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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Respiratory Agents	**Original Policy Date:**	December 1, 2009
Subject:	Xolair	**Page:**	1 of 12

Last Review Date: June 13, 2024

Xolair

Description

Xolair (omalizumab)

Background
Xolair (omalizumab) is a monoclonal antibody that prevents binding of IgE to the high-affinity receptors on basophils and mast cells by forming complexes with circulating free IgE (1-2). Xolair is a treatment option for asthmatic patients with a pre-treatment IgE level of ≥ 30 IU/mL with a positive skin test or *in vitro* reactivity to a perennial aeroallergen such as pollen, mold spores, dust mites, or animal allergens (2).

Current asthma guidelines state that Xolair may be considered as adjunctive therapy in patients who have allergies and severe persistent asthma that is inadequately controlled with the combination of high-dose inhaled corticosteroids and long acting $beta_2$ agonists, the preferred treatment for moderate persistent and severe persistent asthma. Alternative options include either a leukotriene modifier or theophylline in combination with inhaled corticosteroids for moderate persistent asthma (2).

Xolair has shown to be effective against allergy-induced asthma only. Allergy tests are required to identify patients who may be candidates for Xolair therapy. Allergic asthma is identified as testing positive to at least one perennial aeroallergen according to either a skin test (e.g., prick/puncture test, intracutaneous test) or a blood test (e.g., RAST) and having an IgE level between 30 and 700 IU/ml in patients 12 years of age and older and between 30 and 1300 IU/ml in patients between 6 and 11 years of age (1).

Xolair was evaluated in several clinical studies for safety and efficacy. Dosing for asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and IgE-mediated food allergy was based on body weight and baseline serum IgE concentration (1).

Regulatory Status

FDA-approved indications: Xolair (omalizumab) is an anti-IgE antibody indicated for: (1)

- Moderate to severe persistent asthma in patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.
- Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.
- IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance.
- Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

Limitations of Use: (1)

- Not indicated for acute bronchospasm or status asthmaticus.
- Not indicated for the emergency treatment of allergic reactions, including anaphylaxis.
- Not indicated for other forms of urticaria.

Xolair has a boxed warning citing the risk of anaphylaxis after administration. Anaphylaxis has occurred as early as after the first dose of Xolair, but also has occurred beyond 1 year after beginning regularly administered treatment. Due to the risk of anaphylaxis, patients should be observed closely for an appropriate period of time after Xolair administration. Health care providers administering Xolair should be prepared to manage anaphylaxis that can be life-threatening. Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair. Management of anaphylaxis may include administration of subcutaneous epinephrine (1).

Malignant neoplasms were observed in 20 of 4127 (0.5%) Xolair-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents 12 years of age and older with asthma and other allergic disorders. The observed malignancies in Xolair-treated patients were a variety of types, with breast, non-melanoma skin, prostate, melanoma, and parotid occurring more than once, and five other types occurring once each. The majority of

patients were observed for less than 1 year. The impact of longer exposure to Xolair or use in patients at higher risk for malignancy (e.g., elderly, current smokers) is not known (1).

FEP adherence is defined as ≥ 50% utilization within the last 180 days.

Prescribers are advised to follow the recommended dosing charts provided in the package insert (see Appendix 1) (1).

The safety and effectiveness of Xolair in pediatric patients less than 1 year of age with IgE-mediated food allergy have not been established. The safety and effectiveness of Xolair in pediatric patients less than 6 years of age with asthma have not been established. The safety and effectiveness of Xolair in pediatric patients less than 12 years of age with urticaria have not been established. The safety and effectiveness of Xolair in pediatric patients less than 18 years of age with CRSwNP have not been established (1).

Related policies
Cinqair, Dupixent, IL-5 Antagonists, Tezspire

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xolair may be considered **medically necessary** if the conditions indicated below are met.

