Xolair (omalizumab) Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date	Date of Origin
03-11-2024	

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Xolair® (omalizumab) Injection for subcutaneous use	Moderate to severe persistent asthma in adults and pediatric 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 Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance Limitations of use: • Not indicated for acute bronchospasms, or status asthmaticus • Not indicated for the emergency treatment of allergic reactions, including anaphylaxis • Not indicated for other allergic conditions or forms of urticaria		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

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.(2,3) The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma. 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.(3) 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

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define moderate asthma as that which is well controlled with Step 3 or Step 4 treatment (e.g., low- or medium-dose inhaled corticosteroids [ICS] in combination with a long-acting beta agonist [LABA] in either treatment track). Severe asthma is defined as asthma that remains uncontrolled despite optimized treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA to prevent it from becoming uncontrolled. Severe asthma must be distinguished from asthma that is difficult to treat due to inadequate or inappropriate treatment, or persistent problems with adherence or comorbidities such as chronic rhinosinusitis or obesity, as they need very different treatment compared with if asthma is relatively refractory to high-dose ICS-LABA or even oral corticosteroids (OCS). Early initiation of low dose ICS in patients with asthma has led to greater improvement in lung function than initiation of ICS after symptoms have been present for more than 2 to 4 years. The 2023 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)

2023 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations and are broken into two tracks based on reliever therapy.

Track 1 is the preferred approach recommended by GINA, because using low dose ICS-formoterol as reliever reduces the risk of exacerbations compared with regimens with short-acting β2-agonist (SABA) as reliever, and is a simpler regimen. Note ICS-formoterol should not be used as the reliever by patients taking any other (non-formoterol) ICS-LABA or ICS-LAMA:(3)

- Step 1:
  - As-needed low dose ICS-formoterol
- Step 2:
  - As-needed low dose ICS-formoterol
- Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up
  - Maintenance: low dose ICS-formoterol
  - Reliever: as-needed low dose ICS-formoterol
- Step 4:
  - Maintenance: medium dose ICS-formoterol
  - Reliever: as-needed low dose ICS-formoterol
- Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment
  - Maintenance: consider high dose ICS-formoterol
  - Reliever: as-needed low dose ICS-formoterol
  - Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers
  - Refer for phenotypic assessment +/- biologic therapy
    - Add-on anti-IgE for severe allergic asthma
    - SC omalizumab in patients greater than or equal to 6 years
    - Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma
      - Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age
      - Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years
      - Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years
    - Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma
      - SC tezepelumab for patients greater than or equal to 12 years

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	○ Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance ○ Maintenance oral corticosteroids (OCS) should be used only as last resort, because short-term and long-term systemic side-effects are common and serious **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; if not, they will be exposed to the higher risk of exacerbations with SABA-only treatment:(3) • Step 1: ○ Take ICS whenever SABA taken ○ Reliever: as-needed ICS-SABA or as needed SABA • Step 2: ○ Preferred maintenance: low dose ICS ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options with limited indications, or less evidence for efficacy and/or safety: ▪ Low dose ICS whenever SABA taken ▪ Daily LTRA. These are less effective than daily ICS, particularly for preventing exacerbations and there is a US FDA boxed warning about the risk of serious mental health effects with montelukast ○ Daily low-dose ICS-LABA as initial therapy leads to faster improvement in symptoms and FEV1 than ICS alone but is costlier, and the reduction in exacerbations compared with SABA is similar to that with ICS ○ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up ○ Preferred maintenance: low dose ICS-LABA ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options: ▪ Medium dose ICS ▪ Low-dose ICS plus LTRA but review US FDA boxed warning ▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding SLIT • Step 4: ○ Preferred maintenance: medium/high dose ICS-LABA ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options: ▪ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium my mist inhaler) • Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium ▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment ○ Maintenance: medium/high dose ICS-LABA ○ Reliever: as-needed ICS-SABA or as-needed SABA ○ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers

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- Refer for phenotypic assessment +/- biologic therapy
  - Add-on anti-IgE for severe allergic asthma
    - SC omalizumab in patients greater than or equal to 6 years
  - Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma
    - Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age
    - Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years
    - Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years
  - Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma
    - SC tezepelumab for patients greater than or equal to 12 years
- Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance
- Maintenance OCS should only be used as last resort, because short-term and long-term systemic side-effects are common and serious

