Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Omalizumab [Xolair®]	MP-RX-FP-105-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: TYPE B DRUG

Service Description

This document addresses the use of Omalizumab (Xolair®), an anti-IgE antibody drug approved by the Food and Drug Administration (FDA) for the treatment of asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), chronic idiopathic urticaria, and IgE-mediated food allergy.

Background Information

This document addresses the use of Xolair (omalizumab), an anti-IgE antibody that binds to IgE, preventing its attachment to FcεRI receptors on mast cells and basophils, thereby inhibiting the release of inflammatory mediators. It is approved by the Food and Drug Administration (FDA) to treat moderate to severe persistent asthma in individuals 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms inadequately controlled with inhaled corticosteroids. Xolair also has FDA approved indications as add-on maintenance treatment of nasal polyps in adults with inadequate response to nasal corticosteroids as well as treatment of chronic idiopathic urticaria in individuals aged 12 and older who remain symptomatic despite H1 antihistamine treatment. In February 2024, the FDA approved a new indication for Xolair (omalizumab) for use in adults and children aged 1 year and older to reduce IgE-mediated food allergies.

Asthma

FDA approval for Xolair for moderate to severe persistent asthma was based in part on the results of three randomized, double-blind, placebo-controlled, multi-center trials where the number of asthma exacerbations was the principal outcome. The trials enrolled subjects with moderate to severe persistent asthma, a positive skin test reaction to a perennial aeroallergen and a total IgE level greater than 30 IU/mL. The number of exacerbations was reduced in those receiving Xolair compared to the placebo group. However, individuals whose forced expiratory volume in 1 second (FEV1) was greater than 80% predicted at enrollment did not experience a reduction in exacerbations.

The 2023 Global Initiative for Asthma (GINA) guidelines list Xolair as a treatment option in Step 5 of their asthma management algorithm. Add-on targeted biologic therapy should be considered for individuals with severe asthma experiencing exacerbations or poor symptom control despite taking at least high-dose inhaled corticosteroid/long acting beta2 –agonists and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids.

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Comparative Doses for Inhaled Corticosteroids (Adults and Adolescents) (Wenzel 2021)

Drug	Low Daily Dose	Medium Daily Dose	High Daily Dose
Beclomethasone 40 or 80 mcg/actuation	80-160 mcg	>160-320 mcg	>320-640 mcg
Budesonide 90 or 180 mcg/actuation	180-360 mcg	>360–720 mcg	>720-1440 mcg
Ciclesonide 80 or 160 mcg/actuation	160 mcg	320 mcg	640 mcg
Fluticasone propionate MDI: 44, 110 or 220 mcg/actuation DPI: 50, 100 or 250 mcg/dose	176–220 mcg 100-250 mcg	>220–440 mcg >250–500 mcg	>440-1760 mcg >500-2000 mcg
Fluticasone furoate 50, 100 or 200 mcg/dose	50 mcg	100 mcg	200 mcg
Mometasone MDI: 50, 100 or 200 mcg/actuation DPI: 110 or 220 mcg/actuation	200 mcg 220 mcg	>200-400 mcg >220-440 mcg	>400-800 mcg >440-880 mcg

DPI = dry powder inhaler, MDI = metered dose inhaler

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

FDA approval for Xolair for chronic rhinosinusitis with nasal polyps (CRSwNP) was based on the results of two randomized, double-blind, placebo-controlled, multi-center trials where nasal polyp score (NPS) and nasal congestion score (NCS) were the principal outcome. The trials enrolled subjects with nasal polyps with inadequate response to nasal corticosteroids and a total IgE level greater than 30 IU/mL. Participants received Xolair or placebo in addition to background nasal mometasone therapy. The Xolair group had a statistically significant greater improvement at week 24 in NPS and NCS compared to the placebo group.

In 2014, the Joint Task Force on Practice Parameters (JTFPP) representing the American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI) and the Joint Council of Allergy, Asthma & Immunology published a practice parameter on the diagnosis and management of rhinosinusitis. In 2015, the American Academy of Otolaryngology Head and Neck Surgery Foundation (AAO-HNS) published a clinical practice guideline on adult sinusitis. Both publications recommend confirming a clinical diagnosis of nasal polyps with imaging using anterior rhinoscopy, nasal endoscopy or computed tomography (CT). Intranasal corticosteroids are recommended for long-term treatment of nasal polyps. A short course of oral corticosteroids is included as a reasonable option to decrease polyp size and alleviate symptoms. Sinonasal surgery is another treatment option. The AAAAI/ACAAI guidance recommends consideration of Xolair for the treatment of nasal polyps when other medical and surgical options have failed.

