Medicare Part B - Xolair (omalizumab) Prior Authorization Criteria

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent(s)	Indication(s)	Dosage^
Xolair® (omalizumab) Injection for subcutaneous use	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 2-4 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.
^ Initiate therapy in a healthcare setting. Once therapy has been safely established, the healthcare provider may determine whether self-administration of Xolair prefilled syringe by the patient or caregiver is appropriate, based on careful assessment of risk for anaphylaxis and mitigation strategies.

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. Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles. 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.[2,3]

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). 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. Early initiation of low dose 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 2021 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]

2021 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations. 2021 GINA guidelines have been updated to include two treatment "tracks", with the key difference being the medication that is used for symptoms relief: as-needed low dose ICS-formoterol in Track 1, and as-needed SABA in Track 2.[3]

Track 1 is the preferred approach recommended by GINA, because using low dose ICS-formoterol as reliever reduces the risk of severe exacerbations compared with regimens with SABA as reliever, with similar symptom control:[3]

- Steps 1 and 2: As-needed low dose ICS-formoterol
    - Alternative options: Daily leukotriene receptor antagonist (LTRA), or add house dust mite (HDM) sublingual immunotherapy (SLIT)
- Step 3: Low dose maintenance ICS-formoterol
    - Reliever: As-needed low dose ICS-formoterol
    - Alternative options: Medium dose ICS, or add LTRA, or add HDM SLIT
- Step 4: Medium dose maintenance ICS-formoterol
    - Reliever: As-needed low dose ICS-formoterol
    - Alternative options: Add long-acting muscarinic antagonist (LAMA) or LTRA, or switch to high dose ICS
- Step 5: Add-on LAMA; refer for phenotypic assessment and consideration of anti-IgE, anti-IL5/5R, anti-IL4R; consider high dose ICS-formoterol
    - Reliever: As-needed low dose ICS-formoterol
    - Alternative options: Add azithromycin (adults) or LTRA; add low dose oral corticosteroids (OCS) but consider side effects

Track 2 is an alternative approach if Track 1 is not possible or is not preferred by a patient with no exacerbations on their current therapy. Before considering a regimen with SABA reliever, the clinician should consider whether the patient is likely to be adherent with their controller therapy, as if not, they will be exposed to the risks of SABA-only treatment:[3]

- Step 1: Take ICS whenever SABA taken
    - Reliever: As-needed short-acting β-2 agonist (SABA)
- Step 2: Low dose maintenance ICS
    - Reliever: As-needed SABA
    - Alternative options: Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT
- Step 3: Low dose maintenance ICS-LABA
    - Reliever: As-needed SABA
    - Alternative options: Medium dose ICS, or add LTRA, or add HDM SLIT
- Step 4: Medium/high dose maintenance ICS-LABA
    - Reliever: As-needed SABA
    - Alternative options: Add LAMA or LTRA, or switch to high dose ICS

- Step 5: Add-on LAMA; refer for phenotypic assessment and consideration of anti-IgE, anti-IL5/5R, anti-IL4R; consider high dose ICS-LABA
    - Reliever: As-needed SABA
    - Alternative options: Add azithromycin (adults) or LTRA; add low dose oral corticosteroids (OCS) but consider side effects

2021 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 with as needed SABA
    - 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 with as-needed SABA as reliever, or
        - Change to a combination low dose ICS-LABA plus as-needed SABA, or
        - Maintenance and reliever therapy (MART) with very low dose ICS-formoterol
- Step 4:
    - Medium dose ICS-LABA, or
    - MART with low dose budesonide-formoterol
    - Alternative options: high dose ICS-LABA; add-on tiotropium
- Step 5:
    - Refer for expert assessment and advice if not controlled on a moderate dose ICS
    - Alternative options: add-on tiotropium

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. Severe asthma is defined by GINA guidelines as asthma that is uncontrolled despite adherence with maximal optimized GINA Step 4 or Step 5 therapy (e.g., medium or high dose ICS with a second controller; maintenance OCS) and treatment of contributory factors (e.g., inhaler technique, smoking or comorbidities), or that worsens when high dose treatment is decreased. Roughly 3% to 10% of adults with asthma have severe asthma. 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.[3,4] The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) mirror the GINA definition of severe asthma, and define uncontrolled asthma as:[2]

- Frequent severe exacerbations (i.e., two or more bursts of systemic corticosteroids within the past 12 months)
- Serious exacerbations (i.e., at least one hospitalization, intensive care unit stay, or mechanical ventilation in the past 12 months)
- Airflow limitation (i.e., FEV1 less than 80% predicted)
- Asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids

A specialist, preferably in a multidisciplinary severe asthma clinic (if available) performs further assessment, which includes the patient's inflammatory phenotype (i.e., Type 2 or non-Type 2).[3]

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]

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[1]
Omalizumab has a boxed warning due to risk of anaphylaxis. Because of the risk of anaphylaxis, therapy should be initiated in a healthcare setting. Selection of patients for self-administration should be based on criteria to mitigate risk from anaphylaxis. Patient-specific factors including the following criteria should be considered:

- Patient should have no prior history of anaphylaxis, including to Xolair or other agents such as foods, drugs, biologics, etc
- Patient should receive at least 3 doses of Xolair under the guidance of a healthcare provider with no hypersensitivity reactions
- Patient or caregiver is able to recognize symptoms of anaphylaxis
- Patient or caregiver is able to treat anaphylaxis appropriately
- Patient or caregiver is able to perform subcutaneous injections with Xolair prefilled syringe with proper technique according to the prescribed dosing regimen and Instructions for Use

Omalizumab is contraindicated in patients with history of hypersensitivity to omalizumab or any ingredients of omalizumab.

REFERENCES

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Document History
Original Prime Standard Part B criteria, approved by P&T UM Committee 06/2021
Annual Review Prime Standard Part B criteria, with changes to criteria approved by P&T UM Committee 12/2021

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Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET AGENT(S)	PREREQUISITE AGENT(S)
Target and prerequisite agent(s) determined by client	Target and prerequisite agent(s) determined by client
Xolair (omalizumab)	For moderate to severe persistent asthma: • Inhaled corticosteroid For chronic idiopathic urticaria (CIU): • second-generation H-1 antihistamine (e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) For chronic rhinosinusitis with nasal polyposis (CRSwNP): • Intranasal corticosteroid

Brand (generic)	GPI	Multisource Code	HCPCS Code
Xolair (omalizumab)			
150 mg vial	44603060002120	M, N, O, or Y	J2357
75 mg / 0.5 mL prefilled syringe	4460306000E510	M, N, O, or Y	J2357
150 mg / 1 mL prefilled syringe	4460306000E520	M, N, O, or Y	J2357

CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents for the requested indication, then ONE of the following:
    a. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    b. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL prerequisite agent(s)
    OR
    c. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL prerequisite agent(s)
    OR

d. The prescriber has submitted documentation indicating ALL prerequisite agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

AND

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

AND

4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months