2023 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:(3)

- Step 1:
  - Low dose ICS taken whenever SABA taken
  - Reliever: as needed SABA
- Step 2
  - Preferred: daily low dose ICS
  - Preferred reliever: as needed SABA
  - Alternative options:
    - Low-dose ICS whenever SABA is taken using separate inhalers
    - Daily LTRA are less effective for exacerbation reduction. Advise parents about US FDA warning on montelukast
- Step 3: after checking inhaler technique and adherence, and treating modifiable risk factors (any of the following):
  - Medium-dose ICS maintenance plus as-needed SABA
  - Low-dose ICS-LABA maintenance plus as-needed SABA
  - Maintenance and reliever therapy (MART) with a very low dose of budesonide-formoterol DPI
- Step 4: Individual children's responses vary, so each of the Step 3 options may be tried before considering a step-up to Step 4. Refer for expert advice
  - Preferred: medium dose ICS-LABA plus as-needed SABA
  - Preferred: low dose ICS-formoterol MART plus as-needed low-dose ICS-formoterol
  - Alternative options:
    - Add-on tiotropium
    - Add-on LTRA
- Step 5:
  - Refer for phenotypic assessment with or without higher dose ICS-LABA
  - Reliever: as needed SABA (or ICS-formoterol reliever for MART)
  - Add on therapy with anti-IgE or anti-IL4R, anti-IL5
  - As a last resort consider add on low dose OCS but consider side effects

Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype

Roughly 3% to 10% of adults with asthma have severe asthma as defined by the GINA 2023 guidelines.(3) The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) and the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group mirror

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	the GINA definition of severe asthma, and defined uncontrolled asthma for adult and pediatric patients 5 years of age and over:(2,12)
	
	• 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)
	
	Type 2 inflammation is characterized by the presence of cytokines such as interleukin (IL)-4, IL-5, and IL-13, which are often produced by the adaptive immune system on recognition of allergens. It is also characterized by eosinophilia or increased fraction of exhaled nitric oxide (FeNO) and may be accompanied by atopy. In many patients with asthma, Type 2 inflammation rapidly improves when ICS are taken regularly and correctly; this is classified as mild or moderate asthma. In severe asthma, Type 2 inflammation may be relatively refractory to high dose ICS. Type 2 inflammation is considered refractory if any of the following are found while the patient is taking high dose ICS or daily OCS:(3)
	
	• Blood eosinophils greater than or equal to 150 cells/microliter
	• FeNO greater than or equal to 20 ppb
	• Sputum eosinophils greater than or equal to 2%
	• Asthma is clinically allergen-driven
	
	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 who have allergic or eosinophilic biomarkers or need maintenance OCS.(3) 2023 GINA recommends the biologics below based on patient eligibility factors:
	
	• Anti-IgE (omalizumab):
	  ○ Sensitization on skin prick testing or specific IgE
	  ○ Total serum IgE and weight within dosage range
	  ○ Exacerbations in the last year
	• Anti-IL5/Anti-IL5R (benralizumab, mepolizumab, reslizumab):
	  ○ Exacerbations in the last year
	  ○ Blood eosinophils greater than or equal to 150 cells/microliter (for benralizumab and mepolizumab) or greater than or equal to 300 cells/microliter (for reslizumab)
	• Anti-IL4R (dupilumab):
	  ○ Exacerbations in the last year
	  ○ Blood eosinophil greater than or equal to 150 cells/microliter but less than or equal to 1500 cells/microliter, or FeNO greater than or equal to 25 ppb, or taking maintenance OCS
	• Anti-TSLP (tezepelumab):
	  ○ Exacerbations in the last year
	
	Patient response should be evaluated 4 months after initiating therapy and follow up should occur every 3 to 6 months thereafter. 2023 GINA recommends the following step-down therapy process in patients responding well to targeted biologic therapy:(3)
	
	• Reevaluate the need for each asthma medication every 3 to 6 months, but inhaled therapy should not be completely stopped

