PREMERA HMO

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PHARMACY / MEDICAL POLICY – 5.01.513

Xolair (omalizumab)

Effective Date:	**Oct. 3, 2025***
Last Revised:	Jun. 10, 2025
Replaces:	N/A

*View the current policy here.

RELATED MEDICAL POLICIES:

5.01.559 IL-5 Inhibitors

5.01.575 Dupixent (dupilumab)

5.01.627 Thymic Stromal Lymphopoietin (TSLP) Inhibitors

The Site of Service Medical Necessity criteria within this policy DOES NOT apply to Alaska fully-insured members; refer to the infusion and injection drug Medical Necessity criteria only.

Site of Service *and* the infusion and injection drug Medical Necessity criteria apply to all other plan members.

Please contact Customer Service for more information.

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Asthma is a long-term lung condition affecting the airways of the lung. Asthma causes the airways to become inflamed. Inhaling certain substances such as tobacco smoke, pet dander, and dust mites can set off a chain reaction. The immune system produces substances — antibodies — to attack the foreign substance that's creating the asthma attack. Xolair is a drug that helps prevent the body from reacting to the substance that would normally cause an asthma attack. It's typically prescribed to treat severe asthma when symptoms aren't controlled by inhaled corticosteroids. Xolair is also used to treat hives without a known cause that don't respond to usual treatments. Hives are itchy red areas on the skin. They can be small as a pencil point to the size of a hand, or even larger. They are often caused by an allergic reaction. Xolair can also be used to treat nasal polyps that do not respond to nasal steroids. Nasal polyps are more common in people with allergies and can cause a runny, stuffy, or blocked nose. This

policy describes when Xolair may be considered medically necessary to treat conditions such as asthma, hives, and nasal polyps.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Site of Service (SOS) Medical Necessity criteria applies ONLY to medical benefit reviews. SOS Medical Necessity criteria does NOT apply to Alaska fully-insured members; refer to the infusion and injection drug Medical Necessity criteria only. Please contact Customer Service for more information.

We will review specific intravenous (IV) and injectable drugs for medical necessity for all ages.

For those age 13 and older, we also will review the site of service for medical necessity. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home.

Drugs subject to site of service review addressed in this policy are:

- Xolair (omalizumab)

Site of Service Administration	Medical Necessity
Medically necessary sites of service • **Physician's office** • **Infusion center** • **Home infusion**	**IV infusion and injection therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost effective site:** • These are the preferred **medically necessary** sites of service for specified drugs.

Site of Service Administration	Medical Necessity
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**IV infusion and injection therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site.** **This site is considered medically necessary for the first 90 days for the following:** • The initial course of infusion or injection of a pharmacologic or biologic agent **OR** • Re-initiation of an agent after 6 months or longer following discontinuation of therapy* **Note:** *This does not include when standard dosing between infusions or injections is 6 months or longer **This site is considered medically necessary when there is no outpatient infusion center within 50 miles of the individual's home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions or injections of this drug.** **This site is considered medically necessary only when the individual has a clinical condition which puts him or her at increased risk of complications for infusions or injections, including any 1 of the following:** • Known cardiac condition (e.g., symptomatic cardiac arrhythmia) or pulmonary condition (e.g., significant respiratory disease, serious obstructive airway disease, %FVC less than or equal to 40%) that may increase the risk of an adverse reaction • Unstable renal function which decreases the ability to respond to fluids • Difficult or unstable vascular access • Acute mental status changes or cognitive conditions that impact the safety of infusion or injection therapy

Site of Service Administration	Medical Necessity

	• A known history of severe adverse drug reactions and/or anaphylaxis to prior treatment with a related or similar drug
	
	This site is considered medically necessary when the individual has cytokine release syndrome (CRS) and all the following are met:
	• CRS is grade 3 or 4 as evidenced by ALL the following:
	  ○ Temperature at least 38 °C
	  ○ Hypotension that requires 1 or more vasopressors
	  ○ Hypoxia that requires oxygen through a high-flow nasal cannula, face mask, non-rebreather mask, or Venturi mask OR positive pressure (continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, or mechanical ventilation)
	AND
	• The individual will be admitted into an inpatient setting as soon as possible

Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**These sites are considered not medically necessary for infusion and injectable therapy services of various medical and biologic agents when the site-of-service criteria in this policy are not met.**

Xolair (omalizumab) may be considered medically necessary for the following The US Food and Drug Administration (FDA)-approved indications:

Indication	Medical Necessity
Moderate to severe persistent asthma	**Xolair (omalizumab) SC is subject to review for** site of service **administration.** **Xolair (omalizumab) may be considered medically necessary for the treatment of moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a**

Indication	Medical Necessity

	perennial aeroallergen, and who also meet the following criteria:
	• The individual is aged 6 years or older
	AND
	• Is using maximum tolerated doses of an inhaled corticosteroid
	AND
	• Is using an inhaled long-acting beta-agonist (LABA)
	AND
	• Meets 1 of the following:
	  ○ 2 or more asthma exacerbations in the previous 12 months requiring use of oral corticosteroids
	  OR
	  ○ 1 or more asthma exacerbations requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous 12 months
	  OR
	  ○ Forced expiratory volume in 1 second (FEV_1) is less than 80% predicted
	  OR
	  ○ FEV_1/forced vital capacity (FVC) less than 0.80
	  OR
	  ○ Has asthma that worsens upon tapering of oral corticosteroid therapy
	AND
	• Has a total serum IgE 30 IU/mL to 1,300 IU/mL for ages 6 to 12 years **OR** 30 IU/mL to 700 IU/mL for aged 12 years and older
	AND
	• Has a positive skin test or RAST (when skin test is not appropriate) to a perennial aeroallergen (i.e., dust mite, cockroach, dog, cat, or molds)
	AND
	• Weighs between 20 kg (44 lbs.) and 150 kg (330 lbs.)
	AND
	• The dose prescribed is limited to 750 mg every four weeks, based on serum IgE and body weight according to the most recent manufacturer's dosing table
	AND

Indication	Medical Necessity
	• Xolair (omalizumab) will not be used in combination with Dupixent (dupilumab), Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), or Tezspire (tezepelumab) when the medications are being used for the treatment of asthma **AND** • Xolair (omalizumab) is prescribed by or in consultation with an allergist/immunologist or pulmonologist

Severe chronic idiopathic urticaria	**Xolair (omalizumab) SC is subject to review for site of service administration.**
	
	Xolair (omalizumab) may be considered medically necessary for the treatment of moderate to severe chronic idiopathic urticaria who remain symptomatic despite treatment with first line agents, when the following criteria are met:
	• The individual is aged 12 years or older
	AND
	• There is no evidence of another cause of the urticarial reaction
	AND
	• Has experienced at least 6-weeks of symptoms including chronic urticaria, itching, hives or angioedema
	AND
	• Has failed to respond to 1 of the following therapeutic regimens (unless contraindicated):
	  ○ 2 or more H1 antihistamines in high doses (2-3 times normal dosing)
	  ○ 1 H1 inhibitor used in combination with any 1 or more of the following: an H2 antihistamine, oral corticosteroids, or leukotriene modifiers
	AND
	• The individual plans to continuing treatment with a low dose of H1 antihistamines
	AND
	• The dose prescribed is 150 mg or 300 mg every four weeks
	AND
	• Xolair (omalizumab) is prescribed by or in consultation with an allergist/immunologist or dermatologist