Xolair may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following **AND** submission of medical records (e.g., chart notes, laboratory values) documenting the following:

1. Moderate or severe Asthma
    a. 6 years of age or older
    b. Positive skin prick test or RAST response to at least one common allergen
    c. Inadequate control of asthma symptoms after a minimum of 3 months of

compliant use with greater than or equal to 50% adherence with **ONE** of the following within the past 6 months:
   i. Inhaled corticosteroids & long acting beta$_2$ agonist
   ii. Inhaled corticosteroids & long acting muscarinic antagonist
d. Baseline serum IgE level ≥ 30 IU/mL
e. **NO** dual therapy with another monoclonal antibody for the treatment of asthma

2. Chronic rhinosinusitis with nasal polyps (CRSwNP)
   a. 18 years of age or older
   b. Inadequate response, intolerance, or contraindication to a 3-month trial of **TWO** nasal corticosteroid sprays (i.e., mometasone, fluticasone, budesonide, or triamcinolone)
   c. Baseline serum IgE level ≥ 30 IU/mL
   d. Used as add-on maintenance treatment

3. IgE-mediated food allergy
   a. 1 year of age or older
   b. Used for the reduction of allergic reactions that may occur with accidental exposure to one or more foods
   c. Patient is allergic to peanut **AND** at least two other foods (e.g., milk, egg, wheat, cashew, hazelnut, or walnut) with positive food specific IgE ≥ 6 kUA/L for each
   d. Baseline serum IgE level ≥ 30 IU/mL
   e. Used in conjunction with food allergen avoidance
   f. **NOT** for emergency treatment of allergic reactions, including anaphylaxis

4. Chronic spontaneous urticaria (CSU)
   a. 12 years of age or older
   b. Symptomatic after at least **TWO** previous trials of H1-antihistamines
   c. Baseline urticaria activity score (UAS)
   (e.g., *https://www.mdcalc.com/urticaria-activity-score-uas*)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following **AND** submission of medical records (e.g., chart notes, laboratory values) documenting the following:

1. Asthma
    a. 6 years of age or older
    b. Decreased exacerbations **OR** improvement in symptoms
    c. Decreased utilization of rescue medications
    d. **NO** dual therapy with another monoclonal antibody for the treatment of asthma
    e. **NO** interruption in therapy 1 year or greater **OR** interruption lasting 1 year or more requires re-testing with a serum IgE level ≥ 30 IU/mL

2. Chronic rhinosinusitis with nasal polyps (CRSwNP)
    a. 18 years of age or older
    b. **NO** interruption in therapy 1 year or greater **OR** interruption lasting 1 year or more requires re-testing with a serum IgE level ≥ 30 IU/mL
    c. Used as add-on maintenance treatment
    d. Improvement in sino-nasal symptoms

3. IgE-mediated food allergy
    a. 1 year of age or older
    b. Used for the reduction of allergic reactions that may occur with accidental exposure to one or more foods
    c. **NO** interruption in therapy 1 year or greater **OR** interruption lasting 1 year or more requires re-testing with a serum IgE level ≥ 30 IU/mL
    d. Used in conjunction with food allergy avoidance
    e. **NOT** for emergency treatment of allergic reactions, including anaphylaxis

4. Chronic spontaneous urticaria (CSU)
    a. 12 years of age or older
    b. Decrease in urticaria activity score (UAS), such as improvement in pruritic wheals, hives, and itching
    (e.g., *https://www.mdcalc.com/urticaria-activity-score-uas*)

All approved requests are subject to review by a clinical specialist for final validation and

coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xolair (omalizumab) is a monoclonal antibody that prevents binding of IgE to the high-affinity receptors on basophils and mast cells by forming complexes with circulating free IgE. Dosing for asthma, CRSwNP, and IgE-mediated food allergy was based on body weight and baseline serum IgE concentration. Xolair has a boxed warning citing the risk of anaphylaxis after administration. Due to the risk of anaphylaxis, patients should be observed closely for an appropriate period of time after Xolair administration. The safety and effectiveness of Xolair in pediatric patients less than 1 year of age with IgE-mediated food allergy have not been established. The safety and effectiveness of Xolair in pediatric patients less than 6 years of age with asthma have not been established. The safety and effectiveness of Xolair in pediatric patients less than 12 years of age with urticaria have not been established. The safety and effectiveness of Xolair in pediatric patients less than 18 years of age with CRSwNP have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Xolair while maintaining optimal therapeutic outcomes.

References

1. Xolair [package insert]. South San Francisco, CA: Genentech, Inc.; February 2024.

2. National Institutes of Health. *National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma - Full Report 2007*. Bethesda, MD: National Heart Lung and Blood Institute; August 2007.
3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available from www.ginasthma.org.

