Medical Drug Clinical Criteria

Subject:	Omalizumab Agents (Xolair, Omlyclo)		
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Overview

This document addresses the use of omalizumab agents (Xolair, Omlyclo), anti-IgE antibodies approved by the Food and Drug Administration (FDA) to treat moderate to severe persistent asthma in individuals 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms inadequately controlled with inhaled corticosteroids. Omalizumab also has FDA approved indications as add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adults with inadequate response to nasal corticosteroids, treatment of chronic spontaneous urticaria in individuals age 12 and older who remain symptomatic despite H1 antihistamine treatment, and IgE-mediated food allergy in adult and pediatric individuals aged 1 year and older for the reduction of allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods. Omlyclo is a biosimilar designated as interchangeable to the reference product Xolair.

Asthma

FDA approval for omalizumab for moderate to severe persistent asthma was based in part on the results of three randomized, double-blind, placebo-controlled, multi-center trials where the number of asthma exacerbations was the principal outcome. The trials enrolled subjects with moderate to severe persistent asthma, a positive skin test reaction to a perennial aeroallergen and a total IgE level greater than 30 IU/mL. The number of exacerbations was reduced in those receiving omalizumab compared to the placebo group. However, individuals whose forced expiratory volume in 1 second (FEV_1) was greater than 80% predicted at enrollment did not experience a reduction in exacerbations.

The 2024 Global Initiative for Asthma (GINA) guidelines list omalizumab as a treatment option in Step 5 of their asthma management algorithm. Add-on targeted biologic therapy should be considered for individuals with severe asthma experiencing exacerbations or poor symptom control despite taking at least high-dose inhaled corticosteroid/long acting $beta_2$–agonists and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids.

Comparative Doses for Inhaled Corticosteroids (Adults and Adolescents) (Wenzel 2021)

Drug	Low Daily Dose	Medium Daily Dose	High Daily Dose
Beclomethasone 40 or 80 mcg/actuation	80-160 mcg	>160-320 mcg	>320-640 mcg
Budesonide 90 or 180 mcg/actuation	180-360 mcg	>360–720 mcg	>720-1440 mcg
Ciclesonide 80 or 160 mcg/actuation	160 mcg	320 mcg	640 mcg
Fluticasone propionate MDI: 44, 110 or 220 mcg/actuation DPI: 50, 100 or 250 mcg/dose	 176–220 mcg 100-250 mcg	 >220–440 mcg >250–500 mcg	 >440-1760 mcg >500-2000 mcg
Fluticasone furoate 50, 100 or 200 mcg/dose	50 mcg	100 mcg	200 mcg
Mometasone MDI: 50, 100 or 200 mcg/actuation DPI: 110 or 220 mcg/actuation	 200 mcg 220 mcg	 >200-400 mcg >220-440 mcg	 >400-800 mcg >440-880 mcg

DPI = dry powder inhaler, MDI = metered dose inhaler

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

FDA approval for omalizumab for chronic rhinosinusitis with nasal polyps (CRSwNP) was based on the results of two randomized, double-blind, placebo-controlled, multi-center trials where nasal polyp score (NPS) and nasal congestion score (NCS) were the principal outcome. The trials enrolled subjects with nasal polyps with inadequate response to nasal corticosteroids and a total IgE level

greater than 30 IU/mL. Participants received omalizumab or placebo in addition to background nasal mometasone therapy. The omalizumab group had a statistically significant greater improvement at week 24 in NPS and NCS compared to the placebo group.

In 2014, the Joint Task Force on Practice Parameters (JTFPP) representing the American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI) and the Joint Council of Allergy, Asthma & Immunology published a practice parameter on the diagnosis and management of rhinosinusitis. In 2015, the American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNS) published a clinical practice guideline on adult sinusitis. Both publications recommend confirming a clinical diagnosis of nasal polyps with imaging using anterior rhinoscopy, nasal endoscopy or computed tomography (CT). Intranasal corticosteroids are recommended for long-term treatment of nasal polyps. A short course of oral corticosteroids is included as a reasonable option to decrease polyp size and alleviate symptoms. Sinonasal surgery is another treatment option. The AAAAI/ACAAI guidance recommends consideration of omalizumab for the treatment of nasal polyps when other medical and surgical options have failed.

