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| **Section:** | Prescription Drugs | **Effective Date:** | January 1, 2024 |
| **Subsection:** | Respiratory Agents | **Original Policy Date:** | December 1, 2009 |
| **Subject:** | Xolair | **Page:** | 1 of 10 |

***Last Review Date:*** December 8, 2023

# 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 and nasal polyps 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.
- Nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.
- Chronic idiopathic urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

Limitations of Use: (1)

- Not indicated for other allergic conditions or other forms or urticaria.
- Not indicated for acute bronchospasm or status asthmaticus.

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 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 nasal polyps 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. Nasal polyps

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. Chronic idiopathic urticaria
    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. Patient has a documented response / improvement in symptoms
    c. Decreased utilization of rescue medications
    d. **NO** dual therapy with another monoclonal antibody for the treatment of asthma

    **AND ONE** of the following:
    a. **NO** interruptions in therapy 1 year or greater
    b. Interruption lasting one year or more require re-testing of total serum IgE levels
        i. Serum IgE level ≥ 30 IU/mL

2. Nasal polyps

a. 18 years of age or older
b. Interruption lasting one year or more require re-testing of total serum IgE levels
    i. Serum IgE level ≥ 30 IU/mL
c. Used as add-on maintenance treatment

3. Chronic idiopathic urticaria
    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 and nasal polyps 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 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 nasal polyps 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.; August 2023.
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.<br>RAST often are used to test for allergies when:<br>• a physician advises against the discontinuation of medications that can interfere with test results or cause medical complications;<br>• a patient suffers from severe skin conditions such as widespread eczema or psoriasis<br>• 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.<br>Addition of the 3 months of inhaled corticosteroids |
| March 2016 | Annual editorial review<br>Policy number change from 5.13.02 to 5.45.02 |

| | |
|---|---|
| September 2016 | Annual editorial review and reference update.<br>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<br>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)<br>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.<br>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 |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 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 | | |
| >600–700 | | 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 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 Nasal Polyps**

| Pretreatment Serum IgE (IU/mL) | Dosing Freq. | Bodyweight | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | >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