Policy History

Date	Action
December 2009	Addition of RAST (radioallergosorbent test) as alternative when skin prick test is not feasible. RAST often are used to test for allergies when: • a physician advises against the discontinuation of medications that can interfere with test results or cause medical complications; • a patient suffers from severe skin conditions such as widespread eczema or psoriasis • a patient has such a high sensitivity level to suspected allergens that any administration of those allergens might result in potentially serious side effects.
November 2010	Addition of serum IgE and weight limits to criteria based on the package insert dosing guidelines
September 2012	Annual editorial review and reference update
March 2013	Annual editorial review and reference update
June 2013	Editorial review and strengthened renewal requirements
March 2014	Editorial review and reference update. Addition of Chronic Idiopathic Urticaria (CIU).
July 2014	Removal of serum IgE weight limits
March 2015	Annual editorial review and reference update. Addition of the 3 months of inhaled corticosteroids
March 2016	Annual editorial review Policy number change from 5.13.02 to 5.45.02
September 2016	Annual editorial review and reference update. Addition of no dual therapy with another monoclonal antibody for asthma, change in age limit.
March 2017	Annual editorial review and reference update
March 2018	Annual editorial review and reference update

June 2018	Annual editorial review Change in serum IgE level for patients 6 – 11 years of age to 30 – 1300 IU/mL for baseline in initiation and re-test in renewal (change from 30 – 700 IU/mL) Addition of 3 months of one of the following: Inhaled corticosteroids & long acting beta$_2$ agonist or Inhaled corticosteroids & long acting muscarinic antagonist
September 2018	Annual review and reference update
March 2019	Annual review and reference update
August 2019	Addition of the 50% adherence requirement to the asthma diagnosis. Addition to the managed PA program
September 2019	Annual review and reference update
October 2019	Addition of initial requirement for baseline urticaria activity score (UAS) and revised requirement to trial at least two H1-antihistamines
December 2019	Annual review
March 2020	Annual review
July 2020	Addition of Appendix 1 with dosing charts and addition of regulatory status statement “Prescribers are advised to follow the recommended dosing charts provided in the package insert” per SME. Updated UAS scoring tool link
September 2020	Annual review
January 2021	Addition of indication: nasal polyps
March 2021	Annual review and reference update
May 2021	Reference update
June 2021	Annual review and reference update
March 2022	Annual editorial review and reference update. Per SME, revised IgE requirements for patients with asthma or nasal polyps to “serum IgE level ≥ 30 IU/mL” with no maximum limit
June 2022	Annual review
September 2022	Annual review
December 2023	Annual review and reference update. Per SME, added anaphylaxis management with subcutaneous epinephrine to regulatory status section
March 2024	Per PI update, added indication of IgE-mediated food allergy. Reworded renewal requirement regarding interruption in therapy. Changed indication of nasal polyps to CRSwNP and chronic idiopathic urticaria to chronic spontaneous urticaria (CSU). Added renewal requirement of “improvement in sino-nasal symptoms” to CRSwNP
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.

Appendix 1 – Xolair Dosing

Table 1. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Patients 12 Years of Age and Older with Asthma

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight			
		30–60 kg	>60–70 kg	>70–90 kg	>90–150 kg
		Dose (mg)			
≥30–100	Every	150	150	150	300
>100–200	4	300	300	300	225
>200–300	weeks	300	225	225	300
>300–400	Every	225	225	300	
>400–500	2	300	300	375	
>500–600	weeks	300	375	**Insufficient Data to Recommend a Dose**	
>600–700		375			

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Table 2. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Pediatric Patients with Asthma Who Begin XOLAIR Between the Ages of 6 to <12 Years

Pre-treatment 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	Every 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300		
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375				
>600-700		300	225	225	300	375					
>700-800	Every 2 weeks	225	225	300	375						
>800-900		225	225	300	375						
>900-1000		225	300	375							
>1000-1100		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

Insufficient Data to Recommend a Dose

*Dosing frequency:

- ☐ Subcutaneous doses to be administered every 4 weeks
- ☐ Subcutaneous doses to be administered every 2 weeks

Table 3. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Adult Patients with CRSwNP

Pretreatment 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 Weeks	300	375	450	450	525	600		
>800 - 900		300	375	450	525	600			
>900 - 1000		375	450	525	600				
>1000 - 1100		375	450	600					
>1100 - 1200		450	525	600					
>1200 - 1300		450	525						
>1300 - 1500		525	600						

Insufficient Data to Recommend a Dose

*Dosing frequency:

- ■ Subcutaneous doses to be administered every 4 weeks
- □ Subcutaneous doses to be administered every 2 weeks

Table 4. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Adult and Pediatric Patients 1 Year of Age and Older with IgE-Mediated Food Allergy

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

Insufficient data to Recommend a Dose

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks