BlueCross BlueShield of Kansas
An Independent Licensee of the Blue Cross and Blue Shield Association.

Xolair® (omalizumab) Prior Authorization Program Summary

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent(s)	Indication(s)	Dose and administration
Xolair® (omalizumab) Subcutaneous injection	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 symptoms that are inadequately controlled with inhaled corticosteroids*	75 mg to 375 mg by subcutaneous injection every 2 or 4 weeks Determine the dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg)
	Chronic idiopathic urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment*	150 or 300 mg by subcutaneous injection every 4 weeks
	Add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids	75 mg to 600 mg by subcutaneous injection every 2 or 4 weeks Determine the dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg)

***** Omalizumab is not indicated for treatment of other allergic conditions, other forms of urticaria, relief of acute bronchospasms, or status asthmaticus.

CLINICAL RATIONALE

Asthma

Asthma is a chronic inflammatory disorder of the airways.[2,3] It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.[2] Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness.[2,3] Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles.[2] The National Asthma Education and Prevention Program (NAEPP) Expert Panel guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma. In addition, differential diagnosis of asthma should be considered.[2]

Markers of asthma that is not adequately controlled in patients receiving therapy include limitation of normal activities, poor lung function with FEV1 of < 80% predicted, at least 2 episodes per year of asthma exacerbations requiring oral systemic corticosteroids.[2] More frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control.[2]

The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma.[3] Long-term goals for asthma management are to achieve good control of

symptoms, maintain normal activity level, and to minimize the future risk of exacerbations, fixed airflow limitation, and side-effects.[7] Allergic asthma is triggered by inhalation of allergens.[4] IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose inhaled corticosteroids (ICS) in combination with a long-acting beta agonist (LABA).[3] Severe asthma is defined as asthma that requires Step 4 or 5 treatment (e.g., with high dose ICS plus a LABA) to prevent it from becoming 'uncontrolled', or which remains uncontrolled despite this therapy.[3] Early initiation of low dose inhaled corticosteroid (ICS) in patients with asthma has led to greater improvement in lung function than if initiation of ICS after symptoms have been present for more than 2 to 4 years. The 2020 GINA guidelines recommend every adult and adolescent with asthma should receive ICS-containing controller medication to reduce the risk of serious exacerbation, even in patients with infrequent symptoms.[3]

2020 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations:[3]

- Step 1:
  - Preferred controller: as-needed low-dose ICS-formoterol
  - Alternative options: as needed low-dose ICS taken at the same time as a short acting β-agonist (SABA)
- Step 2:
  - Preferred controller: daily low dose ICS plus as needed SABA or as needed low dose ICS-formoterol
  - Alternative options: Leukotriene receptor antagonist (LTRA) or as needed ICS taken at the same time as a SABA
  - LTRA are less effective than ICS, particularly for preventing exacerbations
- Step 3:
  - Preferred controller: daily low dose ICS/LABA plus as needed SABA, or low dose ICS-formoterol as maintenance and reliever therapy
  - Alternative options: Medium dose ICS maintenance or low dose ICS plus either LTRA or sustained release theophylline
- Step 4:
  - Preferred controller: low dose ICS-formoterol as maintenance and reliever therapy or daily medium dose ICS/LABA plus as needed SABA
  - Alternative options: High dose ICS, add-on tiotropium, LTRA or sustained-release theophylline
- Step 5:
  - Refer patients for phenotypic assessment and consideration of add on therapy (e.g., tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R)
  - Preferred therapy optimization
  - Add-on controller therapy after optimization of existing therapy: high dose ICS/LABA, add-on tiotropium; add low dose oral corticosteroids (OCS), but consider side effects; add on anti-IgE, anti-IL5/5R, or anti-IL4R
- Reliever therapy:
  - Preferred: ICS-formoterol
  - Alternative: SABA

2020 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:[3]

- Step 1:
  - Possible controller: as needed ICS taken at the same time as a SABA OR regular low dose ICS with as needed SABA (likelihood of poor adherence should be taken into account)
- Step 2:
  - Preferred controller: daily low dose ICS
  - Alternative options: Leukotriene receptor antagonist (LTRA) or as needed ICS taken at the same time as a SABA

    - LTRA are less effective than ICS, particularly for preventing exacerbations
- Step 3:
    - Address and treat modifiable risk factors (e.g., adherence, technique)
    - Preferred controller: daily medium dose ICS or change to a combination low dose ICS-LABA plus as needed SABA
- Step 4:
    - Refer for expert assessment and advice if not controlled on a moderate dose ICS
    - Alternative options: add-on tiotropium

Biologic agents should be considered as add on therapy for patients with refractory type 2 inflammation with exacerbations or poor symptom control despite taking at least high dose ICS/LABA, and that have allergic or eosinophilic biomarkers or need maintenance OCS.[3]

Moderate to Severe Allergic (IgE-mediated) Asthma
Allergic asthma is triggered by inhalation of allergens.[3,4] IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose ICS in combination with a LABA.[3] Severe asthma is defined as "asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy."[3] Guidelines recommend use of omalizumab as add on therapy for patients who have failed to respond to standard therapy and have IgE-mediated allergic asthma.

Chronic Idiopathic Urticaria (CIU)
Urticaria is characterized by the development of wheals (hives), angioedema, or both. Chronic urticaria is defined by the presence of urticaria that has been continuously or intermittently present for more than 6 weeks.[5,6] Treatment goals for CIU involves symptom control and improvement in quality of life that is acceptable to the patient.[6] The 2018 EAACI/GA LEN/EDF/WAO guidelines, endorsed by the American Academy of Allergy, Asthma, and Immunology, American Academy of Dermatology, American College of Asthma, and Allergy, and Immunology, recommend the following for the treatment of CIU:[6]

- Recommend discontinuing medications suspected to worsen CIU (e.g., NSAIDs)
- First line treatment: second-generation H-1 antihistamine (cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) dosed daily
- Second-line treatment: Increase the dose up to 4 times the FDA max if inadequate control after 2-4 weeks of therapy at the FDA max
- Third-line treatment: addition of omalizumab

Chronic Rhinosinusitis with Nasal Polyposis
Chronic rhinosinusitis with nasal polyposis (CRSwNP) is an inflammatory condition affecting the paranasal sinuses. Hallmarks of the disease consist of at least two out of four cardinal symptoms (i.e., facial pain/pressure, hyposmia/anosmia, nasal drainage, and nasal obstruction) for at least 12 consecutive weeks in addition to nasal polyps and sinonasal inflammation.[8-10] Sinus computed tomography (CT) and/or nasal endoscopy are needed to determine the presence of sinonasal inflammation and nasal polyps. The exact cause of CRSwNP is unknown, but biopsies of nasal polyps have shown elevated levels of eosinophils.[8]

First line therapy for CRSwNP consists of nasal saline irrigation in combination with intranasal corticosteroids.[8-10] The American Academy of Family Physicians notes that no one intranasal corticosteroid is superior to another or that increased dosing provides greater effectiveness. The American Academy of Otolaryngology recommends a short course of oral corticosteroids if no response is seen with intranasal corticosteroids after 3-months of appropriate use.[10] Short courses of oral corticosteroids (up to three weeks) can improve sinonasal symptoms and endoscopic findings. Surgical intervention may be required in patients in which medical therapy is ineffective.[8,9]

Safety
Omalizumab has a boxed warning due to risk of anaphylaxis. It is also contraindicated in patients with history of hypersensitivity to omalizumab or any ingredients of omalizumab.[1]

REFERENCES

1. Xolair prescribing information. Genentech, Inc. November 2020.
2. National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. August 2007. Available at https://www.ncbi.nlm.nih.gov/books/NBK7232/pdf/Bookshelf_NBK7232.pdf. Accessed October 2020.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2020. Available at www.ginasthma.org.
4. Lanier B, Bridges T, Kulus M, et al. Omalizumab for the Treatment of Exacerbations in Children with Inadequately Controlled Allergic (IgE-mediated) Asthma. *J Allergy Clin Immunol*. 2009 Dec;124(6):1210-1216.
5. Bernstein J, Lang D, Khan D, et al. The Diagnosis and Management of Acute and Chronic Urticaria: 2014 Update. *J Allergy Clin Immunol*. 2014;133(5):1270-1277.
6. The EAACI/GA^{2}LEN/EDF/WAO Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. *Allergy*. 2018;73:1393–1414. doi: 10.1111/all.13397.
7. National Institute for Health and Care Excellence (NICE). Guideline on Asthma: Diagnosis, Monitoring and Chronic Asthma Management. 2020. Available at https://www.nice.org.uk/guidance/ng80/resources/asthma-diagnosis-monitoring-and-chronic-asthma-management-pdf-1837687975621. Accessed October 2020.
8. Stevens WW, Schleimer RP, and Kern RC. Chronic Rhinosinusitis with Nasal Polyps. *J Allergy Clin Immunol Pract.* 2016;4(4):565–572.
9. Sedaghat AR. Chronic Rhinosinusitis. *Am Fam Physician*. 2017 Oct;96(8):500-506.
10. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical Practice Guideline (Update): Adult Sinusitis. Otolaryngol Head Neck Surg. 2015;152(2 suppl):S1-S39.