Indication	Medical Necessity
Chronic rhinosinusitis with nasal polyps (CRSwNP)	**Xolair (omalizumab) SC is subject to review for site of service administration.** **Xolair (omalizumab) may be considered medically necessary as an add-on maintenance treatment in adult individuals with inadequately controlled chronic rhinosinusitis with nasal polyps when:** • The individual is aged 18 years or older **AND** • Has a pretreatment IgE of at least 30 IU/mL **AND** • Weighs between 30 kg (66 lbs.) and 150 kg (330 lbs.) **AND** • Diagnosis of bilateral nasal polyps is confirmed by physical examination or nasal endoscopy **AND** • Has an adequate trial and failure of 1 intranasal corticosteroid as monotherapy **AND** • Xolair (omalizumab) is prescribed in combination with an intranasal corticosteroid **AND** • The dose is limited to 600 mg every 2 weeks based on the individual's serum IgE and body weight and the most recent Xolair (omalizumab) prescribing information dosing table **AND** • Xolair (omalizumab) will not be used in combination with Dupixent (dupilumab) or Nucala (mepolizumab) when the medications are being used for the treatment of CRSwNP **AND** • Medication is prescribed by or in consultation with an allergist/immunologist or otolaryngologist
Immunoglobulin (Ig)E-mediated food allergy	**Xolair (omalizumab) SC is subject to review for site of service administration.**

Indication	Medical Necessity

	Xolair (omalizumab) may be considered medically necessary to reduce Type I allergic reactions in individuals with an IgE-mediated food allergy when all the following criteria are met:
	• The individual is aged 1 year or older
	AND
	• Is diagnosed with an IgE-mediated food allergy as demonstrated by ALL the following:
	  ○ Has experienced signs and symptoms of a significant systemic allergic reaction within a short period of time following a known ingestion of one or more foods
	  AND
	  ○ A positive skin prick test response to 1 or more foods OR a positive serum IgE test to 1 or more foods
	AND
	• Xolair (omalizumab) will be used in conjunction with a diet that avoids food allergens
	AND
	• Xolair (omalizumab) will not be used concomitantly with Palforzia [peanut (*Arachis hypogaea*) allergen powder-dnfp]
	AND
	• The individual has been prescribed an epinephrine auto-injector
	AND
	• The dose prescribed is limited to to 600 mg every 2 weeks based on the individual's serum IgE and body weight and the most recent Xolair (omalizumab) prescribing information dosing table
	AND
	• Xolair (omalizumab) is prescribed by or in consultation with an allergist/immunologist

Indication	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Indication	Investigational
	Xolair (omalizumab) is considered investigational for all other uses including, but not limited to the following: • Allergic rhinitis • Atopic dermatitis • Other IgE-mediated allergic conditions not listed in this document • Latex allergy • Bullous pemphigoid • Eosinophilic gastrointestinal disorders

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for all drugs listed in the policy may be approved up to 12 months.** **All other reviews may be approved up to 6 months.**
Re-authorization criteria	**Non-formulary exception reviews and all other reviews for moderate to severe persistent asthma may be approved up to 12 months as long as the medical necessity criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy as documented by any of the following parameters:** • Decrease in requirement for oral steroids, exacerbation frequency, ER and urgent care visits, hospitalizations **OR** • Decrease in frequency and severity of asthma symptoms **OR** • Increase in quality of life measures and ability to perform activities of daily living **Non-formulary exception reviews and all other reviews for severe chronic idiopathic urticaria may be approved up to 12 months as long as the medical necessity criteria are met and chart notes demonstrate that the individual continues to show**

Length of Approval	
Approval	**Criteria**
	a positive clinical response to therapy as documented by any of the following parameters: • Decrease in the itch severity **OR** • Decrease in hives **Non-formulary exception reviews and all other reviews for chronic rhinosinusitis with nasal polyps (CRSwNP) may be approved up to 12 months as long as the medical necessity criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy as documented by both of the following parameters:** • Documented decrease from baseline of nasal polyp size **AND** • Improvement in NCS or documented decrease from baseline of nasal congestion **Note:** *NCS scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe **Non-formulary exception reviews and all other reviews for immunoglobulin (Ig)E-mediated food allergy may be approved up to 12 months as long as the medical necessity criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy as documented by a decrease in significant systemic allergic reactions from baseline**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
J2357	Injection, omalizumab (Xolair), 5 mg

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Consideration of Age

The ages stated in this policy for which Xolair (omalizumab) is considered medically necessary is based on the FDA labeling for this drug.

For site of service for medical necessity the age described in this policy is 13 years of age or older. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. The age criterion for site of service for medical necessity is based on the following: Pediatric individuals are not small adults. Pediatric individuals differ physiologically, developmentally, cognitively, and emotionally from adult individuals, and vary by age groups from infancy to teen. Children often require smaller doses than adults, lower infusion rates, appropriately sized equipment, the right venipuncture site determined by therapy and age, and behavioral management during administration of care. Specialty infusion training is therefore necessary for pediatric IV insertions and therapy. Due to pediatrics unique physiology and psychology, site of service review is limited to individuals above the age of 13.

Benefit Application

Xolair is an injectable drug that must be administered in a health care provider's office for at least 3 doses. Once therapy has been safely established, the health care provider can determine whether self-administration of Xolair is appropriate based on assessment of risk for anaphylaxis

and mitigation strategies. Xolair is managed through the pharmacy benefit and the medical benefit.

High Dose Regimens of Inhaled Corticosteroids

High Dose Regimens of Inhaled Corticosteroids			
Drug Name	**Low Dose**	**Medium Dose**	**High Dose**
Beclomethasone HFA (Qvar) 40 mcg per puff 80 mcg per puff	80 to 160 mcg 2 to 4 puffs 1 to 2 puffs	>160 to 320 mcg 3 to 4 puffs	>320 mcg >4 puffs
Budesonide DPI (Pulmicort Flexhaler) 90 mcg per inhalation 180 mcg per inhalation	180 to 360 mcg 2 to 4 inhalations 1 to 2 inhalations	>360 to 720 mcg 3 to 4 inhalations	>720 mcg >4 inhalations
Ciclesonide HFA (Alvesco) 80 mcg per puff 160 mcg per puff	80 to 160 mcg 1 to 2 puffs 1 puff	>160 to 320 mcg 3 to 4 puffs 2 puffs	>320 mcg >2 puffs
Fluticasone propionate HFA (Flovent HFA) 44 mcg per puff 110 mcg per puff 220 mcg per puff	88 to 220 mcg 2 to 5 puffs 1 to 2 puffs	>220 to 440 mcg 3 to 4 puffs 2 puffs	>440 mcg >2 puffs
Fluticasone propionate DPI (Flovent Diskus) 50 mcg per inhalation 100 mcg per inhalation 250 mcg per inhalation 500 mcg per inhalation (strength not available in the U.S.)	100 to 250 mcg 2 to 5 inhalations 1 to 2 inhalations 1 inhalation	>250 to 500 mcg 3 to 5 inhalations 2 inhalations 1 inhalation	>500 mcg 2 inhalations >1 inhalation
Fluticasone furoate DPI	50 mcg	100 mcg	200 mcg

