Xolair® (omalizumab)
(Subcutaneous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed annually, unless otherwise specified.

- Management of Immune Checkpoint Inhibitor-Related Toxicity: Coverage will be provided for 6 months and may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Xolair 75 mg single-dose prefilled syringe/autoinjector: 1 syringe/autoinjector every 14 days
- Xolair 150 mg single-dose prefilled syringe/autoinjector: 4 syringes/autoinjectors every 14 days
- Xolair 150 mg single-dose vial for injection: 4 vials every 14 days
- Xolair 300 mg single-dose prefilled syringe/autoinjector: 2 syringes/autoinjectors every 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Allergic Asthma
- 75 billable units every 14 days

CRSwNP and IgE-Mediated Food Allergy
- 120 billable units every 14 days

All other indications
- 60 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); AND

Universal Criteria [1]

- Will not be used in combination with another anti-IL4, anti-IL5 or IgG2 lambda monoclonal antibody agents (e.g., benralizumab, mepolizumab, reslizumab, dupilumab, tezepelumab etc.); **AND**

Moderate to Severe Persistent Allergic Asthma † [1-3,20,25,29]

- Patient is at least 6 years of age; **AND**
- Will not be used for treatment of acute bronchospasm, status asthmaticus, or allergic conditions (*other than indicated*); **AND**
- Patient has a positive skin test or in vitro reactivity to a perennial aero-allergen; **AND**
- Patient must weigh between 20 kg (44 lbs.) and 150 kg (330 lbs.); **AND**
- Patient has a serum total IgE level, measured before the start of treatment, of either:
    - ≥ 30 IU/mL and ≤ 700 IU/mL in patients age ≥ 12 years; **OR**
    - ≥ 30 IU/mL and ≤ 1300 IU/mL in patients age 6 to <12 years; **AND**
- Patient has documented ongoing symptoms of moderate-to-severe asthma***** with a minimum (3) month trial on previous combination therapy including medium- or high-dose inhaled corticosteroids **PLUS** another controller medication (e.g., long-acting beta-2 agonist**,** leukotriene receptor antagonist, theophylline, etc.); **AND**
- Baseline measurement of at least one of the following for assessment of clinical status:
    - Use of systemic corticosteroids
    - Use of inhaled corticosteroids
    - Number of hospitalizations, ER visits, or unscheduled visits to healthcare provider due to condition
    - Forced expiratory volume in 1 second (FEV_1)

Chronic Idiopathic Urticaria/Chronic Spontaneous Urticaria (CIU/CSU) † [1,4-6,8,28]

- Patient is at least 12 years of age; **AND**
- The underlying cause of the patient's condition is NOT considered to be any other allergic condition(s) or other form(s) of urticaria; **AND**
- Patient is avoiding triggers (e.g., NSAIDs, etc.); **AND**
- Documented baseline score from an objective clinical evaluation tool, such as: urticaria activity score (UAS7), angioedema activity score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), urticaria control test (UCT), angioedema control test (AECT), or Chronic Urticaria Quality of Life Questionnaire (CU-Q_2oL); **AND**
- Patient had an inadequate response to a one or more-month trial on previous therapy with scheduled dosing of a second-generation H1-antihistamine product******; **AND**
- Patient had an inadequate response to a one or more-month trial on previous therapy with scheduled dosing of at least one of the following:

- Up-dosing/dose advancement (up to 4-fold) of a second generation H1-antihistamine**
- Add-on therapy with a leukotriene antagonist (e.g., montelukast, zafirlukast, etc.)
- Add-on therapy with another H1-antihistamine**
- Add-on therapy with a H2-antagonist (e.g., ranitidine, famotidine, etc.)

Note: renewals will require a documented score from an objective clinical evaluation tool (e.g., UAS7, AAS, DLQI, AE-QoL, UCT, AECT, CU-Q_2oL, etc.) recorded within the previous 6 months.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) † [1,22,23, 26-27]

- Patient has bilateral symptomatic sino-nasal polyposis with symptoms lasting at least 8 weeks; **AND**
- Patient has failed at least 8 weeks of daily intranasal corticosteroid therapy; **AND**
- Patient has at least three (3) of the following indicators for biologic treatment:
  - Patient has evidence of type 2 inflammation (e.g., tissue eosinophils ≥10/hpf, blood eosinophils ≥ 150 cells/µL, or total IgE ≥ 100 IU/mL)
  - Patient has required ≥2 courses of systemic corticosteroids per year or >3 months of low dose corticosteroids, unless contraindicated
  - Disease significantly impairs the patient's quality of life
  - Patient has experienced significant loss of smell
  - Patient has a comorbid diagnosis of asthma; **AND**
- Patient does not have any of the following:
  - Antrochoanal polyps
  - Nasal septal deviation that would occlude at least one nostril
  - Disease with lack of signs of type 2 inflammation
  - Cystic fibrosis
  - Mucoceles; **AND**
- Other causes of nasal congestion/obstruction have been ruled out (e.g., acute sinusitis, nasal infection or upper respiratory infection, rhinitis medicamentosa, tumors, infections, granulomatosis, etc.); **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Therapy will be used in combination with intranasal corticosteroids unless not able to tolerate or use is contraindicated

