Medical Policy Manual **Approved Rev: Do Not Implement until 12/2/25**

Omalizumab Products: Omalizumab (Xolair®); Omalizumab-igec (Omlyclo®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Allergic asthma
Indicated for adult and pediatric patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Limitations of use:
Not indicated for the relief of acute bronchospasm or status asthmaticus, or for treatment of other allergic conditions.

Chronic rhinosinusitis with nasal polyps (CRSwNP)
Indicated for add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.

IgE-mediated food allergy
Indicated for the reduction of allergic reactions (Type 1), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric patients aged 1 year and older with IgE-mediated food allergy.

Is to be used in conjunction with food allergen avoidance.

Limitations of use:
Not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

Chronic spontaneous urticaria (CSU)
Indicated for the treatment of adults and adolescents 12 years of age and older with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1 antihistamine treatment.

Limitations of use:
Not indicated for treatment of other forms of urticaria.

Compendial Uses

- Immune checkpoint inhibitor-related toxicities

- Systemic mastocytosis

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

Asthma
Initial requests
- Chart notes or medical record documentation showing pre-treatment IgE level (where applicable).
- Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration.

Continuation requests
Chart notes or medical record documentation supporting improvement in asthma control.

CRSwNP
Initial requests
- Chart notes or medical record documentation showing nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) details (e.g., location, size), Meltzer Clinical Score, or endoscopic nasal polyp score (NPS) (where applicable).
- Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency and duration. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Continuation requests
Chart notes or medical record documentation supporting positive response to therapy.

IgE-Mediated Food Allergy
Initial requests
Chart notes, medical record documentation, or laboratory tests showing the following (where applicable):
- Pre-treatment allergen-specific IgE level.
- Skin-prick test wheal diameter.
- Pre-treatment serum IgE level.
- Positive result of a physician controlled oral food challenge.
- History of a systemic reaction to a food.

Continuation requests
Chart notes or medical record documentation supporting positive response to therapy (e.g., reduction or absence of hypersensitivity to food-allergen).

CSU
Initial requests
Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
Continuation requests
Chart notes or medical record documentation supporting positive response to therapy.

Immune Checkpoint Inhibitor-Related Toxicity
Initial requests
Chart notes or medical record documentation showing pre-treatment IgE level.
Continuation requests
Chart notes or medical record documentation supporting positive response to therapy.

Systemic mastocytosis
Initial requests
- Chart notes or medical record documentation supporting diagnosis of systemic mastocytosis.
- Chart notes, medical record documentation, or claims history supporting previous medications tried (where applicable).

Continuation requests
Chart notes or medical record documentation supporting positive response to therapy.

PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
- Asthma: allergist/immunologist or pulmonologist
- CRSwNP: allergist/immunologist or otolaryngologist
- IgE-mediated food allergy: allergist/immunologist
- Chronic spontaneous urticaria: allergist/immunologist or dermatologist
- Immune checkpoint inhibitor-related toxicity: dermatologist, hematologist, or oncologist

COVERAGE CRITERIA

Asthma

Authorization of 6 months may be granted for members 6 years of age or older who have previously received a biologic drug (e.g., Nucala, Cinqair) indicated for asthma in the past year.

Authorization of 6 months may be granted for treatment of moderate-to-severe asthma when all of the following criteria are met:
- Member is 6 years of age or older.
- Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
- Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
- Member has uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:
  - Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment
  - One or more asthma exacerbation(s) resulting in hospitalization or emergency medical care visit(s)
  - Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
- Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
  - Medium-to-high-dose inhaled corticosteroid
  - Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
- Member will continue to use maintenance asthma treatments (i.e., inhaled corticosteroid and additional controller) in combination with the requested medication.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

Authorization of 6 months may be granted for adult members who have previously received a biologic drug (e.g., Dupixent, Nucala) indicated for chronic rhinosinusitis with nasal polyps (CRSwNP) in the past year.

Authorization of 6 months may be granted for treatment of CRSwNP when all of the following criteria are met:

- Member is 18 years of age or older.
- Member has bilateral nasal polyps and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 4 weeks unless contraindicated or not tolerated.
- Member has one of the following:
  - A bilateral nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril.
  - Meltzer Clinical Score of 2 or higher in both nostrils.
  - A total endoscopic nasal polyp score (NPS) of at least 5 with a minimum score of 2 for each nostril.
- Member has symptoms of nasal blockage, congestion, or obstruction plus one of the following additional symptoms:
  - Rhinorrhea (anterior/posterior).
  - Reduction or loss of smell.
  - Facial pain or pressure.
- Member will continue to use a daily intranasal corticosteroid while being treated with the requested medication, unless contraindicated or not tolerated.

IgE-Mediated Food Allergy

Authorization of 6 months may be granted for reduction of IgE-mediated food allergy reactions when all of the following criteria are met:

- Member is 1 year of age or older.
- IgE-mediated food allergy has been confirmed by either of the following:
  - Pre-treatment food allergen-specific IgE level greater than or equal to 6 IU/mL.
  - Skin-prick test (SPC) with wheal diameter greater than or equal to 4 mm.
- Member has either of the following:
  - A positive physician controlled oral food challenge (e.g., moderate to severe skin, respiratory, or gastrointestinal [GI] symptoms).
  - History of a systemic reaction to a food.
- Member has a pre-treatment serum IgE level greater than or equal to 30 IU/mL.
- Member will continue to follow a food-allergen avoidance diet.

