Medical Policy Bulletin

Title:
Omalizumab (Xolair®)
Policy #:
MA08.025h

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.

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) is 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 in Attachment A are met:

- The individual has a positive skin test or in vitro reactivity to a perennial aeroallergen.
- The individual has a baseline serum 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) 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 Attachment A

Chronic Urticaria

Omalizumab (Xolair) is 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) 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) 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) is 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 in Attachment A are met:

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

Immune Checkpoint Inhibitor–related Pruritus

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the management of 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 listed below, are met:

- The individual is refractory to antihistamines and corticosteroids
- The individual has an elevated baseline serum IgE level
- Omalizmab (Xolair) 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) doses up to 300 mg by subcutaneous injection every 4 weeks

Chronic Rhinosinusitis with Nasal Polyps

Omalizumab (Xolair) is 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 in Attachment A, 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) will be used in combination with intranasal corticosteroids, unless documented failure, contraindication, or intolerance.
- 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])

Systemic Mastocytosis

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

Omalizumab (Xolair) is 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) 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) doses up to 300 mg by subcutaneous injection every 4 weeks.

Prevention of Anaphylaxis

Omalizumab (Xolair) is 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) 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) doses up to 300 mg by subcutaneous injection every 2 weeks.

CONTINUATION THERAPY

Continuation of omalizumab (Xolair) 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) 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) 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 Attachment A for the Dosing and Frequency Requirements for omalizumab (Xolair).

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). 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) 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 post-payment review and audit procedures for any claims submitted for omalizumab (Xolair).

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) 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) is 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) is 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) is 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 percent and less than 80 percent predicted
- FEV1/FVC (forced vital capacity) is reduced 5 percent

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 percent 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 percent

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) 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. Supplemental approvals for Xolair (Omalizumab) have since been issued by the FDA.

PEDIATRIC USE
According to the Drug Manufacturer's Prescribing Information:

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

Description

Omalizumab (Xolair) is 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) 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) 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) is 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 Xolair 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 Xolair 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 Xolair or other agents, such as foods, drugs, biologics, etc.
- Patient should receive at least three 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 with proper technique according to the prescribed dosing regimen and 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: XOLAIR prefilled syringe may be self-administered under adult supervision.
- Pediatric Patients 6 to 11 years of age: XOLAIR 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 the ages of 12 and 76 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.) Since there was 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 since 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 6 to less than 12 years of age. 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 ages 6 to 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, etc. 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 effected 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 a 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 XOLAIR was evaluated in a multi-center, 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 less than or equal to 100mg of peanut protein and less than or equal to 300mg 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 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 3 studied foods and a placebo. The results showed a statistically higher result rate for individuals that had Xolair treatment than those that had the placebo. 68% of individuals who received Xolair were able to consume a single dose of greater than or equal to 600mg 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 greater than or equal to 1000mg of cashew, milk, or egg protein without dose-limiting symptom, Xolair treatment led to a higher response rate than the placebo for all three foods. The study also notes that for 38 pediatric individuals who continued Xolair for 24-28 weeks the ability to consume greater than or equal to 600mg of peanut protein and greater than or equal to 1000mg of milk, egg and 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)

C96.21	Aggressive systemic mastocytosis
D47.02	Systemic mastocytosis
J32.8	Other chronic sinusitis
J32.9	Chronic sinusitis, unspecified
J33.0	Polyp of nasal cavity
J33.1	Polypoid sinus degeneration

J33.8	Other polyp of sinus
J33.9	Nasal polyp, unspecified
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.50	Severe persistent asthma, uncomplicate d
J45.51	Severe persistent asthma with (acute) exacerbation
J45.901	Unspecified asthma with (acute) exacerbation
J45.909	Unspecified asthma, uncomplicated
L29.0	Pruritus ani
L29.1	Pruritus scroti
L29.2	Pruritus vulvae
L29.3	Anogenital pruritus, unspecified
L29.89	Other pruritus
L29.9	Pruritus, unspecified
L50.0	Allergic urticaria
L50.1	Idiopathic urticaria
L50.2	Urticaria due to cold and heat
L50.3	Dermatographic urticaria
L50.5	Cholinergic urticaria
L50.6	Contact urticaria
L50.8	Other urticaria
L50.9	Urticaria, unspecified
L56.3	Solar urticaria
Z91.010	Allergy to peanuts
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

HCPCS Level II Code Number(s)

J2357 Injection, omalizumab, 5 mg

Revenue Code Number(s)

N/A

Policy History

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: o FROM: Do not dose o 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:
12/15/2025
Version Issued Date:
12/15/2025
Version Reissued Date:
N/A