High Dose Regimens of Inhaled Corticosteroids			
Drug Name	**Low Dose**	**Medium Dose**	**High Dose**
(Arnuity Ellipta)* 50 mcg per inhalation 100 mcg per inhalation 200 mcg per actuation	 1 inhalation	 1 inhalation	 2 inhalations 1 inhalation
Mometasone DPI (Asmanex DPI) 110 mcg per inhalation 220 mcg per inhalation	110 to 220 mcg 1 to 2 inhalations 1 inhalation	>220 to 440 mcg 2 inhalations	>440 mcg >2 inhalations
Mometasone HFA (Asmanex HFA) 100 mcg per actuation 200 mcg per actuation	100 to 200 mcg 1 to 2 inhalations 1 inhalation	>200 to 400 mcg 2 inhalations	>400 mcg >2 inhalations

***Note:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.

Evidence Review

Description

Xolair (omalizumab) is a recombinant, humanized construct of murine antibody MaE11 directed against human Immunoglobulin E (IgE). The critical amino acids responsible for the binding of the murine monoclonals to IgE were engrafted onto a human Immunoglobulin GR1R (IgGR1R) subclass framework to yield a humanized antibody with the properties of the selected murine monoclonal. The antibody has a molecular weight of approximately 149 kilo-daltons and is produced by a Chinese hamster ovary cell suspension culture in a nutrient medium containing the antibiotic gentamicin.

Omalizumab inhibits the binding of IgE to the high-affinity IgE receptor (FcRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with omalizumab also reduces the number of FcRI receptors on basophils in atopic individuals.

Maintenance Therapy of Asthma

Asthma is a chronic airway disorder that affects an estimated 17 million Americans. About 10 million of these have allergic asthma, mediated by a cascade in which IgE is bound to high-affinity FcRI receptors on the surface of basophils and mast cells, and is cross-linked by an allergen that results in the degranulation of these effector cells and the release of inflammatory mediators, such as histamine and leukotrienes. These mediators then produce the symptoms of asthma, as well as other related conditions such as allergic rhinitis, atopic dermatitis and anaphylaxis. The severity of the response varies from trivially annoying to immediately life-threatening. As their common mechanism would predict, these diseases share overlapping populations.

Treatment with anti-inflammatory drugs such as inhaled corticosteroids can reverse some of these processes; however, successful response often requires weeks to achieve and sometimes a complete reversal is not achieved, even with optimal combinations of steroids, long-acting beta agonists and other agents. A smaller percentage of individuals may have persistent airflow limitations for which no current therapy has been found to be effective (steroid-resistant asthma). The paradigm of asthma has been expanded from bronchospasm and airway inflammation to include airway remodeling in some individuals. The concept that asthma may be a continuum of these processes that can lead to moderate and severe persistent disease is of critical importance to understanding this disease's pathogenesis and pathophysiology.

Since the asthma individual population is heterogeneous, successful maintenance treatment requires an individualized regimen. Current guidelines suggest that individuals with chronic persistent asthma be started on an inhaled corticosteroid. For individuals with moderate to severe symptoms, a long-acting inhaled beta agonist (salmeterol or formoterol) is generally initiated at the same time as the corticosteroid. Individuals with mild symptoms should receive a beta agonist if they fail to achieve full response with a corticosteroid. Other agents such as leukotriene modifiers and theophylline may be added. Xolair (omalizumab) offers an additional therapeutic option for individuals who have not achieved control with these strategies.

Rationale

In two well-designed pivotal trials over 1000 individuals aged 12 and above with moderate to severe chronic steroid-resistant asthma, Xolair (omalizumab) reduced the overall frequency of asthma exacerbations by 40-50%. Hospitalizations and emergency visits for asthma exacerbation

were also reduced. Reduction in protocol defined exacerbations was observed in approximately 15% of the subjects (NNT = 6); the majority of individuals therefore did not benefit according to the primary endpoint; however reduction in asthma symptom scores and improvement in quality of life scores were observed in the overall population.

After subcutaneous (SC) administration, omalizumab has an average absolute bioavailability of 62%. Following a single SC dose in adult and adolescent individuals with asthma, omalizumab reached peak serum concentrations after an average of 7-8 days. Following multiple doses, areas under the serum concentration-time curve from Day 0 to Day 14 at steady state were up to 6-fold of those after the first dose. In vitro, omalizumab forms complexes with IgE. Precipitating complexes are not observed. Clearance involves IgG clearance processes as well as hepatic clearance of the omalizumab:IgE complexes. Intact IgG is also excreted in bile. In asthma individuals elimination half-life averaged 26 days, with apparent clearance averaging 2.4 ± 1.1 mL/kg/day. Doubling body weight approximately doubled apparent clearance.

Free IgE decrease was greater than 96% using recommended doses. Serum total IgE levels increased due to the formation of omalizumab:IgE complexes, which have a slower elimination rate. The increase in total IgE and decrease in free IgE were reversible, with no observed rebound in IgE levels after drug washout. Total IgE levels did not return to pre-treatment levels for up to one year after discontinuation.

Subsequently published studies continue to affirm the hypothesis that omalizumab is an appropriate last-line agent in individuals who are inadequately controlled, despite best standard therapy with inhaled corticosteroids in combination with other controllers. The bulk of the evidence suggests that many of these individuals will achieve significant benefit when omalizumab is added to their existing treatment.

A published cost-effectiveness analysis concluded that:

> …from a pharmacoeconomic standpoint, omalizumab would be better used in allergic asthmatic individuals with poorly controlled symptoms despite maximal therapy, given the high cost and modest efficacy of this agent. It could be cost saving if given to nonsmoking individuals who are hospitalized 5 or more times or 20 days or longer per year despite maximal asthma therapy.

Chronic Idiopathic Urticaria

The safety and efficacy of Xolair (omalizumab) for the treatment of chronic idiopathic urticaria (CIU) was assessed in two placebo-controlled, multiple-dose clinical trials of 24 weeks' duration

(CIU Trial 1; n= 319) and 12 weeks' duration (CIU Trial 2; n=322). Individuals received Xolair 75 mg, 150 mg, or 300 mg or placebo by SC injection every 4 weeks in addition to their baseline level of H1 antihistamine therapy for 24 or 12 weeks, followed by a 16-week washout observation period. A total of 640 individuals (165 males, 475 females) were included for the efficacy analyses. Most individuals were white (84%) and the median age was 42 years (range 12–72).

Disease severity was measured by a weekly urticaria activity score (UAS7, range 0–42), which is a composite of the weekly itch severity score (range 0–21) and the weekly hive count score (range 0–21). All individuals were required to have a UAS7 of ≥16, and a weekly itch severity score of ≥8 for the 7 days prior to randomization, despite having used an H1 antihistamine for at least 2 weeks.

The mean weekly itch severity scores at baseline were fairly balanced across treatment groups and ranged between 13.7 and 14.5 despite use of an H1 antihistamine at an approved dose. The reported median durations of CIU at enrollment across treatment groups were between 2.5 and 3.9 years (with an overall subject-level range of 0.5 to 66.4 years).

In both CIU Trials 1 and 2, individuals who received Xolair 150 mg or 300 mg had greater decreases from baseline in weekly itch severity scores and weekly hive count scores than placebo at Week 12. The 75-mg dose did not demonstrate consistent evidence of efficacy and is not approved for use.

