoms)
    - Baseline (pre-treatment) serum total IgE level is greater than or equal to 30 IU/mL and less than or equal to 1850 UE/mL
- Omalizumab (Xolair) and related biosimilars are used in conjunction with food allergen avoidance.
- Omalizumab (Xolair) and related biosimilars will not be used as the emergency treatment for allergic reactions (including anaphylaxis, asthma, rhinitis, conjunctivitis, dermatitis) and individual has access to epinephrine.
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair]).
- Dosing and Frequency Requirements: below

Immune Checkpoint Inhibitor–Related Pruritus

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered for the management of refractory cases of moderate (Grade 2) or severe (Grade 3) pruritus related to immunotherapy (e.g., ipilimumab [Yervoy], nivolumab [Opdivo], pembrolizumab [Keytruda]) in adult individuals when all of the following criteria, including the Dosing and Frequency Requirements below, are met:

- The individual has no response to 1 month of gabapentinoids (e.g., gabapentin and pregabalin)
- The individual has an elevated baseline serum IgE level
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) and related biosimilars doses up to 300 mg by subcutaneous injection every 4 weeks

Chronic Rhinosinusitis with Nasal Polyps

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered as add-on maintenance therapy of chronic rhinosinusitis with nasal polyps in adults when all of the following criteria, including Dosing and Frequency Requirements listed below, are met:

- The individual is diagnosed with persistent bilateral nasal polyps characterized by all of the following:
    - Signs and symptoms of rhinosinusitis persisting at least 12 weeks (e.g., nasal and sinus inflammation, nasal drainage/congestion, facial pressure/pain, reduction in sense of smell)
    - Evidence of nasal polyps identified via one of the following visualization techniques: anterior rhinoscopy, nasal endoscopy, sinus computed tomography (CT) or magnetic resonance imaging (MRI)
    - The individual has a Nasal Polyp Score (NPS) of 5 or higher (NPS >2 for each nostril) at baseline
    - The individual has a weekly self-reported Nasal Congestion Score (NCS) average of >1 at baseline
- The individual has a baseline serum IgE level of between 30 IU/mL and 1500 IU/mL
- Documented failure, contraindication, or intolerance to at least a 4-week trial of intranasal corticosteroids
- Omalizumab (Xolair) and related biosimilars will be used in combination with intranasal corticosteroids, unless documented failure, contraindication, or intolerance.
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency Requirements: below

Systemic Mastocytosis

Prophylactic Treatment for Chronic Mast Cell Mediator–Related Cardiovascular and Pulmonary Symptoms

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered for the following conditions in individuals who are at least 12 years of age, when all of the following criteria, including the Dosing and Frequency Requirements listed below, are met:

- As a component of stepwise prophylactic treatment for chronic mast cell mediator–related cardiovascular and pulmonary symptoms (e.g., pre-syncope, tachycardia, wheezing, throat swelling), that are insufficently controlled by H1- and H2-blockers and corticosteroids
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) and related biosimilars doses up to 300 mg by subcutaneous injection every 4 weeks

Prevention of Anaphylaxis

Omalizumab (Xolair) and related biosimilars are considered medically necessary and, therefore, covered for the following conditions in individuals who are at least 12 years of age, when all of the following criteria, including the Dosing and Frequency Requirements listed below, are met:

- Prevention of one of the following conditions:
    - Unprovoked anaphylaxis
    - Hymenoptera (insect venom, e.g., bee or wasp sting) or food-induced anaphylaxis, with negative specific IgE or negative skin test
    - To improve tolerance while on immunotherapy
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) and related biosimilars doses up to 300 mg by subcutaneous injection every 2 weeks.

CONTINUATION THERAPY

Continuation of omalizumab (Xolair) and related biosimilars is considered medically necessary and, therefore, covered when all of the following criteria are met:

- The individual has a documented clinical improvement or stabilization in their disease (e.g., reduction in the frequency of exacerbations, reduction in the reported signs and symptoms)
- The individual continues to receive concomitant drugs, if applicable
- Omalizumab (Xolair) and related biosimilars will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- The Dosing and Frequency Requirements are met

EXPERIMENTAL/INVESTIGATIONAL

All other uses for omalizumab (Xolair) and related biosimilars including, but not limited to, acute bronchospasm or status asthmaticus, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

Refer to this Policy Section (above) or to below for the Dosing and Frequency Requirements for omalizumab (Xolair) and related biosimilars.