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	• Oral treatments: gradually decreased starting with OCS due to significant adverse effects. • Inhaled treatments: consider reducing ICS dose after 3 to 6 months, but do not completely stop inhaled therapy. Continue at least medium dose ICS and remind patients of the importance of continued inhaled controller therapy • Biologic treatments: trial withdrawal after 12 months of treatment and only if patient's asthma remains well controlled on medium dose ICS, and for allergic asthma, there is no further exposure to a previous allergic trigger
Chronic Spontaneous Urticaria (CSU)	Chronic spontaneous urticaria (CSU) can be a debilitating condition that can significantly affect a patient's quality of life. Routine diagnostic work-up for CSU is limited to blood tests for complete blood count and inflammatory markers, such as C-reactive protein and/or erythrocyte sedimentation rate, mostly to rule out other potential diseases. Skin prick testing, typically used to identify specific allergens, is not useful for CSU as the condition is rarely caused by type 1 allergy. CSU is also referred to as chronic urticaria (CU) or chronic idopathic urticaria (CIU).(13) 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 2021 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 First-line treatment with second generation H-1 antihistamines is consistent in other guidelines but recommend omalizumab as second-line treatment and ciclosporin (off-label use) as third-line treatment.(13)

Chronic Rhinosinusitis with Nasal Polyposis	Chronic rhinosinusitis with nasal polyposis (CRSwNP) is an inflammatory condition affecting the paranasal sinuses. The International Consensus Statement on allergy and rhinology: Rhinosinusitis indicates that the diagnostic criteria for chronic rhinosinusitis (CRS) consist of ALL the following:(11)
	
	• Symptoms greater than or equal to 12 weeks
	• Two of the following symptoms:
	  ○ Nasal discharge (rhinorrhea or post-nasal drainage)
	  ○ Nasal obstruction or congestion
	  ○ Hyposmia (loss or decreased sense of smell)
	  ○ Facial pressure or pain
	• One or more of the following findings:
	  ○ Evidence of inflammation on nasal endoscopy or computed tomography
	  ○ Evidence of purulence coming from paranasal sinuses or ostiomeatal complex

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	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.(8,9,10) 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)
Efficacy	**Asthma(1)** The safety and efficacy of Xolair in adult and adolescent patients 12 years of age and older were evaluated in three randomized, double-blind, placebo-controlled, multicenter trials. In all three trials an exacerbation was defined as a worsening of asthma that required treatment with systemic corticosteroids or a doubling of the baseline inhaled corticosteroid dose. In two of these trials patients had a forced expiratory volume in 1 second (FEV1) between 40 and 80% predicted. All patients had a FEV1 improvement of at least 12% following beta-2-agonist administration. All patient were required to have a baseline IgE between 30 and 700 IU/mL and a body weight not more than 150 kg. Dosing information includes weights of at least 30 kg. In both of these trials the number of exacerbations per patient was reduced in patients treated with Xolair compared with placebo. In the third trial there was no restriction on screening FEV1. The number of exacerbations in patients treated with Xolair was similar to that in the placebo-treated patients. The absence of an observed treatment effect may be related to differences in the patient population compared with the other two trials. In all three trials, a reduction of asthma exacerbations was not observed in the Xolair treated patients who had an FEV1 > 80% at the time of randomization. Reductions in exacerbations were not seen in patients who required oral steroids as maintenance therapy. The safety and efficacy of Xolair in pediatric patients 6 to less than 12 years of age with moderate to severe asthma is based on one randomized, double-blind, placebo controlled, multicenter trial and an additional supportive study. The primary efficacy variable was the rate of asthma exacerbations during the 24-week, fixed steroid treatment phase. An asthma exacerbation was defined as a worsening of asthma symptoms as judged clinically by the investigator, requiring doubling of the baseline inhaled corticosteroid dose for at least 3 days and/or treatment with rescue systemic (oral or IV) corticosteroids for at least 3 days. At 24 weeks, the Xolair group had a statistically significantly lower rate of asthma exacerbations (0.45 vs 0.64) with an estimated rate ratio of 0.69 (95% CI). Dosing for pediatric patients between the ages of 6 to less than 12 years is based on weight and IgE level with dosing available for weights less than or equal to 150 kg and IgE levels between 30 and 1300 IU/mL. **Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)(1)** The safety and efficacy of Xolair was evaluated in two, randomized, multicenter, double-blind, placebo-controlled clinical trials that enrolled patients with CRSwNP with inadequate response to nasal corticosteroids. The co-primary endpoints in both trials were nasal polyp score (NPS) and average daily nasal congestion score (NCS) at Week 24. In both trials, patients who received Xolair has statistically significant greater improvement from baseline at Week 24 in NPS and weekly average NCS, than patients who received placebo. **Chronic Spontaneous Urticaria (CSU)(1)** The safety and efficacy of Xolair for the treatment of CSU, previously referred to as chronic idiopathic urticaria (CIU) was assessed in two placebo-controlled, multiple-