In CIU Trial 1, a larger proportion of individuals treated with Xolair 300 mg (36%) reported no itch and no hives (UAS7=0) at Week 12 compared to individuals treated with Xolair 150 mg (15%), Xolair 75 mg (12%), and placebo group (9%). Similar results were observed in CIU Trial 2.

The most common adverse reactions reported in the CIU clinical trials (≥2% Xolair-treated individuals and more frequent than in placebo) included the following: nausea, nasopharyngitis, sinusitis, upper respiratory tract infection, viral upper respiratory tract infection, arthralgia, headache, and cough.

Nasal Polyps

The safety and efficacy of Xolair was evaluated in two, randomized, multicenter, double-blind, placebo-controlled clinical trials that enrolled individuals with CRSwNP with inadequate response to nasal corticosteroids (CRSwNPTrial 1, n=138; CRSwNP Trial 2, n=127). Individuals received Xolair or placebo SC every 2 or 4 weeks, with Xolair for 24 weeks followed by a 4-week

follow-up period. All individuals received background nasal mometasone therapy during both the treatment period and during a 5-week run-in period. Prior to randomization, individuals were required to have evidence of bilateral polyps as determined by a nasal polyp score (NPS) ≥ 5 with NPS ≥ 2 in each nostril, despite use of nasal mometasone during the run-in period. NPS was measured via endoscopy and scored (range 0-4 per nostril: 0= no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity) for a total NPS (range 0-8). Individuals were furthermore required to have a weekly average of nasal congestion score (NCS) > 1 prior to randomization, despite use of nasal mometasone. Nasal congestion was measured by a daily assessment on a 0-to-3-point severity scale (0=none, 1=mild, 2=moderate, 3=severe). Prior sino-nasal surgery or prior systemic corticosteroid usage were not required for inclusion in the trials and sinus CT scans were not performed to evaluate for sinus opacification.

The co-primary endpoints in Trials 1 and 2 were NPS and average daily NCS at Week 24. In both trials, individuals who received Xolair had a statistically significant greater improvement from baseline at Week 24 in NPS and weekly average NCS, than individuals who received placebo. The greater improvements in NPS and NCS in the Xolair group compared to the placebo group were observed as early as the first assessment at Week 4 in both studies.

Xolair had statistically significant improvements in sense of smell score compared to placebo. Sense of smell was measured by a daily assessment on a 0-to-3-point severity scale (0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms). The LS mean difference for change from baseline at Week 24 in sense of smell score in Xolair compared to placebo was -0.3 (95% CI: -0.6, -0.1) in Trial 1 and -0.5 (95% CI: -0.7, -0.2) in Trial 2. Xolair had statistically significant improvements on post-nasal drip compared to placebo. The LS mean difference for change from baseline at Week 24 in post-nasal drip score in Xolair compared to placebo was -0.6 (95% CI: -0.8, -0.3) in Trial 1 and -0.5 (95% CI: -0.8, -0.3) in Trial 2. Xolair had statistically significant improvements in runny nose compared to placebo. The LS mean difference for change from baseline at Week 24 in runny nose score in Xolair compared to placebo was -0.4 (95% CI: -0.7, -0.2) in Trial 1 and -0.6 (95% CI: -0.9, -0.4) in Trial 2.

In a pre-specified pooled analysis of systemic corticosteroid use during the 24-week treatment period, there was no significant reduction in systemic corticosteroid use between the treatment arms. The proportion of individuals taking systemic corticosteroid in Xolair was 2.3% compared to 6.2% in placebo. The odds-ratio of systemic corticosteroid use with Xolair compared to placebo was 0.4 (95% CI: 0.1, 1.5). There were no sino-nasal surgeries reported, in either placebo or Xolair arms, in either Trial.

IgE-Mediated Food Allergies

The safety and efficacy of Xolair (omalizumab) in reducing allergic reactions in individuals with food allergies was evaluated in a multicenter, double-blind, placebo-controlled, National Institute of Allergy and Infectious Diseases (NIAID)-sponsored trial (OUtMATCH; NCT03881696) of 168 individuals between 1 year and 55 years of age who were allergic to peanut and at least two other foods, including milk, egg, wheat, cashew, hazelnut, or walnut. The efficacy of Xolair is based on 165 pediatric individuals who were included in the efficacy analyses of the OUtMATCH trial. For approved use in adults, the effectiveness of Xolair is supported by the adequate and well-controlled trial of Xolair in pediatric individuals, disease similarity in pediatric and adult individuals, and pharmacokinetic (PK) similarity. After 16 to 20 weeks of treatment with either Xolair or placebo, each individual completed a double-blind, placebo-controlled food challenge (DBPCFC) consisting of placebo and each of their three studied foods. Following the DBPCFC, the first 60 individuals (which included 59 pediatric individuals and one adult) who completed the double-blind, placebo-controlled phase of the study could continue to receive Xolair in a 24–28 week open-label extension (OLE). While efficacy cannot be established from uncontrolled, open-label studies, for the 38 pediatric individuals who continued Xolair for 24–28 weeks in the OLE, the percentage of individuals who were able to consume ≥600 mg of peanut protein and ≥1000 mg of egg, milk, and/or cashew protein without moderate to severe dose-limiting symptoms was maintained similarly to the double-blind portion of the trial. The most common side effects of Xolair observed included injection site reactions and fever. Xolair comes with certain warnings and precautions, such as anaphylaxis, malignancy, fever, joint pain, rash, parasitic (worm) infection, and abnormal laboratory tests.

2007 Update

A September 2007 literature review update did not identify any published reports that would change the conclusions of our assessment of the policy statement above.

The Expert Panel Report 3 (EPT-3) from the National Heart Lung and Blood Institute contains updated definitions of asthma.[27]

2008 Update

The American Academy of Allergy Asthma & Immunology supports the FDA labeling of Xolair and states: "Xolair is indicated for the moderate to severe persistent asthmatic individual who is 12 and older, has a positive skin test or in-vitro reaction to a perennial aeroallergen, and does not have control of their symptoms with inhaled corticosteroids. Clinical studies have shown that serum-free IgE levels were reduced by 96% within one hour after using the proper dosing requirements (total serum IgE level and body weight.)

A PubMed literature search through September 2008 did not reveal any published studies which would prompt a reconsideration of the policy statement. The policy was recommended for approval without changes by the P & T Committee (September 2008).

2009 Update

A PubMed literature search through October 2009 did not reveal any published studies which would prompt a reconsideration of the policy statement. The policy was recommended for approval without changes by the P & T Committee in November 2009.

2011 Update

A literature search from Jan 2008 to Jan 2011 did not identify any studies that would prompt reconsideration of the policy statement. A 2011 published review of MEDLINE search spanning from September 2008 to August 2010 revealed investigations and case reports of Xolair (omalizumab) as an add-on agent to standard therapy. The policy statements remain unchanged. The policy was recommended for approval without changes by the P & T Committee in November 2010.