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of omalizumab (Xolair) and related biosimilars. Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of omalizumab (Xolair) and related biosimilars outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for omalizumab (Xolair) and related biosimilars.

ALLERGIC ASTHMA

Dosing for Allergic Asthma: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. See dosing information below:
Peer-reviewed literature and clinical trials recommend a minimum dose of 0.016 mg/kg/IgE (units/mL) subcutaneously per 4 weeks.

Dosing and Frequency for Individuals 6 Years of Age and Older:

Pretreat-ment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)									
30-100		75	75	+75 *150	150	150	150	150	150	300	300

>100-200	Every 4 weeks	150	150	+150 *300	300	300	300	300	300	225	+300 *225
>200-300		150	150	+225 *300	300	300	225	225	225	300	+375 *300
>300-400		225	225	+300 *225	225	225	225	300	300	450	525
>400-500		225	300	+225 *300	+225 *300	300	300	375	375	525	600
>500-600		300	300	+225 *300	300	300	375	450	450	600	
>600-700		300	225	+225 *375	+300 *375	375	450	450	525		
>700-800	Every 2 weeks	225	225	300	375	450	450	525	600		
>800-900		225	225	300	375	450	525	600			
>900-1000		225	300	375	450	525	600				
>1000-1100		225	300	375	450	600			Insufficient data to recommend a dose		
>1100-1200		300	300	450	525	600					
>1200-1300		300	375	450	525						
>1300-1500		300	375	525	600						

Sources: U.S. Prescribing Information, European Prescribing Information, Kornmann 2014, Zielen 2013, Lowe 2015.

Note: There are some dosing differences between age groups that are identified by the following symbols:
+ Individuals 6 – 12 years of age
* Individuals 12 years of age and older

CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

Dosing for Chronic Rhinosinusitis with Nasal Polyps: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. See dosing information below:

Dosing and Frequency for Individuals 18 Years of Age and Older:

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight							
		>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)							
30-100	Every 4 weeks	75	150	150	150	150	150	300	300
>100-200		150	300	300	300	300	300	450	600
>200-300		225	300	300	450	450	450	600	375
>300-400		300	450	450	450	600	600	450	525
>400-500		450	450	600	600	375	375	525	600
>500-600		450	600	600	375	450	450	600	
>600-700		450	600	375	450	450	525		
>700-800	Every 2	300	375	450	450	525	600		
>800-900		300	375	450	525	600			

>900-1000	weeks	375	450	525	600	
>1000-1100		375	450	600		Insufficient Data to Recommend a Dose
>1100-1200		450	525	600		
>1200-1300		450	525			
>1300-1500		525	600			

Refs: U.S. Prescribing Information

IgE- MEDIATED FOOD ALLERGY

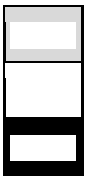
Dosing for IgE-Mediated food allergy: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during treatment with omalizumab (Xolair) and related biosimilars cannot be used as a guide for dose determination. Interruptions lasting less than one year: Dose based on serum IgE levels obtained at the initial dose determination. Interruptions lasting one year or more: Re-test total serum IgE levels for dose determination. See dosing information below:

Peer-reviewed literature and clinical trials recommend a dose of 75mg to 600 mg by subcutaneous injection every 2 or 4 weeks.