In 2022, the JTFPP published guidelines for the medical management of chronic rhinosinusitis with nasal polyposis (CRSwNP). The guidelines focus on select interventions for treatment of CRSwNP including intranasal corticosteroids, biologics and aspirin therapy after desensitization. The guidelines recommend intranasal corticosteroids over no intranasal corticosteroids in individuals with CRSwNP. The guidelines also recommend biologics over no biologics but note it is a conditional recommendation as other treatment options should be considered or used together with biologics (including inhaled corticosteroids and surgery).

Chronic Spontaneous Urticaria (CSU)

Chronic spontaneous urticaria (CSU) is defined as itchy hives that last at least 6 weeks and have no apparent external trigger. The 2014 guidance from the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI) and the Joint Council of Allergy, Asthma & Immunology, provides a step-based approach to the treatment of chronic urticaria. Omalizumab is included as an option in Step 4 of the algorithm when chronic urticaria has been refractory to treatment with potent antihistamines and leukotriene receptor antagonists.

In 2022, the Dermatology Section of the European Academy of Allergology and Clinical Immunology (EAACI), the Global Allergy and Asthma European Network (GA²LEN) and its Urticaria and Angioedema Centers of Reference and Excellence (UCAREs and ACAREs), the European Dermatology Forum (EDF) and the Asia Pacific Association of Allergy, Asthma, and Clinical Immunology (APAAACI) released guidelines on the management of urticaria. The international association suggests second generation H_1 antihistamine as first-line treatment for all types of urticaria. Recommended second-line treatment for chronic urticaria is up dosing of an H_1 antihistamine up to four-fold the standard dose. Omalizuamb can be added on for individuals unresponsive to high dose second generation H_1 antihistamines.

IgE-Mediated Food Allergy

Omalizumab is approved by the FDA for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric individuals aged 1 year and older with IgE-mediated food allergy. IgE-mediated food allergy diagnosis is based on clinical history with confirmation by skin test, blood test or oral food challenge. Omalizumab must be used in combination with allergen avoidance. Xolair is not indicated for emergency treatment of allergic reactions and all individuals must have access to an auto-injectable epinephrine agent.

Omalizumab carries a black box warning for anaphylaxis. Anaphylaxis has been reported after the first dose of omalizumab but also beyond one year after beginning treatment. Omalizumab should be initiated in a healthcare setting and individuals should be closely observed for an appropriate period of time. Health care providers should be prepared to manage anaphylaxis, and individuals should be instructed on anaphylaxis signs and symptoms and to seek immediate medical care should they occur. Selection of individuals for self-administration of Xolair should be based on criteria to mitigate risk from anaphylaxis.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Omalizumab Agents (Xolair, Omlyclo)

Initial requests for omalizumab (Xolair, Omlyclo) for moderate to severe persistent asthma may be if approved if the following criteria are met:

I. Individual is 6 years of age or older; **AND**
II. Individual has a diagnosis of moderate to severe persistent asthma; **AND**
III. Documentation is provided that individual has had a 3 month trial and inadequate response or intolerance to combination controller therapy (high doses of inhaled corticosteroids plus long acting beta$_2$ –agonists, leukotriene modifiers, long-acting muscarinic antagonists or oral corticosteroids) (GINA 2024); **AND**

IV. Individual has a positive skin test or in vitro reactivity to a perennial aeroallergen; **AND**
V. Individual has a pretreatment forced expiratory volume in one second (FEV_1) less than 80% predicted; **AND**
VI. Documentation is provided that individual has a serum Immunoglobulin E (IgE) level equal to or greater than 30 IU/mL.

Continuation requests for omalizumab (Xolair, Omlyclo) for moderate to severe persistent asthma may be if approved if the following criteria are met:

I. Treatment with omalizumab (Xolair, Omlyclo) has resulted in clinical improvement in one or more of the following:
    A. Decreased utilization of reliever medications; **OR**
    B. Decreased frequency of exacerbations (defined as worsening of asthma that requires increase in inhaled corticosteroid dose or treatment with systemic corticosteroids); **OR**
    C. Increase in percent predicted FEV_1 from pretreatment baseline; **OR**
    D. Reduction in reported asthma-related symptoms, including but not limited to wheezing, shortness of breath, coughing, fatigue, sleep disturbance, or asthmatic symptoms upon awakening; **AND**
II. Individual continues to use omalizumab (Xolair, Omlyclo) in combination with inhaled corticosteroid-based controller therapy.

