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Omalizumab

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Overview

This policy supports medical necessity review for omalizumab (**Xolair®**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Omalizumab (Xolair) is considered medically necessary when ONE of the following is met (1, 2, or 3):

1. **Asthma.** Individual meets **ONE** of the following criteria (A or B):
    A. Initial Therapy. Individual meets **ALL** of the following:
        i. Individual is 6 years of age or older
        ii. Diagnosis of asthma is confirmed by **BOTH** of the following (a and b):
            a. Pre-bronchodilator FEV1 below the lower limits of normal for age in the setting of reduced FEV1/FVC (usually less than 80% in adults and 90% in children)

b. Variable expiratory airflow obstruction as documented by **ONE** of the following (1, 2 or 3):
    1. Increase of at least 12% AND 200 mL in FEV1 after the administration of 200 to 400 mcg albuterol or levalbuterol
    2. Increase of at least 12% AND 200 mL in FEV1 from baseline between visits or after 4 weeks of treatment
    3. Positive exercise or bronchial challenge testing

iii. Individual has a baseline immunoglobulin E (IgE) level greater than or equal to 30 IU/mL
"Baseline" is defined as prior to receiving any treatment with Xolair or another monoclonal antibody therapy that may lower IgE levels (e.g., Dupixent [dupilumab subcutaneous injection], Tezspire [tezepelumab-ekko subcutaneous injection])

iv. Individual has a baseline positive skin test or *in vitro* test (i.e., a blood test) for allergen-specific immunoglobulin E (IgE) for one or more aeroallergens
"Baseline" is defined as prior to receiving any Xolair or another monoclonal antibody therapy that may interfere with allergen testing (e.g., Dupixent and Tezspire). Examples of aeroallergens are house dust mite, animal dander, cockroach, feathers, mold spores, grass, pollen, and weeds.

v. Individual has received at least 3 consecutive months of combination therapy with **BOTH** of the following (a and b):
    a. An inhaled corticosteroid
    b. At least one additional asthma controller or asthma maintenance medication (for example, inhaled long-acting beta$_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, theophylline, or monoclonal antibody therapies for asthma [e.g., Cinqair, Dupixent, Fasenra, Nucala, and Tezspire])

    Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting beta$_2$-agonist would fulfill the requirement for both criteria [a] and [b].

vi. Individual has asthma that is uncontrolled or was uncontrolled at baseline as defined by **ONE** of the following (a, b, c, or d):
"Baseline" is defined as prior to receiving Xolair or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Dupixent, Cinqair, Fasenra, Nucala, Tezspire, or Xolair

    a. Poor symptom control as defined by Asthma Control Questionnaire consistently greater than 1.5 or Asthma Control Test less than 20
    b. Individual experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year
    c. Individual experienced one or more asthma exacerbation(s) requiring hospitalization, an emergency department visit, or an urgent care visit in the previous year
    d. Daily or every other day oral corticosteroids are required to prevent asthma exacerbations

vii. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist

B. Individual is Currently Receiving Xolair. Individual meets **ALL** of the following:
    i. Individual has already received at least 4 months of therapy with omalizumab (Xolair) and has documentation of beneficial response (An individual who has received less than 4 months of therapy or who is restarting therapy with Xolair will be considered under criterion 1A [Asthma, Initial Therapy])

Examples of beneficial response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department visits, or urgent care visits due to asthma; decreased reliever/rescue medication use; or improved lung function parameters

ii. Individual continues to receive therapy with one inhaled corticosteroid **OR** one inhaled corticosteroid-containing combination
iii. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist

Dosing for Asthma: Up to a maximum dose of 375 mg administered subcutaneously not more frequently than once every 2 weeks

2. **Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria).** Individual meets **ONE** of the following criteria (A or B):
   A. Initial Therapy. Individual meets **ALL** of the following:
      i. Individual is 12 years of age or older
      ii. Individual has or had urticaria for greater than 6 weeks (prior to treatment with Xolair), despite daily non-sedating H_1 antihistamine therapy with doses that have been titrated up to a maximum of four times the standard FDA-approved dose for at least 2 weeks, unless contraindicated or intolerant
      Examples of non-sedating H_1 antihistamine therapy are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine
      iii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