2012 Update

A literature search from Jan 2011 to Dec 2011 did not identify any studies that would prompt reconsideration of the policy statement. Hanania, et al., reported results of an 850 individual RCT evaluating the impact of Xolair (omalizumab) as add on therapy in individuals with severe asthma treated with high dose inhaled corticosteroid (ICS) plus long-acting beta agonist (LABA), with or without other controllers. Individuals were followed for 48 weeks. Asthma exacerbations

were significantly reduced in the omalizumab arm (RRR=0.75, p=0.006). Individuals on omalizumab also reported improved quality of life (AQLQ) scores, reduced albuterol use and decreased mean asthma symptom score. In Feb 2011, a disturbing report from the ongoing EXCELS prospective cohort study, suggested that they might be seeing an imbalance of arterial thrombotic events; however, the finding was not statistically significant at the time of report. As of this update, no further information on this report is available.

2013 Update

A Phase III, multicenter, double-blind RCT evaluated the efficacy and safety of Xolair (omalizumab) in individuals with moderate-to-severe chronic idiopathic urticaria refractory to H1-antihistamine therapy. 323 individuals were randomized to receive 3 subcutaneous injections at 4 week intervals of omalizumab 75 mg, 150 mg, or 300 mg or placebo, followed by a 16-week observation period. The primary endpoint was change weekly itch-severity score (ISS, ranging from 0 to 21, with higher scores indicating more severe itching). Baseline weekly ISS was ~14 in all groups. At week 12, the mean (±SD) change from baseline in weekly ISS was −5.1±5.6 in the placebo group, −5.9±6.5 in the 75-mg group (P = 0.46), −8.1±6.4 in the 150-mg group (P = 0.001), and −9.8±6.0 in the 300-mg group (P<0.001). Adverse events were similar across groups. Serious AE were infrequent but higher in the 300-mg group (6%). A literature search from Jan 2012 to Dec 2012 did not identify other studies that would prompt reconsideration of the policy statement.

2014 (April) Update

A literature search conducted from 1/1/2013 through 2/28/2014 found no new evidence that would change this policy. An updated Cochrane meta-analysis published in January 2014 confirmed a reduction in both the frequency of asthma exacerbations and hospitalizations in individuals treated with Xolair (omalizumab) versus placebo. Individuals dependent on systemic corticosteroids were able to reduce or eliminate the requirement for systemic steroids. The authors identified a need for double-dummy trials and more studies in pediatric individuals. Given the drug's high cost it would be valuable to identify biomarkers predictive of response.

2014 (May) Update

In November 2013 two additional Phase II clinical trials were presented at the European Academy of Dermatology and Venerology combined with the study reported above[40]. The three studies included close to 1,000 individuals between the ages of 12 and 75 years, who were severely affected by chronic idiopathic/spontaneous urticaria despite treatment with high doses of H1- antihistamines. The results were consistent across the studies with 80-90% response rate of symptomatic improvement (decreased itching, wheals, and increased days without angioedema). The response was does dependent, with most response to the highest dose tested (400 mg q 4 weeks). Individuals were able to decrease the daily dose of H1 antihistamines.

On March 21, 2014, the FDA approved Xolair (omaluzimab) for use in the treatment of chronic idiopathic urticarial for people aged 12 and older who have failed first line treatment with H1 antihistamine therapy.

2015 Update

A literature search conducted from 1/1/2013 through 2/28/2014 found no new evidence that would change this policy.

2017 Update

A literature search conducted from 1/1/2014 through 10/31/2017 found no new evidence that would change this policy.

2018 Update

A literature search conducted from 1/1/2015 through 09/10/2018 found no new evidence that would change this policy.

2019 Update

Reviewed the Xolair prescribing information and conducted a literature search from 9/1/2018 through 10/31/2019 and no new evidence was identified that would change this policy.

2020 Update

Reviewed the Xolair prescribing information and articles from UpToDate on "Anti-IgE therapy" and "Chronic spontaneous urticaria: Treatment of refractory symptoms". Updated from "severe persistent asthma" to "moderate to severe persistent asthma" as FDA approved indication. Added to coverage criteria for moderate to severe persistent asthma that this results in "commonly requiring urgent care visits, ER visits and/or hospitalizations". Added clinical trial information for chronic idiopathic urticaria to evidence review section of policy. Updated drug names documented in the appendix table.

2021 Update

Reviewed the Xolair prescribing information and articles from UpToDate on "Anti-IgE therapy" and "Chronic spontaneous urticaria: Treatment of refractory symptoms" and "Treatment of severe asthma in adolescents and adults. Updated weight requirements based on available dosing data from FDA label and added smoking restriction for treatment of asthma, as it was an exclusion criteria in the clinical trials. Updated verbiage in chronic idiopathic urticaria for clarity.

2022 Update

Reviewed the Xolair prescribing information and added the clinical trial information to the evidence review for the treatment of nasal polyps. No new information was identified that would require changes to this policy.

2023 Update

Reviewed the Xolair prescribing information and conducted a literature review. Updated definition of moderate to severe persistent asthma to include individuals with one or more asthma exacerbations in the previous 12 months requiring use of oral corticosteroids. Updated the indication "nasal polyps" with "chronic rhinosinusitis with nasal polyps" to match the FDA Label. Updated initial approval length for Xolair for CIU to 6 months.

2024 Update

Reviewed the Xolair prescribing information and conducted a literature review. Updated criteria that Xolair (omalizumab) is not to be used in combination with Tezspire (tezepelumab) for the treatment of asthma. Updated criteria that Xolair (omalizumab) is not to be used in combination with Dupixent (dupilumab) for the treatment of nasal polyps. Updated criteria to include treatment of certain individuals with IgE-mediated food allergies. The following updates are effective January 3, 2025. Updated asthma criteria to remove the requirement for adults to not be a current smoker or is currently enrolled in a smoking cessation program. Updated asthma diagnostic criteria to the following: Individual has two or more asthma exacerbations in the previous 12 months requiring use of oral corticosteroids, one or more asthma exacerbations requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous 12 months, forced expiratory volume in 1 second (FEV_1) <80% predicted, or has a dependence on oral corticosteroids of at least 5 mg per day of prednisone or equivalent.

2025 Update

Reviewed the Xolair prescribing information and conducted a literature review. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Updated the asthma coverage criteria from using maximum doses of an inhaled corticosteroid to using maximum tolerated doses of an inhaled corticosteroid. Added site of service review. Clarified that the Site of Service Medical Necessity criteria can apply to injection drugs. Updated asthma coverage criteria by adding an FEV1/FVC less than 0.80 as an option to the requirement to meet one of the following. Updated asthma coverage criteria by changing the meets one of the following option from has a dependence on oral corticosteroids of at least 5 mg per day of prednisone or equivalent to has asthma that worsens upon tapering of oral corticosteroid therapy.

References

1. Presta LG, Lahr SJ, Shields RL, et al. Humanization of an antibody directed against IgE. J Immunol 1993 Sep 1; 151(5):2623-32.
2. Nayak AS. A common pathway: asthma and allergic rhinitis. Allergy Asthma Proc 2002 Nov-Dec; 23(6):359-65.
3. National Asthma Education and Prevention Program. Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 2. Bethesda, MD: National Institutes of Health; 1997. NIH publication 97-4051.