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	dose clinical trials of 24 and 12 weeks duration. Disease severity was measured by a weekly urticaria activity score (UAS7), which is a composite of the weekly itch severity score and the weekly hive count score. All patients were required to have a UAS7 of greater than or equal to 16 and a weekly itch severity score greater than or equal to 8 for the 7 days prior to randomization, despite having used an H1 antihistamine for at least 2 weeks. In both trials patients who received Xolair 150 mg and 300 mg had greater decreases from baseline in weekly itch severity score and weekly hive count scores than placebo at week 12.
Safety	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:(1) • 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.(1)

REFERENCES

Number	Reference
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2	International European Respiratory Society (ERS)/American Thoracic Society (ATS) Guidelines on Management of Severe Asthma. *Eur Resp J*. 2020;55:1900588. Available at https://erj.ersjournals.com/content/55/1/1900588.
3	Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2023. Available at www.ginasthma.org
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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.
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7	Reference no longer used
8	Stevens WW, Schleimer RP, and Kern RC. Chronic Rhinosinusitis with Nasal Polyps. *J Allergy Clin Immunol Pract.* 2016;4(4):565–572.
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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. Reaffirmed by American Academy of Family Physicians April 2020.
11	Orlandi, RR, Kingdom, TT, Smith, TL, et al. International consensus statement on rhinology and allergy: rhinosinusitis. *Int Forum Allergy Rhinol*. 2021; 11: 213– 739. https://doi.org/10.1002/alr.22741
12	National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. 2020 Focused updates to the asthma management guidelines. National Heart, Lung, and Blood Institute, 2007. Available at: https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines

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Number	Reference
13	Guideline for Diagnosis and Management of Chronic Spontaneous Urticaria. Physician's Weekly. April 2021.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J2357	Xolair	omalizumab for inj ; omalizumab subcutaneous soln auto-injector ; omalizumab subcutaneous soln prefilled syringe	150 MG ; 150 MG/ML ; 300 MG/2ML ; 75 MG/0.5ML	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Xolair	omalizumab for inj ; omalizumab subcutaneous soln auto-injector ; omalizumab subcutaneous soln prefilled syringe	150 MG ; 150 MG/ML ; 300 MG/2ML ; 75 MG/0.5ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All Target Agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following: 1. ONE of the following: A. The patient is 6 to less than 12 years of age AND BOTH of the following: 1. The pretreatment IgE level is 30 IU/mL to 1300 IU/mL **AND** 2. 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: 1. The pretreatment IgE level is 30 IU/mL to 700 IU/mL **AND** 2. The patient's weight is 30 kg to 150 kg **AND** 2. Allergic asthma has been confirmed by a positive skin test or in vitro reactivity test to a perennial aeroallergen **AND** 3. 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**

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Module	Clinical Criteria for Approval
	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 (prior to therapy with the requested agent) Forced Expiratory Volume (FEV1) that is less than 80% of predicted **AND** 4. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 375 mg every 2 weeks **OR** C. The patient has a diagnosis of chronic spontaneous urticaria (CSU) (otherwise known as chronic idiopathic urticaria [CIU]) AND ALL of the following: 1. The patient has had over 6 weeks of hives and itching **AND** 2. 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** 3. ONE of the following: A. The patient has tried and had an inadequate response to the FDA labeled maximum 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 titrated up to 4 times the FDA labeled maximum dose of a second-generation H-1 antihistamine **OR** 2. The prescriber has provided information indicating the patient cannot be treated with a dose titrated up to 4 times the FDA labeled maximum dose of a second-generation H-1 antihistamine **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** 4. The requested dose is within FDA labeled dosing for the requested indication AND does NOT exceed 300 mg every 4 weeks **OR** D. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND ALL of the following: 1. The patient has at least TWO of the following symptoms consistent with chronic rhinosinusitis (CRS): A. Nasal discharge (rhinorrhea or post-nasal drainage) B. Nasal obstruction or congestion C. Loss or decreased sense of smell (hyposmia) D. Facial pressure or pain **AND** 2. The patient has had symptoms consistent with chronic rhinosinusitis (CRS) for at least 12 consecutive weeks **AND** 3. 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** 4. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **OR** E. The patient has another FDA approved indication for the requested agent AND the requested dose is within FDA labeled dosing for the requested indication **OR**