   B. Individual is Currently Receiving Xolair. Individual meets **BOTH** of the following:
      i. Individual has already received at least 4 months of therapy with Xolair and has documentation of beneficial response (An individual who has received less than 4 months of therapy or who is restarting therapy with Xolair will be considered under criterion 2A [Chronic Idiopathic Urticaria, Initial Therapy])

      Examples of a response to Xolair therapy are decreased severity of itching, decreased number and/or size of hives

      ii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

Dosing for Chronic Idiopathic Urticaria: ONE of the following dosing regimens (A or B):
   A. 150 mg administered subcutaneously once every 4 weeks
   B. 300 mg administered subcutaneously once every 4 weeks

3. **Nasal Polyps.** Individual meets **ONE** of the following criteria (A or B):
   A. Initial Therapy. Individual meets **ALL** of the following:
      i. Individual is 18 years of age or older
      ii. Individual has chronic rhinosinusitis with nasal polyposis as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan
      iii. Individual has experienced **TWO** or more of the following symptoms for at least 6 months: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell
      iv. Individual has a baseline immunoglobulin E (IgE) level greater than or equal to 30 IU/mL
      "Baseline" is defined as prior to receiving any treatment with Xolair or another monoclonal antibody therapy that may lower IgE levels (e.g., Dupixent, Tezspire)
      v. Individual meets **BOTH** of the following (a and b):

a. Individual has received at least 3 months of therapy with an intranasal corticosteroid
b. Individual will continue intranasal corticosteroid therapy concomitantly with Xolair, unless contraindicated or intolerant

vi. Individual meets **ONE** of the following (a or b):
a. Individual has received at least one course of treatment with a systemic corticosteroid within the previous two years or has a contraindication or intolerance to systemic corticosteroid therapy
b. Individual has had prior surgery for nasal polyps

vii. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] specialist)

B. Individual is Currently Receiving Xolair. Individual meets **ALL** of the following:
i. Individual has already received at least 6 months of therapy with Xolair and has documentation of beneficial response (An individual who has received less than 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 3A [Nasal Polyps, Initial Therapy])

Examples of beneficial response to Xolair therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sinonasal symptoms, improved sense of smell

ii. Continued concomitant therapy with an intranasal corticosteroid
iii. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] specialist)

Dosing for Nasal Polyps: Up to a maximum dose of 600 mg administered subcutaneously not more frequently than once every 2 weeks.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Authorization Duration

Approval duration for initial therapy: up to 12 months
Approval duration for individuals currently receiving Xolair: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Atopic Dermatitis.** One single-center, double-blind, placebo-controlled trial, Atopic Dermatitis Anti-IgE Pediatric Trial (ADAPT) evaluated the efficacy of Xolair in patients 4 to 19 years of age with severe atopic dermatitis (n = 62).[25] After 24 weeks of therapy, the difference in the objective Scoring Atopic Dermatitis [SCORAD] index with Xolair vs. placebo was -6.9 (P = 0.01). This was statistically significant; however, the clinical significance is unknown. Quality of life measurements were also improved with Xolair. Smaller studies have not shown benefit and case studies have yielded mixed results.[25-27] Additional larger, well-designed clinical trials are needed to determine if Xolair has a role in the treatment of atopic dermatitis. Atopic dermatitis guidelines from the American Academy Dermatology (2014) note that data are limited to determine if Xolair is efficacious.[28] These guidelines do not make a recommendation regarding Xolair use in this patient population.

European consensus guidelines for the treatment of atopic dermatitis (2018) also note the mixed data and state that they cannot recommend Xolair for the treatment of atopic dermatitis.[2]

2. **Concurrent use with another Monoclonal Antibody Therapy (for example, Adbry, Cinqair, Dupixent, Fasenra, Nucala, or Tezspire).** The efficacy and safety of Xolair used in combination with other monoclonal antibody therapies such as Adbry, Cinqair, Dupixent, Fasenra, Nucala, or Tezspire have not been established. There are very limited case reports describing the combined use of Nucala and Xolair for severe asthma as well as off-label indications.[30-32] Further investigation is warranted.