IgE-Mediated Food Allergic Reactions (Type 1) [1,30]

- Patient is at least 1 year of age; **AND**
- Patient is avoiding known food allergens; **AND**

- Patient is allergic to peanut and at least one other food (e.g., milk, egg, wheat, tree nuts, etc.); **AND**
- Patient's allergy must be confirmed by all of the following:
    - Positive skin prick test (SPT), defined as wheal ≥4 mm larger than saline control
    - Positive peanut and food specific IgE, defined as ≥6 IU/mL at screening or within three months of screening
    - Positive double-blind placebo-controlled food challenge (DBPCFC), defined as experiencing dose-limiting symptoms at a single dose of ≤100 mg of peanut protein and ≤300 mg of food protein; **AND**
- Will not be used for the emergency treatment of allergic reactions, including anaphylaxis

Management of Immune Checkpoint Inhibitor-Related Toxicity ‡ [9,10]

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g., nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, dostarlimab, tremelimumab, nivolumab/relatlimab-rmbw, retifanlimab etc.); **AND**
- Patient has refractory and severe (i.e., grade 3: intense or widespread, constant, limiting self-care activities of daily living or sleep) pruritus; **AND**
- Patient has an increased serum IgE level above the upper limit of normal of the laboratory reference value

Systemic Mastocytosis ‡ [9,11]

- Used for the prevention of one of the following:
    - Chronic mast cell mediator-related cardiovascular (e.g., pre-syncope, tachycardia, etc.) or pulmonary (e.g., wheezing, throat-swelling, etc.) symptoms insufficiently controlled by conventional therapy (e.g., H1 or H2 blockers or corticosteroids); **OR**
    - Unprovoked anaphylaxis; **OR**
    - Hymenoptera or food-induced anaphylaxis in patients with a negative test for specific IgE antibodies or a negative skin test; **OR**
- Used to improve tolerance while on immunotherapy (i.e., venom immunotherapy [VIT])

***Components of severity for classifying asthma as moderate may include any of the following (not all inclusive):** [2,25]
• Daily symptoms • Nighttime awakenings > 1x/week but not nightly • SABA use for symptom control occurs daily • Some limitation to normal activities • Lung function (percent predicted FEV_1) >60%, but <80% • Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to mild asthma
***Components of severity for classifying asthma as severe may include any of the following (not all inclusive):** [2,25]

• Symptoms throughout the day • Nighttime awakenings, often 7x/week • SABA use for symptom control occurs several times daily • Extremely limited in normal activities • Lung function (percent predicted FEV_1) <60% • Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma	
****H1 Antihistamine Products (not all inclusive)** [5,8]	
First Generation H1 • bromphineramine • carbinoxamine • clorpheniramine • clemastine • cyproheptadine • dexchlorpheniramine • diphenhydramine • doxepin • hydroxyzine • triprolidine	Second Generation H1 • cetirizine • desloratadine • fexofenadine • levocetirizine • loratadine

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of anaphylaxis (bronchospasm, hypotension, syncope, urticaria, and/or angioedema), malignancy, symptoms similar to serum sickness (fever, arthralgia, and rash), parasitic (helminth) infection, eosinophilic conditions (e.g., vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy, especially upon reduction of oral corticosteroids), etc.; **AND**

Moderate to Severe Persistent Allergic Asthma [1-3,20,25]

- Patient must weigh between 20 kg (44 lbs.) and 150 kg (330 lbs.); **AND**
- Improvement in asthma symptoms or asthma exacerbations as evidenced by decrease in one or more of the following:
  - Use of systemic corticosteroids
  - Two-fold or greater decrease in inhaled corticosteroid use for at least 3 days
  - Hospitalizations
  - ER visits
  - Unscheduled visits to healthcare provider; **OR**
- Improvement from baseline in forced expiratory volume in 1 second (FEV_1)

Chronic Idiopathic Urticaria/Chronic Spontaneous Urticaria (CIU/CSU) [1,4-6,8,28]