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Module	Clinical Criteria for Approval
	F. The patient has another indication that is supported in compendia for the requested agent AND the requested dose is supported in compendia for the requested indication **AND** 2. If the patient has a diagnosis of moderate to severe persistent asthma, ALL of the following: A. ONE of the following: 1. 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** 2. 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** 3. The patient has an intolerance or hypersensitivity to inhaled corticosteroid therapy **OR** 4. The patient has an FDA labeled contraindication to ALL inhaled corticosteroids **AND** B. ONE of the following: 1. 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. Long-acting muscarinic antagonist (LAMA) **OR** C. A Leukotriene receptor antagonist (LTRA) **OR** D. Theophylline **OR** 2. The patient has an intolerance or hypersensitivity to therapy with long-acting beta-2 agonists (LABA), long-acting muscarinic antagonists (LAMA), leukotriene receptor antagonist (LTRA), or theophylline **OR** 3. The patient has an FDA labeled contraindication to ALL long-acting beta-2 agonists (LABA) AND long-acting muscarinic antagonists (LAMA) **AND** C. The patient will continue asthma control therapy (e.g., ICS, ICS/LABA, LTRA, LAMA, theophylline) in combination with the requested agent **AND** 3. If the patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP), BOTH of the following: A. ONE of the following: 1. The patient has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone) used for at least a 3-month trial **OR** 2. The patient has an intolerance or hypersensitivity to therapy with intranasal corticosteroids (e.g., fluticasone) **OR** 3. The patient has an FDA labeled contraindication to ALL intranasal corticosteroids **AND** B. BOTH of the following: 1. The patient is currently treated with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) **AND** 2. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **AND** 4. If the patient has an FDA approved indication, then 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 for the requested indication **AND** 5. 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** 6. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following:

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Module	Clinical Criteria for Approval
	1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 6 months for asthma, chronic idiopathic urticaria, and nasal polyps 12 months for all other indications **Renewal Evaluation** **Target Agent(s)** 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 Medical Drug Review process **AND** 2. ONE of the following: A. The patient has a diagnosis of moderate to severe persistent asthma AND ALL of the following: 1. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. Increase in percent predicted Forced Expiratory Volume (FEV_1) **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** 2. The patient is currently treated and is compliant with standard therapy [i.e., inhaled corticosteroids (ICS), ICS/long-acting beta-2 agonist (ICS/LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline] **AND** 3. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 375 mg every 2 weeks **OR** B. The patient has a diagnosis of chronic spontaneous urticaria (CSU) (otherwise known as chronic idiopathic urticaria [CIU]) AND BOTH of the following: 1. The patient has had clinical benefit with the requested agent **AND** 2. The requested dose is within FDA labeled dosing for the requested indication 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: 1. The patient has had clinical benefit with the requested agent **AND** 2. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **AND** 3. The requested dose is based on the patient's pretreatment serum IgE level and body weight as defined in FDA labeling AND does NOT exceed 600 mg every 2 weeks **OR** D. The patient has another FDA approved indication for the requested agent AND BOTH of the following:

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Module	Clinical Criteria for Approval
	1. The patient has had clinical benefit with the requested agent **AND** 2. The requested dose is within FDA labeled dosing for the requested indication **OR** E. The patient has another indication that is supported in compendia for the requested agent AND BOTH of the following: 1. The patient has had clinical benefit with the requested agent **AND** 2. The requested dose is supported in compendia 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. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 12 months

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab)

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Contraindicated as Concomitant Therapy
Cosentyx (secukinumab)
Cyltezo (adalimumab-adbm)
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Litfulo (ritlecitinib)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)

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Contraindicated as Concomitant Therapy
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)

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