3. **Eosinophilic Gastroenteritis, Eosinophilic Esophagitis, or Eosinophilic Colitis.** There are limited and conflicting data from very small studies and case series on the use of Xolair for the treatment of eosinophilic gastrointestinal conditions.[33-36] Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association and the Joint Task Force on Allergy-Immunology Practice Parameters (2020) recommend against the use of Xolair in patients with this condition.[37]

4. **Latex Allergy in Health Care Workers with Occupational Latex Allergy.** A small European study assessed the effects of Xolair treatment in health care workers (n = 18) with occupational latex allergy.[38] Xolair use in these patients resulted in a reduction in mean conjunctival challenge test scores as compared with placebo-treated patients after 16-weeks of therapy. Also, three patients who did not respond to Xolair treatment during the double-blind phase responded during the 16-week open-label phase. Thus, the overall ocular response rate for all patients in the open-label phase was 93.8% (n = 15/16). Also 11 of 15 patients in the open-label phase had a negative response to a latex glove challenge test (4 patients had a mild response). Well-controlled trials are needed.

5. **Peanut and Other Food Allergies.** Limited data are available regarding the use of Xolair to facilitate desensitization to food allergens. A Phase II multicenter clinical trial was initiated using Xolair in patients with peanut allergy; however, it was discontinued prematurely due to concerns regarding the safety of the oral peanut challenges in some patients.[39] Insufficient data were obtained to reach any conclusions about the efficacy of Xolair. Data are also available from a small pilot study examining the use of Xolair to facilitate rapid oral desensitization in high-risk peanut-allergic patients.[40] There are also minimal data (a Phase I study and a case series) on the use of Xolair to facilitate desensitization in patients with severe cow's milk allergy.[41-44] Additionally, a Phase I study and a Phase II study have evaluated the use of Xolair to facilitate desensitization in patients with multiple food allergies.[45,46] Guidelines for the diagnosis and management of food allergy in the US from the National Institute of Allergy and Infectious Diseases (2010; 2017 addendum) indicate there are currently no medications recommended to prevent IgE-mediated or non-IgE-mediated food-induced allergic reactions from occurring in an individual with existing food allergies.[47] The Practice Parameter on Food Allergy from the JTFPP (2014) also states that immunotherapies (such as the oral immunotherapy desensitization described above) show promise for the treatment of food allergy; however, there is currently inadequate evidence that the therapeutic benefit outweighs the risk.[48] Trials of these have been uncontrolled, small studies, which are subject to selection bias and uncertain safety profiles. However, treatment with anti-IgE monoclonal antibodies might increase the threshold for doses needed to stimulate an allergic reaction and potentially may enhance the safety profile for patients. Additional well-controlled trials are needed.

Coding

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2357	Injection, omalizumab, 5 mg

Background

OVERVIEW

Xolair, an anti-immunoglobulin E (IgE) monoclonal antibody, is indicated for the following uses:[1]

- **Asthma,** in patients ≥ 6 years of age with moderate to severe persistent disease who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids (ICSs). Xolair has been shown to decrease the incidence of asthma exacerbations in these patients. Limitations of Use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus. It is also not indicated for the treatment of other allergic conditions.
- **Chronic idiopathic urticaria**, in patients ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment. Limitation of Use: Xolair is not indicated for the treatment of other forms of urticaria.
- **Nasal polyps**, as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids.

Dosing of Xolair for the treatment of asthma or nasal polyps is based on body weight and the serum total IgE level measured before the start of treatment.[1] Dosing for these indications is only provided for patients with a pretreatment serum IgE level ≥ 30 IU/mL. Dosing of Xolair in patients with chronic idiopathic urticaria is not dependent on serum IgE level or body weight.

