P&T Date: 06/05/2025

Omalizumab Products
Omalizumab-igec
Omlyclo® (omalizumab-igec)
Xolair® (omalizumab)

HCPCS: Omlyclo**:** J3590**;** Xolair: J2357

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of uncontrolled moderate to severe allergic asthma
      i. Positive skin test or in-vitro reactivity to a perennial aeroallergen
      ii. Chronic administration of systemic corticosteroids or high dose inhaled corticosteroids (listed in table 1) in combination with
         1. Long acting inhaled β2 agonist (LABA) modifier for at least 3 months fails to maintain adequate control
            OR
         2. Leukotriene modifier for at least 3 months fails to maintain adequate control
            OR
         3. Long acting muscarinic antagonists (LAMA) in adults and children 12 years of age and older for at least 3 months fails to maintain adequate control
      iii. IgE level greater than 30 but less than 700 IU/mL for patients 12 years of age and older
         OR
         IgE level greater than 30 but less than 1,300 IU/mL for patients 6 years to less than 12 years of age
   c. Diagnosis of chronic idiopathic urticaria (CIU)
      i. Must have occurrence of almost daily hives and itching for at least 6 weeks
      ii. Past trial and failure of all of the following for at least 2 months:
         1. Trial and failure of a second-generation antihistamine at the maximal tolerated dose
            AND
         2. Trial and failure of one of the following at maximal dosing:
            a) Another second-generation antihistamine
            b) H2 antagonist
            c) Leukotriene receptor antagonist
            d) First generation antihistamine given at bedtime
            e) Hydroxyzine
            f) Doxepin
      iii. Other diagnoses have been ruled out

d. Diagnosis of nasal polyps
    i. Patient is currently receiving and will continue to receive the standard of care regimen
    ii. Inadequate response to treatment with intranasal corticosteroids
    iii. Baseline serum total IgE level of 30 IU/mL to 1,500 IU/mL prior to initiating treatment with omalizumab
e. Diagnosis of IgE-mediated food allergy
    i. Documentation of clinical history of allergic reaction following consumption of at least one of the following: peanuts, milk, eggs, wheat, cashews, hazelnuts, and walnuts
    ii. Documentation of a confirmed diagnosis of an allergy to either peanuts, milk, eggs, wheat, cashews, hazelnuts, or walnuts confirmed by one of the following:
        1. IgE specific antibodies greater than or equal to 6 kU_A/L
        2. Food-specific skin prick test (SPT)
    iii. Provider attestation that the member will be on an allergen avoidant diet while on omalizumab therapy
    iv. Must have a current prescription for epinephrine and access to an epinephrine autoinjector while using omalizumab
    v. Serum total IgE level greater than 30 but less than or equal to 1850 IU/mL
    vi. Must not be used in combination with any other food allergy desensitization therapy
f. Not to be used in combination with other biologics or targeted DMARDs for the same indication
g. For self-administration of omalizumab prefilled syringe: the patient has received the first 3 doses under the guidance of a health care provider
    i. After the first 3 doses under the guidance of a health care provider, the member will self-administer omalizumab unless clinically unable to do so
h. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met.
i. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in WyoBlue Advantage's utilization management medical drug list and/or WyoBlue Advantage's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
    a. Quantity Limits: Align with FDA recommended dosing
    b. Authorization Period: One year at a time
    c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Omalizumab is an anti-IgE antibody indicated for: moderate to severe persistent asthma in adults and pediatric patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids; chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids as add-on maintenance treatment; IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (type I), including anaphylaxis, that may occur with accidental exposure to one or more foods; and chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment. Omalizumab is not indicated for acute bronchospasm or status asthmaticus, the emergency treatment of allergic reactions, including anaphylaxis, or other forms of urticaria.

- Uncontrolled Moderate to Severe Allergic Asthma

    - Per the Global Institute for Asthma (GINA) 2024 guidelines, severe asthma is a subset of difficult-to-treat asthma that is uncontrolled despite adherence with maximal optimized high-dose inhaled corticosteroid (ICS)-LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased. Severe asthma requires treatment with high dose ICS plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains uncontrolled despite therapy. Add-on treatment for severe asthma include LAMA, leukotriene receptor antagonist (LTRA), low dose azithromycin (adults) and biologic agents for severe allergic or severe type 2 asthma. Type 2 inflammation is found in a majority of people with severe asthma and is characterized by production of cytokines such as interleukin and can also include immunoglobulin E (IgE)-mediated events involving mast cells and basophils (in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells). Anti-IgE monoclonal antibodies reduce the levels of circulating IgE and inhibit the binding of IgE to mast cells to prevent activation of the allergic cascade and decrease inflammation.