Xolair (omalizumab) Prior Authorization

TARGET AGENT
Xolair® (omalizumab)

Brand (generic)	GPI	Multisource Code
Xolair (omalizumab)		
150 mg vial	44603060002120	M, N, O, or Y
75 mg / 0.5 mL prefilled syringe	4460306000E510	M, N, O, or Y
150 mg / 1 mL prefilled syringe	4460306000E520	M, N, O, or Y

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent will be approved when ALL of the following are met:

1. ONE of the following:
    A. The patient's age is within FDA labeling for the requested indication for the requested agent
    OR
    B. The prescriber has provided information in support of using the requested agent for the patient's age

AND

2. ONE of the following:
    A. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following:
        i. ONE of the following:
            a. The patient is 6 to less than 12 years of age AND BOTH of the following:
                a. The pretreatment IgE level is 30 IU/mL to 1300 IU/mL
                AND
                b. The patient's weight is 20 kg to 150 kg
            OR
            b. The patient is 12 years of age or over AND BOTH of the following:
                a. The pretreatment IgE level is 30 IU/mL to 700 IU/mL
                AND
                b. The patient's weight is 30 kg to 150 kg

        AND

        ii. Allergic asthma has been confirmed by a positive skin test or in vitro reactivity test (RAST) to a perennial aeroallergen
        AND
        iii. The patient has a history of uncontrolled asthma while on asthma control therapy as demonstrated by ONE of the following:
            a. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months
            OR
            b. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months
            OR
            c. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered
            OR
            d. The patient has baseline Forced Expiratory Volume (FEV1) that is less than 80% of predicted

        AND

        iv. ONE of the following:

a. The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months
OR
b. The patient is currently being treated with the requested agent AND ONE of the following:
    a. Is currently treated with an inhaled corticosteroid for at least 3 months that is adequately dosed to control symptoms
    OR
    b. Is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months
OR
c. The patient has an intolerance or hypersensitivity to inhaled corticosteroid therapy
OR
d. The patient has an FDA labeled contraindication to ALL inhaled corticosteroids

AND

v. ONE of the following:
    a. The patient is currently being treated for at least 3 months with ONE of the following:
        a. A long-acting beta-2 agonist (LABA)
        OR
        b. A Leukotriene receptor antagonist (LTRA)
        OR
        c. Long-acting muscarinic antagonist (LAMA)
        OR
        d. Theophylline
    OR
    b. The patient has an intolerance or hypersensitivity to therapy with long-acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonists (LAMA), or theophylline
    OR
    c. The patient has an FDA labeled contraindication to ALL long-acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonists (LAMA), AND theophylline

AND

vi. The patient will continue asthma control therapy (e.g., ICS, LABA, LTRA, LAMA, theophylline) in combination with the requested agent

AND

vii. The requested dose is based on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling AND does NOT exceed 375 mg every 2 weeks

OR

B. The patient has a diagnosis of chronic idiopathic urticaria (CIU) AND ALL of the following:
    i. The patient has had over 6 weeks of hives and itching

    AND

    ii. If the patient is currently being treated with medications known to cause or worsen urticaria, then ONE of the following:
        a. The prescriber has reduced the dose or discontinued any medications known to cause or worsen urticaria (e.g., NSAIDs)
        OR
        b. The prescriber has provided information indicating that a reduced dose or discontinuation of any medications known to cause or worsen urticaria is not appropriate

    AND

    iii. ONE of the following:

a. The patient has tried and had an inadequate response to the FDA max dose of a second-generation H-1 antihistamine (e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) after at least a 2-week trial **AND** ONE of the following:
    1. The patient has tried and had an inadequate response to a dose above the FDA labeled maximum dose (e.g., up to 4 times the FDA labeled maximum dose)
    OR
    2. The prescriber has provided information indicating the patient cannot be treated with a dose above the FDA labeled maximum dose

OR

b. The patient has an intolerance or hypersensitivity to second-generation H-1 antihistamine therapy

OR

c. The patient has an FDA labeled contraindication to ALL second-generation H-1 antihistamines