In 2022, the JTFPP published guidelines for the medical management of chronic rhinosinusitis with nasal polyposis (CRSwNP). The guidelines focus on select interventions for treatment of CRSwNP including intranasal corticosteroids, biologics and aspirin therapy after desensitization. The guidelines recommend intranasal corticosteroids over no intranasal corticosteroids in individuals with CRSwNP. The guidelines also recommend biologics over no biologics but note it is a conditional recommendation as other treatment options should be considered or used together with biologics (including inhaled corticosteroids and surgery).

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Chronic Spontaneous Urticaria (CSU)

Chronic spontaneous urticaria (CSU) is defined as itchy hives that last at least 6 weeks and have no apparent external trigger. The 2014 guidance from the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI) and the Joint Council of Allergy, Asthma & Immunology, provides a step-based approach to the treatment of chronic urticaria. Xolair is included as an option in Step 4 of the algorithm when chronic urticaria has been refractory to treatment with potent antihistamines and leukotriene receptor antagonists.

In 2022, the Dermatology Section of the European Academy of Allergology and Clinical Immunology (EAACI), the Global Allergy and Asthma European Network (GA²LEN) and its Urticaria and Angioedema Centers of Reference and Excellence (UCAREs and ACAREs), the European Dermatology Forum (EDF) and the Asia Pacific Association of Allergy, Asthma, and Clinical Immunology (APAAACI) released guidelines on the management of urticaria. The international association suggests second generation H1 antihistamine as first-line treatment for all types of urticaria. Recommended second-line treatment for chronic urticaria is up dosing of an H1 antihistamine up to four-fold the standard dose. Xolair can be added on for individuals unresponsive to high dose second generation H1 antihistamines.

Ig-E-mediated Food Allergy

Xolair is approved by the FDA for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric individuals aged 1 year and older with IgE-mediated food allergy. IgE-mediated food allergy diagnosis is based on clinical history with confirmation by skin test, blood test or oral food challenge. Xolair must be used in combination with allergen avoidance. Xolair is not indicated for emergency treatment of allergic reactions and all individuals must have access to an auto-injectable epinephrine agent.

Xolair carries a black box warning for anaphylaxis. Anaphylaxis has been reported after the first dose of Xolair but also beyond one year after beginning treatment. Xolair should be initiated in a healthcare setting and individuals should be closely observed for an appropriate period of time. Health care providers should be prepared to manage anaphylaxis, and individuals should be instructed on anaphylaxis signs and symptoms and to seek immediate medical care should they occur. Selection of individuals for self-administration of Xolair should be based on criteria to mitigate risk from anaphylaxis.

Approved Indications

A. Moderate to Severe Persistent Asthma
B. Chronic Idiopathic Urticaria (CIU)
C. Nasal Polyps
D. IgE-Mediated Food Allergy

Other Uses

i. N/A

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J2357	Injection, omalizumab, 5 mg [Xolair]

ICD-10	Description
J33.0-J33.9	Nasal polyp
J44.0-J44.9	Other chronic obstructive pulmonary disease [with asthma]
J45.20-J45.998	Asthma
L50.0-L50.9	Urticaria
Z91.010	Allergy to peanuts
Z91.011	Allergy to milk products
Z91.012	Allergy to eggs
Z91.013	Allergy to seafood
Z91.014	Allergy to mammalian meats
Z91.018	Allergy to other foods

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

B vs D Criteria: All drugs included in this PA are subject to B vs D evaluation. Medication must be furnished "incident to" physician service provided and usually not self-administered to be covered by Medicare and to be eligible to be evaluated through part B. If not, medication must be evaluated through part D.

Omalizumab (Xolair®)

I. Asthma

A. Criteria for Initial Approval

Initial requests for Xolair (omalizumab) for moderate to severe persistent asthma may be approved if the following criteria are met:

i. Individual is 6 years of age or older; **AND**
ii. Individual has a diagnosis of moderate to severe persistent asthma; **AND**
iii. Documentation is provided that individual has had a 3-month trial and inadequate response or intolerance to combination controller therapy (high doses of inhaled corticosteroids plus long acting beta2 –agonists, leukotriene modifiers, long-acting muscarinic antagonists or oral corticosteroids) (GINA 2023); **AND**
iv. Individual has a positive skin test or in vitro reactivity to a perennial aeroallergen; **AND**
v. Individual has a pretreatment forced expiratory volume in one second (FEV_1) less than 80% predicted; **AND**
vi. Documentation is provided that individual has a serum Immunoglobulin E (IgE) level equal to or greater than 30 IU/mL.

