PRIOR AUTHORIZATION POLICY

POLICY: Immunologicals – Xolair Prior Authorization Policy
- Xolair® (omalizumab subcutaneous injection – Genentech/Novartis)

REVIEW DATE: 03/07/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xolair, an anti-immunoglobulin (Ig)E 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.
- **Chronic rhinosinusitis with nasal polyps** (CRSwNP), as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids.
- **IgE-mediated food allergy**, in patients ≥ 1 year of age, for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. Xolair is to be used in conjunction

with food allergen avoidance. Limitation of Use: Xolair is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

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.

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. In the pivotal study of Xolair for food allergy, patients were required to have a positive skin prick test response to a food and to have a positive IgE test (blood test) to food.[15] Patients were provided with an epinephrine auto-injector throughout the study.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2023) proposes a step-wise approach to asthma treatment.[16] 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., patients with symptoms and/or exacerbations despite medium- or high-dose ICS/long-acting beta2-agonist [LABA] or who require maintenance oral corticosteroid). 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.[17,18] 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: forced expiratory volume in 1 second (FEV_1) < 80% predicted after appropriate bronchodilator withholding.

Chronic Urticaria Guidelines

Guidelines for the definition, classification, diagnosis, and management of urticaria have been published by the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/Asia Pacific Association of Allergy, Asthma and Clinical Immunology (2022).[19] The American Academy of Dermatology was involved in the development of these guidelines and endorses their recommendations. Chronic spontaneous urticaria is defined as the appearance of wheals, angioedema, or both for > 6 weeks due to known or unknown causes. Signs and symptoms may be present daily/almost daily or have an intermittent recurrent course. Second generation H1-antihistamines taken regularly are the recommended first-line treatment for all types of urticaria following elimination of possible underlying causes. If standard doses do not eliminate urticaria signs and symptoms, the dose of the antihistamine should be increased up to 4-fold. If symptoms persist following 2 to 4 weeks of antihistamine therapy, the addition of Xolair may be considered. For patients with refractory chronic urticaria, the addition of Xolair may be considered. Short courses of rescue systemic corticosteroids are recommended for treatment of patients with acute exacerbations of chronic urticaria. However, guidelines recommend against the long-term use of systemic steroids.

Chronic Rhinosinusitis with Nasal Polyps Guidelines

The Joint Task Force on Practice Parameters (JTFPP) published a focused guideline update for the medical management of CRSwNP (2023), which updated recommendations regarding intranasal corticosteroids and biologic therapies.[20] Intranasal corticosteroids are recommended for the treatment of CRSwNP. Use of biologics (e.g., Xolair) are also recommended. However, in patients who derived a sufficient benefit from other therapies such as intranasal corticosteroids, surgery, or aspirin therapy after desensitization, biologics may not be preferred. Conversely, biologics may be preferred over other medical treatment options in patients who continue to have a high burden of disease despite receiving at least 4 weeks of treatment with an intranasal corticosteroid.

The diagnosis of CRSwNP was not addressed in this focused guideline update. Previous guidelines have noted that 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 of chronic rhinosinusitis likely.[21-24] However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Oral corticosteroids and surgical intervention were not specifically addressed in this update. Prior guidelines recommend short courses of oral corticosteroid as needed and consideration of surgical removal as an adjunct to medical therapy in patients with CRSwNP that is not responsive or is poorly responsive to medical therapy.[21,22,24]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xolair. All approvals are provided for the duration noted below. In cases where approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xolair, as well as the monitoring required for adverse events and long-term efficacy, approval requires Xolair to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Xolair® (omalizumab subcutaneous injection (Genentech/Novartis) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

FDA-Approved Indications

1. **Asthma.** Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
      i. Patient is ≥ 6 years of age; AND
      ii. Patient has a baseline immunoglobulin E (IgE) level ≥ 30 IU/mL; AND
      Note: "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]).
      iii. Patient 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 perennial aeroallergens and/or for one or more seasonal aeroallergens; AND
      Note: "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 perennial aeroallergens are house dust mite, animal dander, cockroach, feathers, and mold spores. Examples of seasonal aeroallergens are grass, pollen, and weeds.
      iv. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
         a) An inhaled corticosteroid; AND
         b) At least one additional asthma controller or asthma maintenance medication; AND
         Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting beta$_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, and monoclonal antibody therapies for asthma (e.g., Xolair, Cinqair [reslizumab intravenous infusion], Dupixent, Fasenra [benralizumab subcutaneous injection], Nucala [mepolizumab subcutaneous injection], and Tezspire. Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfil the requirement for both criteria a and b.

v. Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, or e):
Note: "Baseline" is defined as prior to receiving Xolair or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Cinqair, Dupixent, Fasenra, Nucala, Tezspire, and Xolair.
- **a)** Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
- **b)** Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR
- **c)** Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR
- **d)** Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR
- **e)** Patient has asthma that worsens upon tapering of oral corticosteroid therapy; AND

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

B) Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has already received at least 4 months of therapy with Xolair; AND
Note: A patient who has received < 4 months of therapy or who is restarting therapy with Xolair should be considered under criterion 1A (Asthma, Initial Therapy).

ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND

iii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department, urgent care, or medical clinic visits due to asthma; decreased reliever/rescue medication use; and improved lung function parameters.

2. Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria). Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 12 years of age; AND

ii. Patient has/had urticaria for > 6 weeks (prior to treatment with Xolair), with symptoms present > 3 days per week 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; AND
Note: 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) Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has already received at least 4 months of therapy with Xolair; AND
Note: A patient who has received < 4 months of therapy or who is restarting therapy with Xolair should be considered under criterion 2A (Chronic Idiopathic Urticaria, Initial Therapy).

ii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Xolair therapy are decreased severity of itching, decreased number and/or size of hives.

3. Chronic Rhinosinusitis with Nasal Polyps. Approve Xolair for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has chronic rhinosinusitis with nasal polyps as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND

iii. Patient 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; AND

iv. Patient has a baseline immunoglobulin E (IgE) level ≥ 30 IU/mL; AND
Note: "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]).

v. Patient meets BOTH of the following (a and b):

a) Patient has received at least 4 weeks of therapy with an intranasal corticosteroid; AND

b) Patient will continue to receive therapy with an intranasal corticosteroid concomitantly with Xolair; AND

vi. Patient meets ONE of the following (a, b, or c):

a) Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR

b) Patient has a contraindication to systemic corticosteroid therapy; OR

c) Patient has had prior surgery for nasal polyps; AND

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

B) Patient is currently receiving Xolair. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has already received at least 6 months of therapy with Xolair; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 3A (Nasal Polyps, Initial Therapy).

ii. Patient continues to receive therapy with an intranasal corticosteroid; AND

iii. Patient has responded to Xolair therapy as determined by the prescriber.
Note: Examples of a response to Xolair therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, and/or improved sense of smell.

4. **Immunoglobulin (Ig)E-Mediated Food Allergy**. Approve Xolair for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   - **A)** Patient is ≥ 1 year of age; AND
   - **B)** Patient has a baseline immunoglobulin (Ig)E level ≥ 30 IU/mL; AND
     Note: "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]).
   - **C)** Patient meets BOTH of the following(i and ii):
     - **i.** Patient has a positive skin prick test response to one or more foods; AND
     - **ii.** Patient has a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods; AND
   - **D)** According to the prescriber, the patient has a history of an allergic reaction to a food that met each of the following (i, ii, and iii):
     - **i.** Patient demonstrated signs and symptoms of a significant systemic allergic reaction; AND
       Note: Signs and symptoms of a significant systemic allergic reaction include hives, swelling, wheezing, hypotension, and gastrointestinal symptoms.
     - **ii.** This reaction occurred within a short period of time following a known ingestion of the food; AND
     - **iii.** The prescriber deemed this reaction significant enough to require a prescription for an epinephrine auto-injector; AND
       Note: Examples of epinephrine auto-injectors include EpiPen, EpiPen Jr., Auvi-Q, and generic epinephrine auto-injectors.
   - **E)** Patient has been prescribed an epinephrine auto-injector; AND
     Note: Examples of epinephrine auto-injectors include EpiPen, EpiPen Jr., Auvi-Q, and generic epinephrine auto-injectors.
   - **F)** According the prescriber, Xolair will be used in conjunction with a food allergen-avoidant diet; AND
   - **G)** The medication is prescribed by or in consultation with an allergist or immunologist.

CONDITIONS NOT COVERED

- **Xolair® (omalizumab subcutaneous injection (Genentech/Novartis) is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

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 (2023) note that there are insufficient data to make a recommendation regarding the use of Xolair.[28]

2. **Concurrent use of Xolair with another Monoclonal Antibody Therapy.** The efficacy and safety of Xolair used in combination with other monoclonal antibody therapies 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.[29-32] One limited case series also reported the use of Xolair and Dupixent in patients with asthma or chronic idiopathic urticaria.[33] Further investigation is warranted.
   Note: Monoclonal antibody therapies are Adbry® (tralokinumab-ldrm subcutaneous injection), Cinqair® (reslizumab intravenous infusion), Dupixent® (dupilumab subcutaneous injection), Fasenra® (benralizumab subcutaneous injection), Nucala® (mepolizumab subcutaneous injection), or Teszpire® (tezepelumab-ekko subcutaneous injection).

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.[34-37] 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.[38]

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.[39] 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.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Conditions Not Covered :** Criteria were updated to clarify that use of Xolair with another monoclonal antibody therapy is specific to Cinqair, Fasenra, Nucala, Dupixent, Tezspire, and Adbry.	03/22/2023
Selected Revision	**Chronic Rhinosinusitis with Nasal Polyps:** Approval condition updated from "Nasal Polyps" to "Chronic Rhinosinusitis with Nasal Polyps". Duration of the intranasal corticosteroid requirement was changed from 3 months to 4 weeks.	02/14/2024
Early Annual Revision	**IgE-Mediated Food Allergy:** New approval criteria for this indication were added. **Conditions Not Covered :** "Peanut and Other Food Allergies" was removed as a Condition Not Recommended for Approval.	03/06/2024 and 03/07/2024