A health care professional should initiate omalizumab treatment in a health care setting that is equipped and prepared to identify and treat anaphylaxis until therapy has been safely established. Selection of patients for self-administration should be based on careful assessment of risk for anaphylaxis and mitigation strategies.[1]

Clinical Efficacy

Timing of efficacy assessments varied by indication across the numerous pivotal studies in which Xolair demonstrated benefit. In the majority of the asthma trials, efficacy with Xolair was assessed as early as 16 weeks.[1-11] In chronic idiopathic urticaria, one of the studies included a 12-week double-blind treatment period, while the other was longer with 24 weeks of double-blind treatment.[12,13] Across both studies evaluating Xolair in nasal polyps, efficacy was evaluated at Week 24.[14] Patients continued treatment with intranasal corticosteroids throughout the study.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2022) proposes a step-wise approach to asthma treatment.[15] Xolair is listed as an option for add-on therapy in patients ≥ 6 years of age with difficult-to-treat, severe eosinophilic asthma (i.e., asthma that cannot be managed by therapy with an inhaled corticosteroid [ICS]/long-acting beta$_2$-agonist [LABA] combination with or without an additional controller). Higher blood eosinophil levels, elevated fractional exhaled nitric oxide, allergy-driven symptoms, and childhood-onset asthma may predict a good asthma response to Xolair.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.[16,17] Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20;
2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;

3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: FEV_1 < 80% predicted after appropriate bronchodilator withholding.

Chronic Urticaria Guidelines
A Practice Parameter on the Diagnosis and Management of Acute and Chronic Urticaria (2014) from the Joint Task Force on Practice Parameters (JTFPP) and guideline from the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/World Allergy Organization (2018) define chronic urticaria as urticaria that has been continuously or intermittently present for at least 6 weeks.[18,19] Continuous therapy with antihistamines (second generation H1-antagonists) is generally recommended as first-line pharmacologic treatment for urticaria following trigger avoidance. If symptoms persist following 2 to 4 weeks of initial therapy, the dose of the second generation H1-antagonist should be increased to up to 4-fold. For patients with refractory chronic urticaria, the addition of Xolair may be considered.

Nasal Polyp Guidelines
A 2014 Practice Parameter on the Diagnosis and Management of Rhinosinusitis (2014) and a Practice Parameter for the Management of Rhinitis from the JTFPP (2020), and a 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology (AAO), make similar recommendations regarding the diagnosis and management of chronic rhinosinusitis with nasal polyposis (CRSwNP).[20-24] The presence of two or more signs and symptoms of chronic rhinosinusitis (e.g., rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge) that persist for an extended period of time makes the diagnosis CRS likely. However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography scan. Nasal corticosteroids are recommended for the management of CRSwNP, as they decrease nasal polyp size, prevent regrowth of nasal polyps following surgical removal, and improve nasal symptoms. Short courses of oral corticosteroids are also recommended. Endoscopic surgical intervention may be considered as an adjunct to medical therapy in patients with chronic rhinosinusitis that is not responsive or is poorly responsive to medical therapy. The JTFPP parameter lists Xolair as a therapy that may be considered for the treatment of nasal polyps based on the limited data available at the time of publication. The AAO guidelines do not address Xolair.

The European Forum for Research and Education in Allergy expert board on uncontrolled severe CRSwNP and biologics (2021) recommends that these agents, including Xolair, only be used for severe uncontrolled CRSwNP when Type 2 inflammation is present.[49] Severe CRSwNP is defined as bilateral CRSwNP with a nasal polyp score ≥ 4 and persistent symptoms (e.g., loss of smell/taste, nasal obstruction, secretion or postnasal drip, facial pain or pressure) with the need for add-on treatment to supplement intranasal corticosteroids. Severe CRSwNP is considered to be uncontrolled if the patient has received continuous treatment with an intranasal corticosteroid and has needed at least one course of systemic corticosteroids in the previous 2 years (or has a medical contraindication or intolerance) and/or has a previous sinonasal surgery.

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