Initial requests for omalizumab (Xolair, Omlyclo) for chronic rhinosinusitis with nasal polyps (CRSwNP) may be if approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP); **AND**
III. Documentation is provided that presence of nasal polyps demonstrated on one of the following (AAO-HNS 2015):
    A. Anterior rhinoscopy; **OR**
    B. Nasal endoscopy; **OR**
    C. Computed tomography (CT); **AND**
IV. Individual has had a trial and inadequate response to maintenance intranasal corticosteroids; **AND**
V. Individual is refractory to or is ineligible or intolerant to the following (AAAAI/ACAAI 2014, JTFPP 2022):
    A. Systemic corticosteroids; **OR**
    B. Sinonasal surgery; **AND**
VI. Individual is requesting omalizumab (Xolair, Omlyclo) as add-on therapy to maintenance intranasal corticosteroids; **AND**
VII. Documentation is provided that individual has a serum Immunoglobulin E (IgE) level greater than or equal to 30 IU/mL.

Continuation requests for omalizumab (Xolair, Omlyclo) for chronic rhinosinusitis with nasal polyps (CRSwNP) may be if approved if the following criterion is met:

I. Treatment with omalizumab (Xolair, Omlyclo) has resulted in clinically significant improvement in clinical signs and symptoms of disease (including but not limited to improvement in nasal congestion or reduced nasal polyp size; **AND**
II. Individual continues to use omalizumab (Xolair, Omlyclo) in combination with maintenance intranasal corticosteroids.

Initial requests for omalizumab (Xolair, Omlyclo) for chronic spontaneous idiopathic urticaria (CSU) may be approved if the following criteria are met:

I. Individual is 12 years of age or older; **AND**
II. Individual has a diagnosis of chronic spontaneous idiopathic urticaria (CSU); **AND**
III. Individual has had an inadequate response to a two week trial of a second generation H_1 antihistamine up dosed to a maximum of four times the approved dose (EAACI 2022).

Continuation requests for omalizumab (Xolair, Omlyclo) for chronic spontaneous urticaria (CSU) may be approved if the following criterion is met:

I. Treatment with omalizumab (Xolair, Omlyclo) has resulted in clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to itch severity and hive count); **AND**
II. Individual continues to use omalizumab (Xolair, Omlyclo) in combination with second generation H_1 antihistamine therapy.

Initial requests for omalizumab (Xolair, Omlyclo)for IgE-mediated food allergy may be if approved if the following criteria are met:

I. Individual is 1 year of age or older; **AND**
II. Individual has a diagnosis of IgE-mediated food allergy; **AND**
III. Documentation is provided that diagnosis is confirmed via:

A. Clinical history of IgE-mediated food allergy demonstrated by moderate to severe symptoms (including but not limited to throat tightness, dyspnea/wheezing, clinically signification hypotension, generalized urticaria) or requiring administration of epinephrine or emergency medical care; **AND**
B. Positive skin prick test or positive serum IgE test or positive food challenge; **AND**

IV. Documentation is provided that undividual has a serum Immunoglobulin E (IgE) level equal to or greater than 30 IU/mL; **AND**
V. Individual will use omalizumab (Xolair, Omlyclo) in combination with food allergen avoidance; **AND**
VI. Individual has a prescription for an auto-injectable epinephrine agent.

Continuation requests for omalizumab (Xolair, Omlyclo) for IgE-mediated food allergy may be if approved if the following criteria are met:

I. Individual will use omalizumab (Xolair, Omlyclo) in combination with food allergen avoidance; **AND**
II. Individual has a prescription for an auto-injectable epinephrine agent.

Omalizumab (Xolair, Omlyclo) may not be approved for the following;

I. In combination with Cinqair, Dupixent, Fasenra, Nucala, Tezspire, Palforzia or oral immunotherapy (OIT); **OR**
II. May not be approved with the above criteria are not met and for all other indications.