4. National Asthma Education and Prevention Program. Guidelines for the Diagnosis and Management of Asthma—Update on Selected Topics 2002. Bethesda, MD: National Institutes of Health; 2002. NIH publication 02-5075.
5. Finn A, Gross G, van Bavel J et al. Omalizumab improves asthma-related quality of life in patients with severe allergic asthma. J Allergy Clin Immunol 2003 Feb; 111(2):278-84.
6. Corren J, Casale T, Deniz Y, Ashby M. Omalizumab, a recombinant humanized anti-IgE antibody, reduces asthma-related emergency room visits and hospitalizations in patients with allergic asthma. J Allergy Clin Immunol 2003 Jan; 111(1):87-90.
7. Buhl R, Hanf G, Solèr M, et al. The anti-IgE antibody omalizumab improves asthma-related quality of life in patients with allergic asthma. Eur Respir J 2002 Nov; 20(5):1088-94.
8. Buhl R, Solèr M, Matz J et al. Omalizumab provides long-term control in patients with moderate-to-severe allergic asthma. Eur Respir J 2002 Jul; 20(1):73-8.
9. Solèr M, Matz J, Townley R et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. Eur Respir J 2001; Aug; 18(2):254-61.
10. Lemanske RF Jr, Nayak A, McAlary M et al. Omalizumab improves asthma-related quality of life in children with allergic asthma. Pediatrics 2002 Nov; 110(5):e55.
11. Noga O, Hanf G, Kunkel G. Immunological and clinical changes in allergic asthmatics following treatment with omalizumab. Int Arch Allergy Immunol 2003 May; 131(1):46-52.
12. Plewako H, Arvidsson M, Petruson K et al. The effect of omalizumab on nasal allergic inflammation. J Allergy Clin Immunol 2002 Jul; 110(1):68-71.
13. Kuehr J, Brauburger J, Zielen S et al. Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis. J Allergy Clin Immunol 2002 Feb; 109(2):274-80.
14. Casale TB, Condemi J, LaForce C et al. Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. JAMA 2001 Dec 19; 286(23):2956-67.
15. Busse W, Corren J, Lanier BQ et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol 2001 Aug; 108(2):184-90.
16. Milgrom H, Berger W, Nayak A et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). Pediatrics 2001 Aug; 108(2):E36.
17. Buhl R. Omalizumab (Xolair) improves quality of life in adult patients with allergic asthma: a review. Respir Med 2003 Feb; 97(2):123-9.
18. Milgrom H. Is there a role for treatment of asthma with omalizumab? Arch Dis Child 2003 Jan; 88(1):71-4.
19. Vignola AM, Humbert M, Bousquet J et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. Allergy 2004;59(7):709-717.
20. Ayres JG, Higgins B, Chilvers ER et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with poorly controlled (moderate-to-severe) allergic asthma. Allergy 2004;59(7):701-708.
21. Walker S, Monteil M, Phelan K et al. Anti-IgE for chronic asthma in adults and children. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD003559.
22. Humbert M, Beasley R, Ayres J et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. Allergy 2005;60:309–316.
23. Bousquet , Cabrera P, Berkman N et al. The effect of treatment with omalizumab, an anti-IgE antibody, on asthma exacerbations and emergency medical visits in patients with severe persistent asthma. Allergy 2005:60:302–308.
24. Oba Y and Salzman GA. Cost-effectiveness analysis of omalizumab in adults and adolescents with moderate-to-severe allergic asthma. J Allergy Clin Immunol 2004;114:265-9.

25. National Heart Lung and Blood Institute. Clinical Practice Guidelines: Guidelines for the Diagnosis and Management of Asthma (EPR-3). Last updated 2007. Available at: **http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines** Accessed January 8, 2025.

26. National Institute for Health and Clinical Excellence (NICE). Omalizumab for severe persistent allergic asthma. Technology Appraisal Guidance No. 278. London, UK. April 2013. Available at: **https://www.nice.org.uk/guidance/ta278**. Accessed January 8, 2025.

27. Li JT, Oppenheimer J, Bernstein IL, Nicklas RA. Attaining optimal asthma control: A practice Parameter. 7 October 2005. Accessed via the Practice Guidelines section of the American Academy of Allergy Asthma & Immunology.

28. Morjaria JB, Proiti M, Polosa R. Stratified medicine in selecting biologics for the treatment of severe asthma. Current Opinion in Allergy and Clinical Immunology 2011,11:58–63.

29. Hanania NA, Alpan O, Hamilos DL, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy. Ann Intern Med. 2011;154:573-582.

30. Drug Safety Update. Omalizumab: potential risk of arterial thrombotic events. 2011;4(7):A4.

31. Saini S, Rosén KE, Hsieh HJ, et al., A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria.JACI 2011;128:567-573.

32. Maurer M, Rosén KE, Hsieh H, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. NEJM, epublished February 24, 2013.

33. Normansell R, Walker S, Milan SJ, et al. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev 2014 Jan 13;1:CD003559.

34. Norman G, Faria R, Paton F, et al. Omalizumab for the treatment of severe persistent allergic asthma: a systematic review and economic evaluation. Health Technol Assess 2013;17(52):1-342.

35. Maurer M. Phase III randomized, double-blind, placebo-controlled study evaluating efficacy and safety of omalizumab in H1-antihistamine-refractory chronic idiopathic/spontaneous urticaria. European Academy of Dermatology and Venereology (EADV) annual meeting 2013. Oral Presentation. 5 October 2013, 11:30 a.m.

36. Long A, Rahmaoui A, Rothman KJ, et al. Incidence of malignancy in patients with moderate-to-severe asthma treated with or without omalizumab. J Allergy Clin Immunol. 2014 Sep;134(3):560-567.

37. Omalizumab (Xolair). Package Insert. Genentech, Inc. A Member of the Roche Group. South San Francisco, CA. Revised March 2023. Available at: **http://www.gene.com/download/pdf/xolair_prescribing.pdf.** Accessed January 8, 2025.

38. Cleveland Clinic: Available at: **https://my.clevelandclinic.org/health/diseases/8630-urticaria-hives-and-angioedema** Accessed January 8, 2025.

39. UpToDate: Anti-IgE therapy. **https://www.uptodate.com/contents/anti-ige-therapy?search=anti%20ige%20therapy&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1**. Accessed January 8, 2025.

40. UpToDate: Chronic spontaneous urticaria. **https://www.uptodate.com/contents/chronic-spontaneous-urticaria-treatment-of-refractory-symptoms?search=chronic%20spontaneous%20urticaria&source=search_result&selectedTitle=3~14&usage_type=default&display_rank=3**. Accessed January 8, 2025.

41. Cherian S, Konstantinova T, Hu J, Khan SH. Safety Profile of Dual Biologic Therapy with Omalizumab and a Second Biologic Agent. Journal of Allergy and Clinical Immunology. 2020;145(2).

42. Ortega G, Tongchinsub P, Carr T. Combination Biologic Therapy for Severe Persistent Asthma. Annals of Allergy, Asthma & Immunology. 2019;123(3):309-311.

43. Thomes R, Darveaux J. Combination Biologic Therapy in Severe Asthma: A Case Series. Annals of Allergy, Asthma & Immunology. 2018;121(5).