Dosing and Frequency for Individuals 1 year of Age and Older:

Pre-treatment 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							

Refs: U.S. Prescribing Information



Subcutaneous doses to be administered every 4 weeks

Subcutaneous doses to be administered every 2 weeks

Insufficient data to Recommend a Dose

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of omalizumab (Xolair) and related biosimilars is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

There is no Medicare coverage criteria addressing this service; therefore, the Company policy is applicable.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, omalizumab (Xolair) and related biosimilars are covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

Omalizumab (Xolair) and related biosimilars are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when omalizumab (Xolair) is covered under a member's medical benefit. It does not address instances when omalizumab (Xolair) and related biosimilars are covered under a member's pharmacy benefit.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

DEFINITIONS

Moderate persistent asthma is defined by the National Heart, Lung, and Blood Institute (NHLBI) for treatment purposes as any of the below:

- Daily symptoms
- Nocturnal symptoms that occur more than one time a week but not nightly
- Daily use of inhaled, short-acting, beta2-agonist for symptom control
- Some limitation with normal activity
- Forced expiratory volume in 1 second (FEV1) or peak expiratory flow (PEF) is greater than 60% and less than 80% predicted
- FEV1/FVC (forced vital capacity) is reduced 5%

Severe persistent asthma is defined by the NHLBI for treatment purposes as any of the below:

- Symptoms throughout the day

- Nocturnal symptoms are frequent (often 7 times per week)
- Extreme limitation with normal activity
- FEV1 or PEF less than 60% predicted
- Daily use of an inhaled, short-acting, beta2-agonist for symptom control (can be several times/day)
- FEV1/FVC is reduced more than 5%

The NHLBI also recommends that individuals who have had two or more asthma exacerbations requiring oral systemic corticosteroid in the past year be considered the same for treatment purposes as individuals who have persistent asthma.

NASAL POLYPS

Nasal congestion score (NCS) is a daily self-reported measurement of an individual's congestion and obstruction severity using a 0- to 3-point severity scale (0=none, 1=mild, 2=moderate, 3=severe).

Nasal polyp score (NPS) is a measurement of the extent/severity of nasal polyps based on evaluation by nasal 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).

OTHER INFORMATION REGARDING TREATMENT

Omalizumab (Xolair) and related biosimilars treatment should be initiated by a professional provider within one of the following specialties: Allergy/Immunology, Dermatology, Otolaryngology (Ear/Nose/Throat), or Pulmonology. Maintenance treatment should be administered by a professional provider within the areas of Primary Care (e.g., Family Medicine, Internal Medicine, Pediatrics) or any of the aforementioned specialties.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Omalizumab (Xolair) was approved by the FDA on June 24, 2003, for the treatment of allergic asthma. Supplemental approvals for omalizumab (Xolair) have since been issued by the FDA. The FDA has issued subsequent approvals for related biosimilar products (e.g., omalizumab-igec [Omlyclo]).

PEDIATRIC USE

According to the drug manufacturer's prescribing information:

The safety and effectiveness of omalizumab (Xolair) and related biosimilars in pediatric individuals aged 6 years and older with allergic asthma have been established. The safety and effectiveness of omalizumab (Xolair) in pediatric individuals younger than 6 years of age with allergic asthma have not been established.

The safety and effectiveness of omalizumab (Xolair) and related biosimilars in adolescent individuals ages 12 to 17 years old with chronic idiopathic urticaria have been established. The safety and effectiveness of omalizumab (Xolair) in pediatric individuals younger than 12 years of age with chronic idiopathic urticaria have not been established.

The safety and effectiveness of omalizumab (Xolair) and related biosimilars in pediatric individuals younger than 18 years of age with chronic rhinosinusitis with nasal polyps have not been established.

The safety and effectiveness of omalizumab (Xolair) and related biosimilars for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods have been established in pediatric individuals aged 1 year and older with IgE-mediated food allergy. Safety and effectiveness in pediatric individuals with IgE-mediated food allergy below 1 year of age have not been established.

Description

Omalizumab (Xolair) and related biosimilars are a monoclonal antibody that binds to naturally occurring human immunoglobulin E (IgE), thus reducing an allergic response. For the treatment of allergic (extrinsic) asthma and nasal polyps, omalizumab (Xolair) and related biosimilars inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils. A reduction in the number of surface-bound IgE on the high-affinity IgE receptor-bearing cells limits the release of mediators of the allergic response. For the treatment of chronic urticaria, omalizumab (Xolair) and related biosimilars binds to IgE, which reduces free IgE levels and causes the high-affinity IgE receptors on the surface of mast cells and basophils to downregulate.

Omalizumab (Xolair) and related biosimilars are administered by subcutaneous injection under the guidance of a professional provider. The US Food and Drug Administration (FDA) prescribing information states the following: Initiate therapy in a healthcare setting and once therapy has been safely established, the healthcare provider may determine whether self-administration of omalizumab (Xolair) and related biosimilars prefilled syringe by the patient or caregiver is appropriate, based on careful assessment of risk for anaphylaxis and mitigation strategies.

Healthcare providers should consider known risk factors for anaphylaxis to omalizumab and mitigation strategies when selecting patients for self-administration. Patient-specific factors including the following criteria should be considered:

- Patient should have no prior history of anaphylaxis, including to omalizumab or other agents, such as foods, drugs, biologics, etc.
- Patient should receive at least three doses of omalizumab 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 omalizumab-prefilled syringe with proper technique according to the prescribed dosing regimen and the instructions for use

Instruct patients or caregivers to follow the directions provided in the "Instructions for Use" for preparation and administration of Xolair Prefilled Syringe [see Instructions for Use].

- Adolescents 12 years of age and older: omalizumab prefilled syringe may be self-administered under adult supervision.
- Pediatric Patients 6 to 11 years of age: omalizumab prefilled syringe should be administered by a caregiver.

ALLERGIC ASTHMA

Omalizumab (Xolair) was approved by the FDA on June 24, 2003, for treatment of moderate-to-severe persistent allergic asthma in individuals who are at least 12 years of age. The safety and efficacy of omalizumab (Xolair) were evaluated in three randomized, double-blind, placebo-controlled multicenter trials. The trials consisted of individuals between 12 and 76 years old who had experienced moderate-to-severe persistent asthma, as defined by the National Heart, Lung, and Blood Institute (NHLBI) criteria, for at least 1 year, had a baseline IgE between 30 and 700 IU/mL, and who exhibited a positive skin test reaction to a perennial aeroallergen.

Results from the first two studies demonstrated that the number of exacerbations per individual was reduced in those who were treated with omalizumab (Xolair) compared with a placebo. In the third study, results illustrated that the number of exacerbations experienced by individuals treated with omalizumab (Xolair) was similar to the number of exacerbations experienced by individuals treated with the placebo. The absence of an observed treatment effect in the third study may be related to differences in patient population, study sample size, and/or other factors that existed, in comparison to the first two studies.

In all three studies, the majority of exacerbations were managed in the outpatient setting and were treated with systemic steroids. Hospitalization rates were not significantly different between the individuals who were treated with omalizumab (Xolair) and the patients who were treated with the placebo; however, the overall hospitalization rate was low. Among those individuals who experienced an exacerbation, the distribution of exacerbation severity was similar between treatment groups.

The initial clinical trials that supported the approval of omalizumab (Xolair) found a higher incidence in malignancies. To assess the long-term safety in those with moderate-to-severe persistent asthma and a positive skin test or in vitro reactivity to a perennial aeroallergen, a 5-year follow-up observational cohort study of 5007 individuals treated with omalizumab (Xolair) and a control group of 2829 individuals treated without omalizumab (Xolair) was performed. The study reported similar rates of primary malignancies among both groups of individuals. The study also found that individuals treated with omalizumab (Xolair) had a disproportionate increase in cardiovascular and cerebrovascular events (i.e., transient ischemic attacks, myocardial infarction, pulmonary embolism/venous thrombosis, unstable angina, and pulmonary hypertension.) Because of selection bias and a high rate of discontinuation in this study, a

pooled analysis of 25 randomized, double-blind, placebo-controlled clinical trials was conducted to confirm the incidence of these cardiovascular and cerebrovascular events. A total of 3342 individuals were treated with omalizumab (Xolair) and 2895 treated without omalizumab (Xolair). This study reported no differences in the rates of cardiovascular and cerebrovascular events. Conclusions about the validity of the previous observational study cannot be made because the pooled analysis were based on a low number of events, a younger population, and a shorter duration of follow-up compared to the observational cohort study.