- Provider attests that the patient has been reassessed and continued therapy is necessary for the maintenance treatment of this condition; **AND**
- Treatment has resulted in clinical improvement as documented by improvement from baseline using objective clinical evaluation tools such as the urticaria activity score (UAS7), angioedema activity score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), urticaria control test (UCT), angioedema control test (AECT), or Chronic Urticaria Quality of Life Questionnaire(CU-Q_2oL); **AND**
- Provider has current UAS7, AAS, DLQI, AE-QoL, UCT, AECT, or Cu-Q_2oL recorded within the past 6 months

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) [1,22,23, 26-27]

- Disease response as indicated by improvement in signs and symptoms compared to baseline in one or more of the following: nasal/obstruction symptoms, improvement of sinus opacifications as assessed by CT-scans and/or an improvement on a disease activity scoring tool (e.g., nasal polyposis score (NPS), nasal congestion (NC) symptom severity score, sino-nasal outcome test-22 (SNOT-22), etc.); **OR**
- Patient had an improvement in at least one (1) of the following response criteria:
  - Reduction in nasal polyp size
  - Reduction in need for systemic corticosteroids
  - Improvement in quality of life
  - Improvement in sense of smell
  - Reduction of impact of comorbidities

IgE-Mediated Food Allergic Reactions (Type 1) [1,30]

- Provider attests that the patient has been reassessed and continued therapy is necessary for the maintenance treatment of this condition; **AND**
- Patient has had a reduction in allergic reaction, including anaphylaxis, and/or symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) associated with accidental exposure of known food allergens

Management of Immune Checkpoint Inhibitor-Related Toxicity [9,10]

- May not be renewed

Systemic Mastocytosis [9,11]

- Disease response as indicated by improvement in signs and symptoms compared to baseline or a decreased frequency of exacerbations

V. Dosage/Administration [1,11-13]

Indication	Dose

Allergic Asthma	75 to 375 mg administered subcutaneously by a health care provider§§ every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See tables below.
Chronic Idiopathic Urticaria/Chronic Spontaneous Urticaria	150 or 300 mg administered subcutaneously by a health care provider§§ every 4 weeks. Dosing is not dependent on serum IgE (free or total) level or body weight.
Chronic Rhinosinusitis with Nasal Polyps	75 to 600 mg administered subcutaneously by a health care provider§§ every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See table below.
IgE-Mediated Food Allergy	75 to 600 mg administered subcutaneously by a health care provider§§ every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). See table below.
Management of Immune Checkpoint Inhibitor-Related Toxicity & Systemic Mastocytosis	150 or 300 mg administered subcutaneously every 4 weeks. Dosing is not dependent on serum IgE (free or total) level or body weight. **Must ONLY be administered by a health care provider.

§§ Criteria for Selection of Patients for Self-Administration of Xolair Prefilled Syringe or Autoinjector

The pre-filled syringe or autoinjector formulation may be self-administered after the initial 3 doses are administered in the healthcare setting AND the healthcare provider determines that self-administration is appropriate based on assessment of risk for anaphylaxis and mitigation strategies criteria below:

- **Asthma, CRSwNP and CIU/CSU:** Patient should have no prior history of anaphylaxis to Xolair or other agents, such as foods, drugs, biologics, etc.
- **IgE-Mediated Food Allergy:** Patient should have no prior history of anaphylaxis to Xolair or other agents (except foods), such as drugs, biologics, etc.
- Patient should receive at least 3 doses of Xolair under the guidance of a healthcare provider with no hypersensitivity reactions; **AND**
- Patient or caregiver is able to recognize symptoms of anaphylaxis; **AND**
- Patient or caregiver is able to treat anaphylaxis appropriately; **AND**
- Patient or caregiver is able to perform subcutaneous injections with Xolair prefilled syringe or autoinjector with proper technique according to the prescribed dosing regimen and Instructions for Use

Note: Xolair prefilled syringes for patients under 12 years of age should be administered by a caregiver. Xolair autoinjectors (all doses) are not intended for use in pediatric patients under 12 years of age.

Asthma Omalizumab Doses Administered Every 4 Weeks (mg) in patients ≥ 12 years

Pre-treatment serum IgE (IU/mL)	Body weight (kg)			
	30 to 60	> 60 to 70	> 70 to 90	> 90 to 150
≥ 30 to 100	150	150	150	300
> 100 to 200	300	300	300	See the following table.
> 200 to 300	300	See the following table.	See the following table.	See the following table.