Appendix

Drug Class	Drug Names
Inhaled corticosteroids	Alvesco (ciclesonide), Arnuity Ellipta (fluticasone furoate), Asmanex HFA (mometasone), Asmanex Twisthaler (mometasone), Flovent Diskus (fluticasone propionate), Flovent HFA (fluticasone propionate), Pulmicort Flexhaler (budesonide), and QVAR Redihaler (beclomethasone)
Long Acting Bronchodilators	Severent Diskus (salmeterol xinafoate)
H1 Antihistamines	brompheniramine, chlorpheniramine (Chlor-Trimeton), clemastine (Tavist), cyproheptadine (Periactin), dexbrompheniramine, dexchlorpheniramine, diphenhydramine (Benadryl), hydroxyzine (Vistaril), cetirizine (Zyrtec), desloratadine (Clarinex), fexofenadine (Allegra), loratadine (Claritin)
H2 Antihistamines	famotidine, nizatidine, cimetidine
Combination Long-acting Bronchodilator and Corticosteroid	Advair (fluticasone/salmeterol), Breo Ellipta (fluticasone/vilanterol), Dulera (mometasone/formoterol), Symbicort (budesonide/fomoterol fumarate)
Oral Corticosteroids	methylprednisolone, prednisone, prednisolone
Leukotriene Modifiers	Singulair (montelukast sodium), Accolate (zafirlukast)

H1 and H2 Antihistamines (Only Dosing for Adults and Children ≥ 12 Years is Included in the Following Table).

Drug Class	Drug Name	Standard Drug Dosage
H1	J-Tan PD (brompheniramine): 1mg/mL (30mL); Respa-BR (brompheniramine): 11 mg ER tablet)	Adult dosing varies depending on product type/combination. Some combination products contain 2mg per 5 mL of the brompheniramine Maleate component, with standard dosing for adults and children 12 years and older of 10mL every 4 hours (i.e. 4mg of brompheniramine component every 4 hours).
H1	Chlor-Trimeton (chlorpheniramine)+ multiple other brand names	Adult Immediate Release: 4mg every 4 to 6 hours; NTE 24mg/24 hours. Adult Extended Release: 12mg every 12 hours; NTE 24mg/24 hours. Children Immediate/Extended Release:

Drug Class	Drug Name	Standard Drug Dosage
		> or = 12 years: see adult dosing above.
H1	Tavist; Dayhist (clemastine)	Adult: 1.34mg (1mg base*) twice daily to 2.68mg three times daily; NTE 8.04mg/day (6mg base). OTC labeling: 1.34mg (1mg base*) twice daily; NTE 2mg base/24 hours. Children > or = 12: see adult dosing above.
H1	Periactin (cyproheptadine)	Adult: 4 to 20mg daily divided every 8 hours (NTE: 0.5mg/kg/day). Some individuals may require up to 32mg daily for optimal symptom management. Children 7 to 14 years: 4mg every 8 to 12 hours (NTE: 16mg daily). Children > or = 15 years: start with 4mg every 8 hours; range 12 to 16mg/day. Some individuals may require up to 32mg; Max daily dose: 0.5mg/kg/day.
H1	Polaramine (dexchlorpheniramine)	Adult: 2mg every 4 to 6 hours. Children > or = 12 years: see adult dosing above.
H1	Benadryl (diphenhydramine)	Adult Oral: 25 to 50mg ever 4 to 8 hours, max: 300mg daily. Adult IM/IV: 10 to 50mg per dose; single doses up to 100mg may be used; NTE: 400mg daily. Children > or = 12 years: see adult dosing above.
H1	Vistaril (hydroxyzine)	Adult: 25mg three to four times daily. Children > or = 6 years: 50 to 100mg daily in divided doses.
H1	Zyrtec (cetirizine)	Adult: 5 to 10mg once daily; Max: 10mg daily. Children > or = 6 years to adults: 5 to 10 mg/day as a single dose or divided into 2 doses.
H1	Clarinex (desloratadine)	Adult: 5mg once daily. Children > or = 12 years: see adult dosing above.
H1	Allegra (fexofenadine)	Adult: 60mg twice daily OR 180mg once daily. Children > or = 12 years: see adult dosing above.
H1	Claritin (loratadine)	10mg once daily or 5mg twice daily. Children > or = 6 years: see adult dosing above.
H2	Pepcid (famotidine)	**Dosing for adults and children > or = 12 years depends on the indication and may vary. Dosing for common indications is as follows: Adult: 20mg twice daily or 20 to 40mg once before bedtime. Children > or = 12 years: see adult dosing above.

Drug Class	Drug Name	Standard Drug Dosage
H2	Axid (nizatidine)	**Dosing for adults and children > or = 12 years depends on the indication and may vary. Dosing for common indications is as follows: Adult: 150mg twice daily or 300mg once before bedtime. Children > or = 12 years: see adult dosing above.
H2	Tagamet (cimetidine)	**Dosing for adults and children > or = 12 years depends on the indication and may vary. Dosing for common indications is as follows: Adult: 400mg twice daily or 400 to 800mg once before bedtime. Children > or = 12 years: see adult dosing above.

*Note: dosage differs depending on clemastine base versus clemastine fumarate formulation.
**Note: dosage differs depending on indication, and if therapy is used for prophylaxis versus active treatment vs. maintenance. Please double check dosages provided in this table based on the case-specific information.

Dosage for Asthma

Administration Every 4 Weeks

Pre-treatment Serum IgE (I/mL)	Body Weight (kg)			
	30 – 60	>60 – 70	>70 – 90	>90 – 150
≥30 – 100	150	150	150	300
>100 – 200	300	300	300	N/A
>200 – 300	300	N/A	N/A	N/A

Administration Every 2 Weeks

Xolair (omalizumab) Doses (milligrams) Administered by Subcutaneous Injection Every 2 Weeks for Adults and Adolescents (12 years of age and older) with Asthma

Pre-treatment Serum IgE (I/mL)	Body Weight (kg)			
	30 – 60	>60 – 70	>70 – 90	>90 – 150
≥30 – 100	N/A	N/A	N/A	N/A
>100 – 200	N/A	N/A	N/A	225
>200 – 300	N/A	225	225	300

Pre-treatment Serum IgE (I/mL)	Body Weight (kg)			
	30 – 60	>60 – 70	>70 – 90	>90 – 150
>300 – 400	225	225	300	N/A
>400 – 500	300	300	375	N/A
>500 – 600	300	375	N/A	N/A
>600 – 700	375	N/A	N/A	N/A

Subcutaneous Xolair (omalizumab) Doses Every 2 or 4 Weeks* for Pediatric Individuals with Asthma Who Begin Xolair (omalizumab) Between the Ages of 6 to <12 Years

Pre-treatment Serum IgE (I/mL)	Dosing Freq	Body Weight (kg)									
		20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
>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

Dosing Adjustments

Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during Xolair treatment cannot be used as a guide for dose determination. Dose determination after treatment interruptions

lasting less than 1 year should be based on serum IgE levels obtained at the initial dose determination. Total serum IgE levels may be re-tested for dose determination if treatment with Xolair has been interrupted for one year or more.

Doses should be adjusted for significant changes in body weight. (See tables above.)

Dosage for Chronic Idiopathic Urticaria

Administer Xolair 150 or 300 mg by subcutaneous injection every 4 weeks.

Dosing of Xolair in CIU individuals is not dependent on serum IgE (free or total) level or body weight. The appropriate duration of therapy for CIU has not been evaluated. Periodically reassess the need for continued therapy.