B. Criteria for Continuation Therapy

Continuation requests for Xolair (omalizumab) for moderate to severe persistent asthma may be if approved if the following criteria are met:

i. Treatment with Xolair has resulted in clinical improvement in one or more of the following:
   A. Decreased utilization of rescue medications;
   OR
   B. Decreased frequency of exacerbations (defined as worsening of asthma that requires increase in inhaled corticosteroid dose or treatment with systemic corticosteroids);
   OR
   C. Increase in percent predicted FEV_1 from pretreatment baseline;
   OR
   D. Reduction in reported asthma-related symptoms, such as but not limited to wheezing, shortness of breath, coughing, fatigue, sleep disturbance, or asthmatic symptoms upon awakening; **AND**

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ii. Individual continues to use Xolair in combination with inhaled corticosteroid-based controller therapy.

II. Chronic Rhinosinusitis with nasal polyps (CRSwNP)

A. Criteria for Initial Approval

Initial requests for Xolair (omalizumab) for nasal polyps may be if approved if the following criteria are met:

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of nasal polyps; **AND**
iii. Documentation is provided that presence of bilateral nasal polyps demonstrated on by one of the following (AAO-HNS 2015):
    A. Anterior rhinoscopy; OR
    B. Nasal endoscopy; OR
    C. Computed tomography (CT); **AND**
iv. Individual has had a trial and inadequate response to maintenance intranasal corticosteroids; **AND**
v. Individual is refractory to or is ineligible or intolerant to the following (AAAAI/ACAAI 2014, JTFPP 2022):
    A. Systemic corticosteroids; **OR**
    B. Sinonasal surgery; **AND**
vi. Individual is requesting Xolair as add-on therapy to maintenance intranasal corticosteroids; AND
vii. Documentation is provided that individual has a serum Immunoglobulin E (IgE) level greater than or equal to 30 IU/mL.

B. Criteria for Continuation of Therapy

Continuation requests for Xolair (omalizumab) for chronic rhinosinusitis with nasal polyps (CRSwNP) may be if approved if the following criterion is met:

i. Treatment with Xolair has resulted in clinically significant improvement in clinical signs and symptoms of disease (including but not limited to improvement in nasal congestion or reduced nasal polyp size; **AND**
ii. Individual continues to use Xolair in combination with maintenance intranasal corticosteroids.

III. Chronic Spontaneous Urticaria (CSU)

A. Criteria for Initial Approval

Initial requests for Xolair (omalizumab) for chronic spontaneous idiopathic urticaria (CSU) may be approved if the following criteria are met:

i. Individual is 12 years of age or older; **AND**

ii. Individual has a diagnosis of chronic spontaneous idiopathic urticaria (CSU); **AND**
iii. Individual has had an inadequate response to a two week trial of a second generation H1 antihistamine up dosed to a maximum of four times the approved dose (EAACI 2022).

B. Criteria for Continuation of Therapy

Continuation requests for Xolair (omalizumab) for chronic spontaneous urticaria (CSU) may be approved if the following criterion is met:

i. Treatment with Xolair has resulted in clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to itch severity and hive count); **AND**
ii. Individual continues to use Xolair in combination with second generation H1 antihistamine therapy.

IV. IgE-mediated Food Allergy

A. Criteria for Initial Approval

Initial requests for Xolair (omalizumab) for IgE-mediated food allergy may be if approved if the following criteria are met:

i. Individual is 1 year of age or older; **AND**
ii. Individual has a diagnosis of IgE-mediated food allergy; **AND**
iii. Diagnosis is confirmed via:
    A. Clinical history of IgE-mediated food allergy demonstrated by moderate to severe symptoms (including but not limited to throat tightness, dyspnea/wheezing, clinically signification hypotension, generalized urticaria) or requiring administration of epinephrine or emergency medical care; **AND**
    B. Positive skin prick test or positive serum IgE test or positive food challenge; **AND**
iv. Individual has a serum Immunoglobulin E (IgE) level equal to or greater than 30 IU/mL; **AND**
v. Individual will use Xolair in combination with food allergen avoidance; **AND**
vi. Individual has a prescription for an auto-injectable epinephrine agent.