    - The GINA 2024 guidelines stepwise approach recommend those in STEP 5 to add therapy with LAMAs such as tiotropium, to refer for phenotypic assessment for biologic therapy (anti-IgE therapy, anti-IL5 therapy, or anti-IL4 therapy, or anti-thymic stromal lymphopoietin (TSLP) therapy) and to consider high-dose maintenance ICS-formoterol with as-needed low-dose ICS-formoterol as a reliever. Using ICS-formoterol as MART (maintenance and rescue therapy) as recommended by the 2024 GINA guidelines allows for budesonide products to reach high-dose per Table 1. The GINA 2024 guidelines recommend omalizumab as an add-on anti-IgE maintenance therapy option for patients with severe allergic asthma uncontrolled on high-dose ICS-LABA.

    - The IgE levels in the coverage criteria are based on the efficacy data from the clinical trials of these medications and where they were found to be most effective.

    - Review response to biologic therapy after 4 months of treatment. If the patient had a good response, the need for each medication should re-evaluated, but do not completely stop inhaled therapy. Consider gradually decreasing or stopping oral steroids first.

- Chronic Spontaneous Urticaria

    - In the United States approximately 1.5 million people suffer from chronic spontaneous urticaria (CSU; previously referred to as chronic idiopathic urticaria). CSU is characterized by red, swollen, itchy and sometimes painful hives on the skin that spontaneously present and re-occur for more than 6 weeks. Up to 40% of these patients may also experience angioedema.

    - Per 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; EuroGuiDerm), and the Asia Pacific Association of Allergy, Asthma and Clinical Immunology guideline for the definition, classification, diagnosis, and management of urticaria (2022) that is endorsed by the American Academy of Dermatology and the American College of Allergy, Asthma and Immunology, CSU is defined as the appearance of wheals, angioedema, or both for more than 6 weeks due to known or unknown causes. Signs and symptoms may occur daily or almost daily or follow an intermittent/recurrent course. CSU may recur after a month or years of a patient achieving full remission.

    - The above guidelines recommend a 2nd generation H_1-antihistamine as first-line treatment for all types of urticaria and recommend updosing of a 2nd generation H_1-antihistamine up to fourfold in patients with chronic urticaria unresponsive to a standard-dosed 2nd generation H_1-antihistamine as second-line treatment

before other treatments are considered. It is recommended to add omalizumab for the treatment of patients with chronic urticaria unresponsive to high-dose 2nd generation H_1-antihistamines

- Though the guidelines strongly recommend treating according to the aforementioned algorithm, they also recognize that the use of omalizumab may be cost prohibitive. The guidelines therefore acknowledge that other more affordable alternatives with lower levels of evidence may still be relevant in certain contexts based on clinical experience and may be added if the urticaria is unresponsive to 2nd generation H_1-antihistamines alone. The most widely used of these alternatives include doxepin, H_2-antihistamines, immunosuppressives (i.e., methotrexate, mycophenolate mofetil), and leukotriene receptor antagonists (e.g., montelukast).

- 2014 guidelines from the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology recommend a similar approach to the 2022 international guidelines; however, the following alternatives are suggested prior to recommending the addition of omalizumab if the urticaria is unresponsive to 2nd generation H_1-antihistamines alone: adding a different second-generation antihistamine, adding an H_2-antihistamine, adding a leukotriene receptor antagonist, adding a first generation H_1-antihistamine at bedtime, or other adjunctive therapies like hydroxyzine or doxepin.

- Omalizumab and dupilumab are the only other drugs besides H_1-antihistamines that are FDA approved for treatment of CSU. Guidelines have not yet been updated to include dupilumab's place in therapy

- Nasal Polyps

  - Chronic rhinosinusitis with nasal polyps (CRSwNP, also referred to as nasal polyposis or nasal polyps) is a chronic inflammatory disease of the nasal passage lining or sinuses that leads to bilateral, benign soft tissue growth referred to as nasal polyps. It affects 5-12% of the general population worldwide, often occurring with other immunologic conditions such as allergies and/or asthma. The polyps are characterized by elevated eosinophil levels and are most commonly seen in the third and fourth decade of life.