History

Date	Comments
08/12/03	Add to Prescription Drug Section. - New policy developed at time FDA approved the drug.
01/01/04	Replace Policy - HCPC code updates only.
09/01/04	Replace Policy - Policy renumbered from PR.5.01.113. No changes to dates.
09/14/04	Replace Policy - Scheduled review; policy statement unchanged. Reference section updated.
10/11/05	Replace Policy - Scheduled review, policy statement unchanged.
02/06/06	Codes updated - No other changes.
06/16/06	Update Scope and Disclaimer - No other changes.
10/10/06	Replace Policy - Policy updated with literature search; no change in policy statement. Reviewed by P&T committee on September 26, 2006.
11/13/07	Replace Policy - Policy updated with literature search. Policy statement includes changes in severity, “long-acting beta-agonists” as medically necessary; also includes “Peanut and other food allergies” and “Latex allergy” as investigational. References updated.
10/14/08	Replace Policy - Policy updated with literature search; no change to policy statement. References and codes added.

Date	Comments
12/08/09	Replace Policy - Policy updated with literature search; no change to policy statement. References added. Reviewed by P&T committee on November 24, 2009.
02/08/11	Replace Policy - Policy updated with literature review; no change in policy statement. Reviewed by P&T in November 2010.
02/14/12	Replace policy. Policy updated with literature search. References added. Reviewed by P&T January 24, 2012.
10/11/12	Minor Update – Medco is now Express Scripts.
03/11/13	Replace policy. Policy updated with an additional medically necessary off-label indication: Antihistamine-refractory chronic idiopathic urticaria. Policy Guidelines section updated with dosing guidelines on the new indication. Supporting rationale added; reference 36 updated; references 37-38 added. Reviewed by P&T in March 2013.
02/24/14	Replace policy. Policy updated with literature review; no change in policy statement.
04/14/14	Interim update. Policy updated with literature; no change in policy statement. References 39 and 40 added.
05/12/14	Interim update. Policy section updated. The indication for severe persistent asthma rewritten; criteria moved from Policy Guidelines and is now listed within the Policy section. A notation was added that Xolair is not FDA-approved for patients under age 12 in the US; however, cases may be approved on an individual member basis for those with severe persistent asthma with informed consent by a responsible adult on behalf of the child based upon approval for children age 6 and above in the EU. A new indication is added for treatment of severe chronic idiopathic urticaria for those aged 12 and above when the indicated criteria are met and documentation provided; this indication was approved by the FDA in March 2014. Reference 40 added. HCPCS code J3590 removed; there is a specific code for Xolair (J2357) which is listed in the policy.
05/22/15	Annual Review. Policy updated with literature review, policy statements unchanged.
06/09/15	Interim update. Table added to the Policy Guidelines section to provide dosage information for brand/generic names for H1 and H2 antihistamines and normal dosage ranges for H1 antihistamines. ICD-9 diagnosis codes removed; these were informational only.
09/09/15	Minor edit. Clarification made to policy statement, added “of” to: Severe allergic asthma (FEV1 40-80% of predicted).
10/01/16	Annual Review, approved September 13, 2016. Age limit update for Xolair in the setting of moderate to severe asthma.
11/08/16	Minor update. Information added to the Rationale section to indicate the age limit of application for this drug is based on FDA-labelling. No change in policy statements.
09/01/17	Minor update, changed title from Omalizumab (Xolair) to Xolair (omalizumab).

Date	Comments
12/01/17	Annual Review, approved November 21, 2017. Information added to Appendix section for dosing children aged 6 to <12 years for asthma and dosage for chronic idiopathic urticaria.
11/01/18	Annual Review, approved October 26, 2018. Policy updated with literature review, policy statements unchanged.
12/01/19	Annual Review, approved November 21, 2019. No change in policy statements.
08/01/20	Annual Review, approved July 23, 2020. Updated coverage criteria from "severe persistent asthma" to "moderate to severe persistent asthma" as the FDA approved indication. Added to coverage criteria for moderate to severe persistent asthma that this results in "commonly requiring urgent care visits, ER visits and/or hospitalizations".
10/01/20	Interim Review, approved September 17, 2020. For moderate to severe persistent asthma updated to FEV1 < 80% of predicted. Added criteria that Xolair (omalizumab), Dupixent (dupilumab), Cinqair (reslizumab), Fasenra (benralizumab), and Nucala (mepolizumab) are not to be used as combination therapy with each other for the treatment of asthma.
02/01/21	Interim Review, approved January 12, 2021. Added new indication for the treatment of nasal polyps in adults with inadequate response to nasal corticosteroids.
04/01/21	Interim Review, approved March 23, 2021. Updated criteria for the treatment of chronic idiopathic urticaria to at least 6-weeks of documented symptoms.
11/01/21	Annual Review, approved October 5, 2021. Updated CIU criteria to clarify verbiage for prior medications to step through. Updated criteria for moderate to severe asthma to include body weight requirement based on available dosing and added non-smoker or enrollment in a smoking cessation program requirement. Updated criteria for nasal polyps to include body weight requirement based on available dosing and removed nasal polyp score and nasal congestion score requirement from criteria. Updated coverage criteria become effective for dates of service on or after February 4, 2022, following 90-day provider notification.
01/01/23	Annual Review, approved December 23, 2022. No changes to policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
05/01/23	Interim Review, approved April 11, 2023. Updated definition of moderate to severe persistent asthma to include individuals with one or more asthma exacerbations in the previous 12 months requiring use of oral corticosteroids.
08/01/23	Annual Review, approved July 24, 2023. Updated the indication "nasal polyps" with "chronic rhinosinusitis with nasal polyps" to match the FDA Label. Updated initial approval length for Xolair for CIU to 6 months.
07/01/24	Annual Review, approved June 11, 2024. Updated criteria that Xolair (omalizumab) is not to be used in combination with Tezspire (tezepelumab) for the treatment of

Date	Comments
	asthma. Updated criteria that Xolair (omalizumab) is not to be used in combination with Dupixent (dupilumab) for the treatment of nasal polyps.
08/01/24	Interim Review, approved July 9, 2024. Updated criteria to include treatment of certain individuals with IgE-mediated food allergies.
10/01/24	Interim Review, approved September 10, 2024. The following policy changes are effective January 3, 2025, following a 90-day provider notification. Updated asthma criteria to remove the requirement for adults to not be a current smoker or is currently enrolled in a smoking cessation program. Updated asthma diagnostic criteria to the following: Individual has two or more asthma exacerbations in the previous 12 months requiring use of oral corticosteroids, one or more asthma exacerbations requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous 12 months, forced expiratory volume in 1 second (FEV1) <80% predicted, or has a dependence on oral corticosteroids of at least 5 mg per day of prednisone or equivalent.
02/01/25	Annual Review, approved January 27, 2025. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.
04/01/25	Interim Review, approved March 11, 2025. Updated the asthma coverage criteria from using maximum doses of an inhaled corticosteroid to using maximum tolerated doses of an inhaled corticosteroid.
07/01/25	Interim Review, approved June 10, 2025. Updated asthma coverage criteria by adding an FEV1/FVC less than 0.80 as an option to the requirement to meet one of the following. Updated asthma coverage criteria by changing the meets one of the following option from has a dependence on oral corticosteroids of at least 5 mg per day of prednisone or equivalent to has asthma that worsens upon tapering of oral corticosteroid therapy. The following policy changes are effective October 3, 2025, following 90-day provider notification. Added site of service review. Clarified that the Site of Service Medical Necessity criteria can apply to injection drugs.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to

the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.