B. Criteria for Continuation of Therapy

Continuation requests for Xolair (omalizumab) for IgE-mediated food allergy may be approved if the following criterion is met:

i. Individual will use Xolair in combination with food allergen avoidance; **AND**
ii. Individual has a prescription for an auto-injectable epinephrine agent.

Conditions not Covered:

Xolair (omalizumab) may not be approved for the following:

i. In combination with Cinqair, Dupixent, Fasenra, Nucala, or Tezspire; **OR**

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ii. May not be approved with the above criteria are not met and for all other indications.

Authorization Duration

i. Initial Approval Duration: 6 months
ii. Reauthorization Approval Duration: 12 months

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Limits or Restrictions

A. Therapeutic Alternatives
The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Xolair (omalizumab) 75 mg/0.5 mL prefilled syringe/autoinjector	2 prefilled syringes/autoinjectors per 28 days
Xolair (omalizumab) 150 mg vial, 150 mg syringes	4 vials/prefilled syringes/autoinjectors per 28 days
Xolair (omalizumab) 300 mg/2 mL prefilled syringe/autoinjector 2	2 prefilled syringes/autoinjectors per 28 days
Exceptions	
For chronic rhinosinusitis with nasal polyps or IgE-mediated fold allergy, may approve up to 600 mg every 2 weeks.	

Reference Information

1. Bernstein JA, Lang DM, Khan DA, et al. Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology. Practice parameter: the diagnosis and management of acute and chronic urticaria: 2014 update. JAllerg Clin Immunol. 2014; 133(5):1270-1277.
2. Chinthrajah RS, Jones SM, Kim EH, et al. Updating the CoFAR Grading Scale for Systemic Allergic Reactions in Food Allergy. J Allergy Clin Immunol. 2022 June;149(6): 2166–2170.
3. Chung KF, Wenzel SE, Brozek JL, et al. International European Respiratory Society/American Thoracic Society (ERS/ATS) guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014; 43(2):343-373.
4. Cloutier MM, Baptist AP, Blake KV, et. al. 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program (NAEPP) Coordinating Committee Expert Panel Working Group. J Allergy Clin Immunol. 2020 Dec;146(6):1217-1270.
5. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 26, 2023.
6. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
7. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: https://ginasthma.org/2023-gina-main-report/. Accessed on: January 5, 2024.
8. Holguin F, Cardet JC, Chung KF, et. al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020 Jan 2;55(1):1900588.
9. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
10. National Asthma Education and Prevention Program (NAEPP). Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. NIH Publication Number 08-5846. Updated: August 5, 2008. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm. Accessed: February 5, 2023.
11. Peters AT, Spector S, Hsu J, et al. Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of llergy, Asthma & Immunology (AAAAI), the American College of Allergy, Asthma & Immunology (ACAAI) and the Joint Council of Allergy, Asthma & Immunology. Diagnosis and management of rhinosinusitis: a practice parameter update. American College of Allergy, Asthma & Immunology. 2014;113:347-385.
12. Rank MA, Chu DK, Bognanni A, et. al. The Joint Task Force on Practice Parameters (JTFPP) GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. J Allergy Clin Immunol. 2022;S0091-6749(22)01484-1.
13. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et.al. American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNS). Clinical Practice Guideline (Update): Adult Sinusitis. Otolaryngology-Head and Neck Surgery. 2015;152(2S)SI-S39.
14. Wenzel S. Treatment of severe asthma in adolescents and adults. Last updated: October 21, 2022. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: January 27, 2023.
15. Wood RA, Togias A, Sicherer SH, et al. Omalizumab for the Treatment of Multiple Food Allergies. N Engl J Med. 2024;390(10):889-899.
16. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022;77:734–766.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Choose an item.		Click or tap to enter a date.	Click or tap to enter a date.
Annual Review 3/20/2024	Wording and formatting changes. Update all sections to accommodate format. Update guideline references. Update prior trial requirement in Xolair urticaria criteria. Update continuation criteria, conditions not covered and approval duration. Update criteria for nasal polyp indication and urticaria indication to reflect updated labeling. Convert from dosing limits to quantity limits. Add quantity limits for 300 mg injection and autoinjectors. Update guideline references. Update background information, medication necessity guidelines (initial and continuation criteria) and quantity limit for new IgE-mediated food allergy indication. Coding Reviewed: Added ICD-10-CM Z91.010, Z91.011, Z91.012, Z91.013, Z91.014, Z91.018.	3/14/2025	4/2/2025
Policy Inception 2/24/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023