  - The cornerstone of treatment for nasal polyps is intranasal corticosteroids as well as nasal saline sprays or irrigation. Systemic corticosteroids may also be used short term (10-15 days) to reduce severe polyp inflammation and symptoms like impaired sense of smell or severe nasal blockage.

  - For patients with refractory disease that has not responded to intranasal and oral corticosteroids, biologic therapy and/or functional endoscopic sinus surgery (FESS) may be considered. Surgery must be followed with maintenance therapy with intranasal corticosteroids and other appropriate therapies to prevent recurrence of polyps. No comparative studies or guidelines are available that recommend one treatment option over another for refractory cases.

  - Maintenance therapies are initiated once symptoms have been controlled to minimize inflammation and prevent the regrowth of nasal polyps after surgery. The mainstay of maintenance treatment is intranasal glucocorticoids. Leukotriene inhibitors may also be of benefit as adjunctive therapy, particularly if allergic rhinitis or aspirin-exacerbated respiratory disease are suspected contributing factors.

- IgE-Mediated Food Allergy

  - The 2010 National Institute of Allergy and Infectious Disease Guidelines for the Diagnosis and Management of Food Allergies in the United States recommend suspecting a food allergy in patients presenting with anaphylaxis upon ingestion of food within minutes to hours of ingesting food; in infants, young children, and selected older children diagnosed with certain disorders, such as moderate to severe atopic dermatitis, eosinophilic esophagitis, enterocolitis, enteropathy, and food protein-induced allergic proctocolitis; and in

adults diagnosed with eosinophilic esophagitis. Guidelines state the causative food must be identified through one of the following tests: skin prick tests, intradermal tests, total serum IgE, allergen-specific IgE, atrophy patch test, food elimination diets, or oral food challenges. In clinical trials for Xolair, the diagnosis of food allergy was confirmed through serum specific IgE levels or positive SPT for the following foods: peanuts, milk, eggs, wheat, cashews, hazelnuts, and walnuts. Patients must have had a 4 mm wheal or greater than saline control on SPT or a serum specific IgE greater than or equal to 6 kU_A/L in combination with clinical history of allergic reaction following consumption of peanuts and two other foods to be enrolled in the clinical trial.

- Omalizumab does not provide a cure for food allergies but reduces the risk of potentially life-threatening accidental exposure to food allergens. Omalizumab was superior to placebo in increasing the reaction threshold for peanut, cashew, egg, and milk. Sixty-seven percent of the participants who received omalizumab were able to successfully consume at least 600 mg of peanut protein (cumulative dose, 1044 mg, equivalent to approximately 4 peanuts). This protection still requires ongoing dosing of omalizumab as well as continued avoidance of allergenic foods. Despite the reduced risk of life-threatening reactions, omalizumab does have several serious warnings related to its use, including anaphylaxis. Because of the risk of anaphylaxis, patients should still have a current prescription for epinephrine and access to an epinephrine autoinjector.

- Omalizumab requires patients have total IgE levels of 30 but less than or equal to 1850 IU/mL to adequately dose them based on their body weight. Omalizumab should not be used for IgE-mediated food allergy in those with total IgE levels less than 30 IU/mL or greater than 1850 IU/mL.

- Omalizumab has not been studied and there is no data to support use in combination with other medications used for desensitization of food allergy.

- Omalizumab prefilled syringes for self-administration by certain patients or their caregiver have been approved for all of the indications as the healthcare administered product. Omalizumab prefilled syringes were previously for clinician administration only. Omalizumab's lyophilized powder in single-dose vials can still only be administered by a healthcare provider. Patients should receive 3 doses of omalizumab under the guidance of a healthcare provider due to risk of anaphylaxis before transitioning to self-administration.

- Omalizumab has not been studied and there is no data to support use in combination with other biologic agents and targeted DMARD indicated for any of Omalizumab's approved indications.

References:

1. Xolair [package insert]. South San Francisco, CA: Genentech Omalizumab; February 2024.
2. Omlyclo [package insert]. Jersey City, NJ; Celltrion; March 2025.
3. Novartis. Novartis reports new Phase III data showing omalizumab significantly improves itch in patients with severe form of chronic skin disease CSU. Media Releases. July 2013. Available at: http://www.novartis.com/newsroom/media-releases/en/2013/1712004.shtml. Accessed October 15, 2013.
4. AAAA. Omalizumab: well tolerated and effective in refractory chronic idiopathic spontaneous urticaria. American Academy of Allergy Asthma and Immunology Release. July 2013. Available at: https://www.aaaai.org/global/latest-research-summaries/Current-JACI-Research/omalizumab.aspx. Accessed October 15, 2013.
5. Blumchen K, Ulbricht H, Staden U, et al. Oral peanut immunotherapy in children with peanut anaphylaxis. J Amer Clin Immunol. 2010; 126: 83 - 91.
6. U.S. Department of Health and Human Services – National Institutes of Health. National Asthma Education and Prevention Program Expert Panel Report 3: 2020 Focused Updates to the Asthma Management Guidelines. December 2020. Available at: https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates. Accessed May 19, 2021.
7. Greaves M. Chronic idiopathic urticaria. Curr Opin Allergy Clin Immunol. 2003; 3: 363 - 8.

8. Novartis. Novartis announces US FDA approval of Xolair for chronic idiopathic urticaria (CIU). Thomas Reuters One. March 21, 2014. Available at: http://www.novartis.com/newsroom/media-releases/en/2014/1770973.shtml. Accessed March 22, 2014.
9. The diagnosis and management of acute and chronic urticaria 2014 update. (n.d.). https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Urticaria-2014.pdf. Accessed September 1, 2017.
10. Zuberier T, Aberer W, Asero R, et al. The EAACI/GALEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2018; 73: 1393 – 414.
11. Zuberier T and Bernstein JA. A comparison of the united states and international perspective on chronic urticaria guidelines. J Allergy Clin Immunol Pract. July/August 2018; 6 (4): 1144 – 1511.
12. Dupixent [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals; June 2021.
13. Gevaert P, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. J Allergy Clin Immunol. 2020 Sept; 146 (3): 595-605.
14. Hamilos DL and Holbrook EH. Chronic rhinosinusitis: management. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2020.
15. Bhattacharyya N. Nasal obstruction: diagnosis and management. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2020.
16. IPD Analytics Rx Brief. Xolair for chronic rhinosinusitis with nasal polyps. Published December 2020.
17. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024. Available from: www.ginasthma.org.
18. Clinicaltrials.gov. Omalizumab as monotherapy and as adjunct therapy to multi-allergen oral immunotherapy (OIT) in food allergic children and adults (NCT03881696). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03881696. Accessed on February 23, 2024.
19. Gupta RS, Springston EE, Warrier MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. Pediatrics. 2011; 128 (1): e9 - 17.
20. Gupta RS, Warren CM, Smith BM, et al. The public health impact of parent-reported childhood food allergies in the united states. Pediatrics. 2018; 142 (6): e20181235.
21. Bock SA, Munoz-Furlong A, Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001-2006. J Allergy Clin Immunol. 2007; 119 (4): 1016 - 18.
22. Gupta R, Holdford D, Bilaver L, et al. The economic impact of childhood food allergy in the United States. JAMA Pediatr. 2013; 167 (11): 1026 - 31.
23. Panel NI-SE, Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010; 126 (6 Suppl): S1 - 58.
24. Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update-2014. J Allergy Clin Immunol. 2014; 134 (5): 1016 - 25.
25. 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. doi:10.1111/all.15090

Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Table 1: Comparative cumulative daily dosing of inhaled corticosteroids (mcg/day)

Inhaled Corticosteroid	Ages 12 and up			Ages 6-11		
	Low Dose	Medium Dose	High Dose	Low Dose	Medium Dose	High Dose
Beclometasone dipropionate HFA	100 – 200	>200 – 400	>400	50 – 100	>100 – 200	>200
Budesonide DPI	200 – 400	>400 – 800	>800	100 – 200	>200 – 400	>400
Budesonide nebules	NA	NA	NA	250 – 500	>500 – 1,000	>1,000
Ciclesonide HFA	80 – 160	>160 – 320	>320	80	>80 – 160	>160
Fluticasone furoate DPI	100	NA	200	NA	NA	NA
Fluticasone propionate DPI	100 – 250	>250 – 500	>500	100 – 200	>200 – 400	>400
Fluticasone propionate HFA	100 – 250	>250 – 500	>500	100 – 200	>200 – 500	>500
Mometasone furoate	110 – 220	>220 – 440	>440	110	≥220 - <440	≥440
Triamcinolone acetonide	400 – 1,000	>1,000 – 2,000	>2,000	400 – 800	>800 – 1,200	>1,200