AND

iv. The requested dose is within the FDA labeled dose AND does NOT exceed 300 mg every 4 weeks

OR

C. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND ALL of the following:

i. There is information indicating the patient's diagnosis was confirmed by ONE of the following:
    a. Anterior rhinoscopy or endoscopy
    OR
    b. Computed tomography (CT) of the sinuses

AND

ii. ONE of the following:
    a. The patient has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone) used for at least a 3-month trial
    OR
    b. The patient has an intolerance or hypersensitivity to therapy with intranasal corticosteroids (e.g., fluticasone)
    OR
    c. The patient has an FDA labeled contraindication to ALL intranasal corticosteroids

AND

iii. The patient will continue standard maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent

OR

D. The patient has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested agent AND the requested dose is within the FDA labeled dose for the requested indication

AND

3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

4. The patient will NOT be using the requested agent in combination with another biologic agent for the requested indication [e.g., injectable IL-5 inhibitor (Cinqair, Fasenra, Nucala), injectable IL-4 inhibitor (Dupixent)]

AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of approval: 6 months for asthma, chronic idiopathic urticaria, and nasal polyps
12 months for all other FDA approved indications

Renewal Evaluation

Target Agent will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process
   AND
2. ONE of the following:
   A. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following
      i. The patient's weight is within the FDA indicated range for their age (i.e., 20 kg to 150 kg for patients age 6 to less than 12 years and 30 kg to 150 kg for patients 12 years of age and above)
      AND
      ii. The patient has had clinical response or disease stabilization as defined by ONE of the following:
         a. Increase in percent predicted FEV_1 from baseline
         OR
         b. Decrease in the dose of inhaled corticosteroid required to control the patient's asthma
         OR
         c. Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma
         OR
         d. Decrease in the number of hospitalizations, need for mechanical ventilation, or visits to the emergency room or urgent care due to exacerbations of asthma
      AND
      iii. The patient is currently treated and is compliant with standard therapy [i.e., inhaled corticosteroids, long acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonist (LAMA), theophylline]
      AND
      iv. The requested dose is based on pre-treatment serum IgE level and the patient's body weight as defined in FDA approved labeling AND does not exceed 375 mg every 2 weeks

   OR

   B. The patient has a diagnosis of chronic idiopathic urticaria AND BOTH of the following:
      i. The patient has had clinical benefit with the requested agent
      AND
      ii. The requested dose is within the FDA labeled dose AND does NOT exceed 300 mg every 4 weeks

   OR

   C. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND BOTH of the following:
      i. The patient has had clinical benefit with the requested agent
      AND
      ii. The patient will continue standard maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent

   OR

   D. The patient has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested agent AND BOTH of the following:
      i. The patient has had clinical benefit with the requested agent

AND

ii. The requested dose is within the FDA labeled dose for the requested indication

AND

3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

4. The patient will NOT be using the requested agent in combination with another biologic agent for the requested indication [e.g., injectable IL-5 inhibitor (Cinqair, Fasenra, Nucala), injectable IL-4 inhibitor (Dupixent)]

AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of Approval: 12 months

FDA-Approved Dosing for Patients Age 6 to less than 12 Years

Pre-treatment serum IgE (IU/mL)	Dosing frequency	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								

DO NOT DOSE

FDA-Approved Dosing for Patients 12 years of Age and Above

Pre-treatment serum IgE (IU/mL)	Body weight (kg)			
	30-60	> 60-70	> 70-90	> 90-150
≥ 30-100	150 mg q 4 wks	150 mg q 4 wks	150 mg q 4 wks	300 mg q 4 wks
> 100-200	300 mg q 4 wks	300 mg q 4 wks	300 mg q 4 wks	225 mg q 2 wks
> 200-300	300 mg q 4 wks	225 mg q 2 wks	225 mg q 2 wks	300 mg q 2 wks
> 300-400	225 mg q 2 wks	225 mg q 2 wks	300 mg q 2 wks	
> 400-500	300 mg q 2 wks	300 mg q 2 wks	375 mg q 2 wks	
> 500-600	300 mg q 2 wks	375 mg q 2 wks		
> 600-700	375 mg q 2 wks			

FDA-Approved Dosing for Adult Patients with Nasal Polyps

Pre-treatment serum	Dosing frequency	Body weight (kg)

IgE (IU/mL)									
		>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

Agent(s)	**Contraindication(s)**
Xolair (omalizumab)	Severe hypersensitivity reaction to Xolair or any ingredient of Xolair