Approval Duration
Initial Requests: 6 months
Continuation Requests: 12 months

Quantity Limits

Omalizumab Agents Quantity Limit

Drug	Limit
Xolair (omalizumab) 75 mg/0.5 mL prefilled syringe/autoinjector	2 prefilled syringes/autoinjectors per 28 days
Xolair (omalizumab) 150 mg vial, 150 mg/mL prefilled syringe/autoinjector	4 vials/prefilled syringes/autoinjectors per 28 days
Xolair (omalizumab) 300 mg/2 mL prefilled syringe/autoinjector	2 prefilled syringes/autoinjectors per 28 days
Omlyclo (omalizumab-igec) 75 mg/0.5 mL prefilled syringe	2 prefilled syringes per 28 days
Omlyclo (omalizumab-igec) 150 mg/mL prefilled syringe	4 prefilled syringes per 28 days
Override Criteria	
For chronic rhinosinusitis with nasal polyps or IgE-mediated food allergy, may approve up to 600 mg every 2 weeks.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as Omlyclo (omalizumab-igec)]
J3590	Unclassified biologics [when specified as Omlyclo (omalizumab-igec)]
J2357	Injection, omalizumab, 5 mg [Xolair]

ICD-10 Diagnosis

J32.0-J32.9	Chronic sinusitis
J33.0-J33.9	Nasal polyp
J44.0-J44.9	Other chronic obstructive pulmonary disease [with asthma]
J45.40-J45.42	Moderate persistent asthma
J45.50-J45.52	Severe persistent asthma
L23.6	Allergic contact dermatitis due to food in contact with the skin [IgE-mediated food allergy]

L25.4	Unspecified contact dermatitis due to food in contact with skin [IgE-mediated food allergy]
L27.2	Dermatitis due to ingested food [IgE-mediated food allergy]
L50.0	Allergic urticaria
L50.1	Idiopathic urticaria
L50.6	Contact urticaria
L50.8	Other urticaria [chronic spontaneous urticaria]
T78.00XA-T78.09XS	Anaphylactic reaction due to food
Z91.010-Z91.018	Food allergy status
Z91.02	Food additives allergy status

Document History

Revised: 5/16/2025
Document History:

- 5/16/2025 – Select Review: Add omalizumab biosimilar Omlyclo to clinical criteria and quantity limit. Coding Reviewed: Added HCPCS NOC C9399 and J3590 for Omlyclo. Deleted duplicate ICD-10-CM J44.0-J44.9.
- 2/21/2025 – Annual Review: Remove bilateral from CRSwNP criteria. Update guideline references. Coding Reviewed: Removed J45.20-J45.32 and J45.901-J45-998 from ICD-10-CM range J45.20-J45.998 to only include J45.40-J45.52. Removed L50.2-L50.5 from code range L50.0-L50.8 to only include L50.0, L50.1, L50.6, L50.8 and updated descriptions. Added ICD-10-CM J32.0-J32.9, L23.6, L25.4, L27.2, T78.00XA-T78.09XS, Z91.02. Consolidated Z91.010-Z91.018 into one code range and updated description.
- 3/11/2024 – Select Review: Update clinical criteria and quantity limit for new IgE-mediated food allergy indication. Coding Reviewed: Added ICD-10-CM Z91.010, Z91.011, Z91.012, Z91.013, Z91.014, Z91.018.
- 2/23/2024 – Annual Review: Update prior trial requirement in Xolair urticaria criteria. Update continuation criteria. Update criteria for nasal polyp indication and urticaria indication to reflect updated labeling. Convert from dosing limits to quantity limits. Add quantity limits for 300 mg injection and autoinjectors. Wording and formatting changes. Update guideline references. Coding Reviewed: No changes.
- 2/24/2023 – Annual Review: Wording and formatting changes. Update guideline references. Coding Reviewed: No changes.
- 2/25/2022 – Annual Review: Align nasal polyp continuation criteria with criteria for other biologics. Add may not approve criteria for use with other biologics. Update guideline references. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 02/19/2021 – Annual Review: Update requirements for trial of combination therapy in asthma criteria. Add criteria for nasal polyps. Update quantity limit based on indication. Update references. Coding Reviewed: Added ICD-10-CM J33.0-J33.9.
- 02/21/2020 – Annual Review: Update prior trial requirement for asthma from medium-to-high to high dose ICS. Add continuation criteria for chronic idiopathic uticaria. Clarify approval duration. Wording and formatting changes. Update references. Coding Reviewed: No changes.
- 09/23/2019 – Administrative update to add drug specific quantity limit.
- 02/22/2019 – Annual Review: Update Xolair criteria to align prior trial requirements with other agents for severe asthma. Wording and formatting updates for consistency with other agents for severe asthma.
- 08/17/2018 – Selected Review: Initial P&T review of Xolair clinical criteria. Wording updates to prior trial requirements and addition of references. Update continuation criteria by removing requirement to meet initiation criteria.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.