Chronic Spontaneous Urticaria

Authorization of 6 months may be granted for members 12 years of age or older who have previously received a biologic drug (e.g., Dupixent) indicated for chronic spontaneous urticaria in the past year.

Authorization of 6 months may be granted for treatment of chronic spontaneous urticaria when all of the following criteria are met:

- Member is 12 years of age or older.
- Member remains symptomatic despite treatment with up-dosing (in accordance with EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelines) of a second-generation H_1 antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
- Member has been evaluated for other causes of wheals (hives) and /or angioedema, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).
- Member has experienced a spontaneous onset of wheals (hives), angioedema, or both, for at least 6 weeks.

Immune Checkpoint Inhibitor-Related Toxicity

Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when both of the following criteria are met:

- The member has a refractory case of immune-therapy related severe (G3) pruritus with no response to gabapentinoids in one month.
- The member has elevated IgE levels.

Systemic Mastocytosis

Authorization of 12 months may be granted for treatment of systemic mastocytosis when both of the following criteria are met:

- The major and at least one minor diagnostic criterion for systemic mastocytosis are present or three or more minor diagnostic criteria are present (see Appendix).
- The requested medication will be used in any of the following treatment settings:
  - Used as stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms when the member has tried both of the following:
    - H1 blockers and H2 blockers.
    - Corticosteroids.
  - Used for prevention of recurrent unprovoked anaphylaxis.
  - Used for prevention of hymenoptera or food-induced anaphylaxis, with negative specific IgE or negative skin test.
  - Used to improve tolerability of venom immunotherapy.

CONTINUATION OF THERAPY

Asthma

Authorization of 12 months may be granted for continuation of treatment of moderate-to-severe asthma when all of the following criteria are met:

- Member is 6 years of age or older.
- Asthma control has improved on the requested medication as demonstrated by at least one of the following:
  - A reduction in the frequency and/or severity of symptoms and exacerbations
  - A reduction in the daily maintenance oral corticosteroid dose
- Member will continue to use maintenance asthma treatments (i.e., inhaled corticosteroid and additional controller) in combination with the requested medication.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

Authorization of 12 months may be granted for continuation of treatment of CRSwNP when all of the following criteria are met:

- Member is 18 years of age or older.
- Member has experienced a positive response as evidenced by improvement in signs and symptoms (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sino-nasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).
- Member will continue to use a daily intranasal corticosteroid while being treated with the requested medication, unless contraindicated or not tolerated.

IgE-Mediated Food Allergy

Authorization of 12 months may be granted for reduction of IgE-mediated food allergy reactions when all of the following criteria are met:

- Member is 1 year of age or older.

- Member has achieved or maintained a positive clinical response to therapy as evidenced by a reduction or absence of hypersensitivity (e.g., moderate to severe skin, respiratory or GI symptoms) to food-allergen.
- Member will continue to maintain a food-allergen avoidance diet.

Chronic Spontaneous Urticaria

Authorization of 12 months may be granted for continuation of treatment of chronic spontaneous urticaria when all of the following criteria are met:

- Member is 12 years of age or older.
- Member has experienced a positive response (e.g., improved symptoms, decrease in weekly urticaria activity score [UAS7]) since initiation of therapy.

Immune Checkpoint Inhibitor-Related Toxicity and Systemic Mastocytosis

Authorization of 12 months may be granted for continuation of treatment of refractory immune checkpoint inhibitor-related severe (G3) pruritus or systemic mastocytosis when the member achieves or maintains a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

OTHER

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

Note: If the member is a current smoker or vaper, they should be counseled on the harmful effects of smoking and vaping on pulmonary conditions and available smoking and vaping cessation options.

APPENDIX

2024 WHO Diagnostic Criteria for Systemic Mastocytosis

- Major Criteria: multifocal, dense infiltrates of mast cells (at least 15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organs
- Minor Criteria
  - Atypical mast cell morphology, including spindle shape or immature morphology, present in greater than 25% of all mast cells on bone marrow smears or in other extracutaneous organ(s)
  - KIT p.D816V mutation or other activating KIT mutation(s) detected in peripheral blood, bone marrow, or other extracutaneous organ(s)
  - Mast cells aberrantly express one or more of the following antigens: CD2, CD25, CD30
  - Baseline serum tryptase concentration of greater than 20 ng/mL in the absence of an associated myeloid-neoplasm; in the case of a known HαT, the tryptase level could be adjusted

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Xolair (Omalizumab)	Asthma	Route of Administration: Subcutaneous ≥6 to <12 Year(s) 20-150kg 375mg every 2 weeks

		≥12 Year(s) 30-150kg 375mg every 2 weeks
Xolair (Omalizumab)	Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)	Route of Administration: Subcutaneous ≥18 Year(s) 31-150kg 600mg every 2 weeks
Xolair (Omalizumab)	Chronic Spontaneous Urticaria	Route of Administration: Subcutaneous ≥12 Years 300mg every 4 weeks
Xolair (Omalizumab)	IgE-mediated Food Allergy	Route of Administration: Subcutaneous ≥1 year 10-150kg 600mg every 2 weeks
Xolair (Omalizumab)	Immune Checkpoint Inhibitor-Related Toxicity	Route of Administration: Subcutaneous 600mg every 2 weeks
Xolair (Omalizumab)	Systemic Mastocytosis	Route of Administration: Subcutaneous 600mg every 2 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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EFFECTIVE DATE 12/2/2025

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