Omalizumab (Xolair) was approved by the FDA on July 6, 2017, for the treatment of moderate-to-severe persistent allergic asthma in pediatric individuals aged 6 years to less than 12 years. One of the studies included 628 individuals with moderate-to-severe persistent uncontrolled allergic asthma for at least 1 year, who exhibited a positive skin test reaction to a perennial aeroallergen. After both endpoints of 24 weeks and 52 weeks, there was a statistically significant lower rate of asthma exacerbations in those treated with omalizumab (Xolair), when compared to placebo. Another study of 334 pediatric individuals (298 were 6 to less than 12 years of age) with moderate-to-severe asthma who were well-controlled on inhaled corticosteroids resulted in lower rate of asthma exacerbations at 16 weeks and 28 weeks in those treated with omalizumab (Xolair), when compared to placebo.

Clinical studies with various strengths and weaknesses in study design have been performed in adults and children with baseline IgE levels above 700 IU/mL; most of the studies in the pediatric population had an upper limit of 1300 IU/mL, which is indicated in the product's prescribing information dosing table for children between 6 and 12 years of age. Although there have been studies with IgE levels as high as 2000 IU/mL, the sample size in these trials are sparse, and oftentimes, the outcomes of the subgroup with high IgE levels are not differentiated from the rest of the study population. Omalizumab (Xolair) has been approved for use in Europe and Australia in individuals with a baseline IgE level of 30 to 1500 IU/mL.

CHRONIC URTICARIA

Chronic urticaria is a condition characterized by the presence of hives on most days of the week, for a period of over 6 weeks. In addition, the symptoms of angioedema may occur in 40% to 50% of all cases. This disease has a 1% to 2% prevalence among the United States population and demonstrated in clinical trials that chronic urticaria can cause interruption of daily living and may decrease an individual's quality of life.

Omalizumab (Xolair) was approved by the FDA on March 21, 2014, for the treatment of chronic idiopathic urticaria in individuals who were at least 12 years of age and remained symptomatic despite having used an H1 antihistamine.

According to FDA labeling information, the safety and efficacy of omalizumab (Xolair) was evaluated in two placebo-controlled multiple-dose trials. In addition to H1 antihistamines, injections of omalizumab (Xolair) or placebo were administered every 4 weeks for a period of 12 weeks (n=319) or 24 weeks (n=322) in duration plus a 16-week washout observation period. These studies demonstrated a significant decrease in weekly urticaria activity score (UAS), which combines pruritus intensity and number of hives, when omalizumab (Xolair) was compared to placebo in individuals who had chronic idiopathic urticaria that was resistant to antihistamines.

In addition to chronic idiopathic urticaria, omalizumab (Xolair) has been studied in other types of chronic urticaria, e.g., cholinergic urticaria, chronic autoimmune urticaria, solar urticaria. The published peer-reviewed literature includes a few randomized, placebo-controlled studies, several small case series, and many case reports. These studies have demonstrated a significant decrease in UAS, with minimal adverse events when omalizumab (Xolair) was compared to placebo in individuals who had chronic urticaria that was resistant to antihistamines. Several other small clinical trials are currently underway and are in various stages of development. There have also been guidelines published summarizing the available data and offering algorithms for the treatment of chronic urticaria.

Although there are several types of chronic urticaria, the treatment of each is similar. Routine management usually begins with a second-generation (nonsedating) H1 antihistamine (e.g., cetirizine [Zyrtec®], fexofenadine [Allegra®], loratadine [Claritin®, Alavert®], desloratadine [Clarinex®], levocetirizine [Xyzal®]), followed by dose escalations that exceed the recommended dose. For those individuals requiring further treatment, adjunctive medications are added or substituted to control signs and symptoms of chronic urticaria. Examples of these adjunctive medications may include:

- First-generation (sedating) H1 antihistamine (e.g., chlorpheniramine [Chlor-Trimeton®], cyproheptadine, diphenhydramine [Benadryl®])
- H2 blockers (e.g., cimetidine [Tagamet®], famotidine [Pepcid®], nizatidine)
- Leukotriene modifiers (e.g., zafirlukast [Accolate®], montelukast [Singulair®], zileuton [Zyflo®])

- Systemic glucocorticosteroids (for short periods of time) and other anti-inflammatory agents (e.g., dapsone, sulfasalazine, hydroxychloroquine)
- Immunosuppressants (e.g., cyclosporine, tacrolimus)
- Immunomodulatory agents (e.g., immune globulin, methotrexate)

CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

Chronic rhinosinusitis with nasal polyps (CRSwNP), also known as nasal polyps, is a severe type of chronic rhinosinusitis that affects about 15% of adults. Individuals present with symptoms for 12 weeks or longer with nasal polyps (benign growths) in the nasal sinus tissue, nasal and sinus inflammation, nasal drainage, nasal congestion, facial pressure or pain, and a decrease in sense of smell. Although the exact mechanism is unknown, elevated IgE activates inflammatory cells such as mast cells, basophils, and eosinophils. Diagnosis is based on symptoms and evidence of nasal polyps by visualization via anterior rhinoscopy, nasal endoscopy, sinus computed tomography (CT) or magnetic resonance imaging (MRI). Options for treatment include saline lavage of sinuses, short-term oral corticosteroids, intranasal corticosteroids, and functional endoscopic sinus surgery; however, nasal polyps can regrow despite corticosteroids and surgery.

Omalizumab (Xolair) was approved by the FDA on April 09, 2021, for the treatment of nasal polyps in adults with inadequate response to nasal corticosteroids, as add-on maintenance therapy. On March 17, 2023, the labeling terminology was changed to chronic rhinosinusitis with nasal polyps (CRSwNP).

Gevaert et al. (2020) evaluated the safety and efficacy of omalizumab (Xolair) in two randomized, multicenter, double-blind, placebo-controlled, phase 3 studies of adults (aged 18–75 years) with CRSwNP—characterized by persistent bilateral nasal polyps, nasal congestion, and impaired health-related quality of life due to nasal polyps—who had inadequate response to at least 4 weeks of nasal corticosteroids (POLYP-1, N=138; POLYP-2; n=127) . Inclusion criteria included Nasal Polyp Score (NPS) of 5 or higher (NPS >2 for each nostril) despite use of nasal mometasone at screening visit 1 (day −35). 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 further required to have an NPS of 5 or higher at screening visit 2 (day −7), after 4 weeks of intranasal mometasone during run-in (200 mg twice daily or 200 mg daily if unable to tolerate 200 mg twice daily). A Nasal Congestion Score (NCS) of 2 or higher (with additional symptoms of postnasal drip, runny nose, and/or loss of sense of smell) at day –35 (1-week recall) and a weekly mean NCS higher than 1 at randomization (assessed every morning via an eDiary) were required. Patients were furthermore required to have a weekly average of NCS greater than 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). Participants received subcutaneous (SC) omalizumab (Xolair) and nasal mometasone or SC placebo and nasal mometasone every 2 or 4 weeks, according to dosing schedule (based on weight and IgE levels from 30–1500 IU/mL), for 24 weeks followed by a 4-week follow-up period. The co-primary endpoints in both studies (change from baseline to week 24 in NPS and mean daily NCS) revealed that participants who received omalizumab (Xolair) and nasal mometasone had statistically significant greater improvements in NPS and weekly average NCS, than those who received placebo and nasal mometasone (P<0.001 and P=0.014, respectively).

IgE-Mediated Food Allergy

According to the Centers for Disease Control and Prevention, food allergies in 2021 affected 5.8% of children and 6.2% of adults in the United States. There is no cure for food allergies. Strict avoidance is the only way to prevent an allergic reaction to food. Food allergies can occur within seconds to minutes after ingesting a particular food. Some of the most common food allergies include hives, itching, swelling of the lips, face, tongue or throat, belling pain, nausea or vomiting, wheezing, or trouble breathing. Anaphylaxis is the most severe allergic reaction and is life-threatening if not treated immediately. Prompt administration of epinephrine by injection can save a life.

Omalizumab (Xolair) was approved by the FDA on February 16, 2024, for IgE-mediated food allergy in individuals over the age of 1 year for the reduction of allergic reactions (Type 1), including anaphylaxis, that may occur with accidental exposure to one or more foods. The safety and efficacy of omalizumab (Xolair) was evaluated in a multicenter, randomized, double-blind, placebo-controlled Food Allergy (FA) trial. The trial consisted of 168 individuals between the age of 1 and 55 who were allergic to peanut and at least two other foods, including milk, egg,

wheat, cashew, hazelnut, or walnut. The trial enrolled those individuals who experienced dose-limiting symptoms defined as moderate to severe skin, respiratory, or gastrointestinal symptoms, to a single dose of 100 mg or less of peanut protein and less than or equal to 300 mg protein from two of the other foods studied (e.g., milk, egg, wheat, cashew, hazelnut, or walnut). Anyone with a history of severe anaphylaxis was excluded from the trial. Individuals were given a subcutaneous dose of omalizumab (Xolair) or placebo based on serum total IgE level, measured before the start of treatment and by body weight for 16 to 20 weeks. Upon completion of the treatment, individuals participated in a double-blind placebo-controlled food challenge (DBPCFC) of their three studied foods and a placebo. The results showed a statistically higher result rate for individuals that had omalizumab (Xolair) treatment than those that had the placebo. A total of 68% of individuals who received omalizumab (Xolair) were able to consume a single dose of 600 mg or more of peanut protein without having dose-limiting symptoms compared to only 5% of those that received placebo. For individuals who consumed a single dose of 1000 mg or more of cashew, milk, or egg protein without dose-limiting symptom, omalizumab (Xolair) treatment led to a higher response rate than the placebo for all three foods. The study also noted that for 38 pediatric individuals who continued omalizumab (Xolair) for 24 to 28 weeks, the ability to consume 600 mg or more of peanut protein and 1000 mg or more of milk, egg, or cashew protein without moderate to severe dose-limiting symptoms was maintained.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

HCPCS Level II Code Number(s)
J2357 Injection, omalizumab, 5 mg
Q5154 Injection, omalizumab-igec (Omlyclo), biosimilar, 5 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.025i:

06/18/2026	This version of the policy will become effective 06/18/2026. This policy has been updated to communicate the addition of biosimilar approval for omalizumab-igec (Omlyclo). This policy has been updated to communicate the change to the Medically Necessary coverage position for Immune Checkpoint Inhibitor–Related Pruritus, in accordance with National Comprehensive Cancer Network (NCCN). In addition to severe Grade 3 pruritus related to immunotherapy, there is also coverage for the management of refractory cases of moderate (Grade 2), when individual has no response to 1 month of gabapentinoids (e.g., gabapentin and pregabalin). The pediatric information regarding IgE-mediated food allergy was added. The following HCPCS code has been added to this policy: Q5154 Injection, omalizumab-igec (Omlyclo), biosimilar, 5 mg All of the ICD-10 CM codes have been removed from this policy. Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

Revisions From MA08.025h:

12/15/2025	This version of the policy will become effective 12/15/2025. The following ICD-10 CM codes have been removed from this policy: Z91.011 Allergy to milk products Z91.012 Allergy to eggs The following ICD-10 CM codes have been added to this policy: Z91.0110 Allergy to milk products, unspecified Z91.0111 Allergy to milk products with tolerance to baked milk Z91.0112 Allergy to milk products with reactivity to baked milk Z91.0120 Allergy to eggs, unspecified Z91.0121 Allergy to eggs with tolerance to baked egg Z91.0122 Allergy to eggs with reactivity to baked egg

Revisions From MA08.025g:

06/13/2025	This version of the policy will become effective 06/13/2025. This policy has been updated to communicate the Medically Necessary coverage position for the following indication: • IgE-Mediated Food Allergy The following criteria has been revised: • Prevention of Anaphylaxis: Revised criteria for frequency. The following ICD-10 CM code has been added to this policy: • Z91.010 Allergy to peanuts • Z91.011 Allergy to milk products • Z91.012 Allergy to eggs • Z91.013 Allergy to seafood • Z91.014 Allergy to mammalian meats • Z91.018 Allergy to other foods • Z91.02 Food additives allergy status

Revisions From MA08.025f:

12/16/2024	This version of the policy will become effective 12/16/2024.

	The following ICD-10 CM code has **removed** from this policy: L29.8 Other pruritus The following ICD-10 CM code has been **added** to this policy: L29.89 Other pruritus

Revisions From MA08.025e:

05/07/2024	This version of the policy will become effective 05/07/2024. This Policy has been updated to communicate and clarify the Medically Necessary coverage of Systemic Mastocytosis. Additionally, the terminology for Nasal Polyps was revised by the FDA to Chronic Rhinosinusitis with Nasal Polyps. The following ICD-10 CM codes have been **added** to this policy: C96.21 Aggressive systemic mastocytosis J32.8 Other chronic sinusitis J32.9 Chronic sinusitis, unspecified

Revisions From MA08.025d:

04/20/2022	This policy has been reissued in accordance with the Company's annual review process.

10/04/2021	This version of the policy will become effective 10/04/2021.
	
	This policy has been updated to communicate the Medically Necessary coverage position of the following indications:
	
	• Immune Checkpoint inhibitor-related Pruritus
	• Nasal Polyps
	• Systemic Mastocytosis
	• Continuation Therapy criteria for all indications
	
	Clarification has been made for all indications regarding combination therapy:
	• Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
	
	The following criteria was **revised**:
	
	• Asthma: Revised criteria to allow for the addition of a different second-generation non-sedating H1 antihistamine (In adidition to a substitution to a different second-generation non-sedating H1 antihistamine).
	• Experimental Investigational (E/I) criteria: removed the "treatment of other allergic conditions" as E/I.
	• Dosing and Frequency Requirements: Asthma Dosing and Frequency grid: Language changed in black shaded area, per FDA labeling:
	  ○ FROM: Do not dose
	  ○ TO: Insufficient data to recommend a dose
	
	The following ICD-10 CM codes have been **added** to this policy:
	
	D47.02 Systemic mastocytosis
	J33.0 Polyp of nasal cavity
	J33.1 Polypoid sinus degeneration
	J33.8 Other polyp of sinus
	J33.9 Nasal polyp, unspecified
	L29.0 Pruritus ani
	L29.1 Pruritus scroti
	L29.2 Pruritus vulvae

	L29.3 Anogenital pruritus, unspecified L29.8 Other pruritus L29.9 Pruritus, unspecified

Revisions From MA08.025c:

05/20/2020	The policy has been reviewed and reissued to communicate the Company's continuing position on omalizumab (Xolair®).
05/22/2019	The policy has been reviewed and reissued to communicate the Company's continuing position on omalizumab (Xolair®).
11/21/2018	This policy has been reissued in accordance with the Company's annual review process.
12/13/2017	This Policy has undergone a routine review, and the medical necessity criteria have been revised as follows: • The Policy Section was updated to communicate the modified Dosing and Frequency information. • The Policy Section was also updated to communicate the expanded baseline serum IgE level criteria for the treatment of Allergic Asthma: o **FROM:** between 30 IU/mL and 700 IU/mL o **TO:** between 30 IU/mL and 1500 IU/mL

Revisions From MA08.025b:

06/29/2016	This policy was updated to clarify the dosing and frequency of omalizumab (Xolair®). Information regarding use in pediatrics was also added.

Revisions From MA08.025a:

10/21/2015	This policy has been updated to communicate the Company's position on omalizumab (Xolair®). Criteria for cyclosporine as a prior agent for the treatment of chronic urticaria; information regarding the safety trials of omalizumab (Xolair®); and the dosing and frequency for the FDA-approved indications have been added to the policy.

Revisions From MA08.025:

01/01/2015	This is a new policy.

Version Effective Date:
06/18/2026
Version Issued Date:
06/18/2026
Version Reissued Date:
N/A