Asthma Omalizumab Doses Administered Every 2 Weeks (mg) in patients ≥ 12 years				
Pre-treatment serum IgE (IU/mL)	**Body weight (kg)**			
	30 to 60	**> 60 to 70**	**> 70 to 90**	**> 90 to 150**
> 100 to 200	See previous table.	See previous table.	See previous table.	225
> 200 to 300	See previous table.	225	225	300
> 300 to 400	225	225	300	Do not dose.
> 400 to 500	300	300	375	Do not dose.
> 500 to 600	300	375	Do not dose.	Do not dose.
> 600 to 700	375	Do not dose.	Do not dose.	Do not dose

Asthma Omalizumab Doses Administered Every 2 or 4 Weeks (mg) for Pediatric Patients Who Begin Xolair Between the Ages of 6 to <12 Years											
Pre-treatment serum IgE (IU/mL)	**Dosing Freq. (weeks)**	**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	4	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	Do Not Dose	
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375	Do Not Dose			
>600-700		300	225	225	300	375	Do Not Dose				
>700-900	2	225	225	300	375	Do Not Dose					
>900-1100		225	300	375	Do Not Dose						
>1100-1200		300	300	Do Not Dose							
>1200-1300		300	375	Do Not Dose							

Nasal Polyps Omalizumab Doses Administered Every 2 or 4 Weeks (mg)

Pre-treatment serum IgE (IU/mL)	Dosing Freq. (weeks)	Body Weight (kg)							
		>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
30-100	4	75	150	150	150	150	150	300	300
>100-200		150	300	300	300	300	300	450	600
>200-300		225	300	300	450	450	450	600	375
>300-400		300	450	450	450	600	600	450	525
>400-500		450	450	600	600	375	375	525	600
>500-600		450	600	600	375	450	450	600	
>600-700		450	600	375	450	450	525		
>700-800	2	300	375	450	450	525	600		
>800-900		300	375	450	525	600			
>900-1000		375	450	525	600				
>1000-1100		375	450	600					
>1100-1200		450	525	600					
>1200-1300		450	525						
>1300-1500		525	600						

Do Not Dose

IgE-Mediated Food Allergy Omalizumab Doses Administered Every 2 or 4 Weeks (mg)													
Pre-treatment serum IgE (IU/mL)	Dosing Freq. (weeks)	Body Weight (kg)											
		≥10-12	>12-15	>15-20	>20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
≥30-100	4	75	75	75	75	75	75	150	150	150	150	150	300	300
>100-200		75	75	75	150	150	150	300	300	300	300	300	450	600
>200-300		75	75	150	150	150	225	300	300	450	450	450	600	375
>300-400		150	150	150	225	225	300	450	450	450	600	600	450	525
>400-500		150	150	225	225	300	450	450	600	600	375	375	525	600

>500-600		150	150	225	300	300	450	600	600	375	450	450	600
>600-700		150	150	225	300	225	450	600	375	450	450	525	
>700-800		150	150	150	225	225	300	375	450	450	525	600	
>800-900		150	150	150	225	225	300	375	450	525	600		
>900-1000		150	150	225	225	300	375	450	525	600			
>1000-1100		150	150	225	225	300	375	450	600				
>1100-1200	2	150	150	225	300	300	450	525	600				
>1200-1300		150	225	225	300	375	450	525					
>1300-1500		150	225	300	300	375	525	600					
>1500-1850			225	300	375	450	600						

Do Not Dose

VI. Billing Code/Availability Information

HCPCS Code:

- J2357 – Injection, omalizumab, 5 mg; 1 billable unit = 5 mg

NDC:

- Xolair 75 mg single-dose prefilled syringe or autoinjector: 50242-0214-xx
- Xolair 150 mg single-dose prefilled syringe or autoinjector: 50242-0215-xx
- Xolair 150 mg single-dose vial powder for injection: 50242-0040-xx
- Xolair 300 mg single-dose prefilled syringe or autoinjector: 50242-0227-xx

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C94.30	Mast cell leukemia not having achieved remission
C94.31	Mast cell leukemia, in remission
C94.32	Mast cell leukemia, in relapse
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
D47.02	Systemic mastocytosis
J33.0	Polyp of nasal cavity
J33.1	Polypoid sinus degeneration
J33.8	Other polyp of sinus
J33.9	Nasal polyp, unspecified
J45.40	Moderate persistent asthma, uncomplicated

ICD-10	ICD-10 Description
J45.50	Severe persistent asthma, uncomplicated
L29.8	Other pruritus
L29.9	Pruritus, unspecified
L50.1	Idiopathic urticaria
Z91.010	Allergy to peanuts
Z91.011	Allergy to milk products
Z91.012	Allergy to eggs
Z91.013	Allergy to seafood
Z91.018	Allergy to other foods

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction	NCD/LCA/LCD Document (s)	Contractor
6, K	A52448	National Government Services, Inc

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp. (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp. (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC