RX.PA.037.MPC IMMUNOLOGICALS – XOLAIR (OMALIZUMAB INJECTION FOR SUBCUTANEOUS (SC) USE – GENENTECH/NOVARTIS)

OVERVIEW

Xolair is a recombinant humanized immunoglobulin G (IgG)1κ monoclonal antibody which selectively binds to human immunoglobulin E (IgE), thus inhibiting IgE from binding to the surface of mast cells and basophils (at the high-affinity IgE receptor [FcεRI]), and resulting in a decrease of mediators released in the allergic response.[1] Xolair treatment also reduces the number of FcεRI receptors on basophils in atopic patients. Xolair is indicated for use in patients ≥ 6 years of age with moderate to severe persistent asthma and who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids (ICSs). Xolair decreases the incidence of asthma exacerbations in these patients. Safety and efficacy of Xolair in pediatric patients with asthma aged < 6 years have not been established. Xolair is also indicated for the treatment of adults and adolescents (aged ≥ 12 years) with chronic idiopathic urticaria who remain symptomatic despite H_1 antihistamine treatment. In chronic idiopathic urticaria, Xolair binds to IgE and lowers free IgE levels; subsequently, FcεRI on cells down-regulate. How these effects of Xolair result in an improvement in chronic idiopathic urticaria is not known. Xolair is not indicated for the treatment of other allergic conditions, other forms of urticaria, for relief of acute bronchospasm, or status asthmaticus.

Guidelines

Asthma Guidelines

Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention proposes a step-wise approach to asthma treatment.[2] Patients with persistent symptoms or exacerbations despite a medium-dose ICS/long-acting beta$_2$-agonist (LABA) combination with or without an additional controller, GINA recommends referral of the patient to a specialist with expertise in the management of severe asthma for phenotypic assessment and add-on treatment. Xolair is listed as an option for add-on therapy in patients ≥ 6 years of age with moderate or severe allergic asthma. Blood eosinophil levels ≥ 260 cells per microliter, fractional exhaled nitric oxide (FeNO) ≥20 ppb, allergen-driven symptoms, and childhood-onset asthma may predict a good asthma response to Xolair.

The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014) for the definition, evaluation, and treatment of severe asthma suggest a trial of Xolair in both adults and children with severe allergic asthma.[3] If a trial of Xolair is considered, patients (adults and children ≥ 6 years of age) should have confirmed IgE-dependent allergic asthma that is uncontrolled despite optimal pharmacological and non-pharmacological management and appropriate allergen avoidance and their total serum IgE level should be ≥ 30 IU/mL and < 700 IU/mL. It is also noted that further

administration of Xolair is unlikely to be beneficial if a patient does not respond to therapy within the first 4 months of treatment. The ERS/ATS guidelines also provide a definition of severe asthma. Severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy. Uncontrolled asthma is defined as asthma that meets one of the following four criteria: poor symptom control; frequent severe exacerbations; serious exacerbations; or airflow limitation. Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids.

Urticaria Guidelines
Urticaria guidelines from the European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA[2]LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) [2018] also stress the importance of identification and elimination of underlying causes and trigger avoidance followed by pharmacologic treatment to reduce release of mast cell mediators (e.g. histamine) and/or decrease the effect of these mast cell mediators at target organs.[4] Continuous therapy with antihistamines (second generation H_1-antagonists) is recommended as first-line treatment. If symptoms persist following 2 to 4 weeks of initial therapy, the dose of the second generation H_1-antagonist should be increased to up to 4-fold. If symptoms persist an additional 2 to 4 weeks despite the higher dosing, the addition of Xolair may be considered. Cyclosporine is referenced as an add-on therapy to Xolair if there is inadequate control or symptoms are intolerable within 6 months. Short courses of oral corticosteroids may also be considered if needed to control exacerbations. However, long-term use of systemic corticosteroids is not recommended.

In 2014, the American Academy of Allergy, Asthma, & Immunology (AAAAI); the American College of Allergy, Asthma, & Immunology (ACAAI); and the Joint Council of Allergy, Asthma, & Immunology (JCAAI) published a Joint Task Force Practice Parameter on the diagnosis and management of acute and chronic urticaria.[5] This parameter recommends a four-step approach to treatment of chronic urticaria. Initially, trigger avoidance is indicated along with a second generation antihistamine (Step 1). Step 2 includes increasing the dose of the antihistamine; a 2- to 4-fold increase in the FDA-approved dose of the second-generation antihistamine may be effective to achieve symptom control in some patients. Additionally, adding a second non-sedating antihistamine, an H_2 antagonist, a leukotriene receptor antagonist (LTRA), or a first generation antihistamine to be taken at bedtime may also be beneficial. If the patient's urticarial remains poorly controlled, hydroxyzine or doxepin may be considered as part of Step 3 therapy. Patients with refractory chronic urticaria (Step 4) may consider other alternative therapies, such as Xolair and cyclosporine.

Nasal Polyp Guidelines

A 2014 Practice Parameter on the Diagnosis and Management of Rhinosinusitis and a 2020 Practice Parameter for the Management of Rhinitis from the JTFPP , and a 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology (AAO), make similar recommendations regarding the diagnosis and management of chronic rhinosinusitis with nasal polyposis (CRSwNP).[20-24] The presence of two or more signs and symptoms of chronic rhinosinusitis (e.g., rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge) that persist for an extended period of time makes the diagnosis CRS likely. However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography scan. Nasal corticosteroids are recommended for the management of CRSwNP, as they decrease nasal polyp size, prevent regrowth of nasal polyps following surgical removal, and improve nasal symptoms. Short courses of oral corticosteroids are also recommended. Endoscopic surgical intervention may be considered as an adjunct to medical therapy in patients with chronic rhinosinusitis that is not responsive or is poorly responsive to medical therapy. The JTFPP parameter lists Xolair as a therapy that may be considered for the treatment of nasal polyps based on the limited data available at the time of publication. The AAO guidelines do not address Xolair.

The European Forum for Research and Education in Allergy expert board on uncontrolled severe chronic rhinosinusi CRSwNP and biologics (2021) recommends that these agents, including Xolair, only be used for severe uncontrolled CRSwNP when Type 2 inflammation is present.[49] Severe CRSwNP is defined as bilateral CRSwNP with a nasal polyp score ≥ 4 and persistent symptoms (e.g., loss of smell/taste, nasal obstruction, secretion or postnasal drip, facial pain or pressure) with the need for add-on treatment to supplement intranasal corticosteroids. Severe CRSwNP is considered to be uncontrolled if the patient has received continuous treatment with an intranasal corticosteroid and has needed at least one course of systemic corticosteroids in the previous 2 years (or has a medical contraindication or intolerance) and/or has a previous sinonasal surgery.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Xolair. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xolair, as well as the monitoring required for adverse events and long-term efficacy, initial and continuing approval requires Xolair to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration listed below.

Automation: None.

A. RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Xolair is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Asthma.** Approve Xolair for the duration noted if the patient meets one of the following conditions (A or B):
   - **A)** Initial Therapy. Approve Xolair for 4 months if the patient meets the following criteria (i, ii, iii, iv, v, vi, vii, viii. ix, and x):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Xolair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
     - **iii.** Patient has a baseline (prior to treatment with Xolair or anti-interleukin-4/13 therapy [Dupixent]) immunoglobulin E (IgE) level ≥ 30 IU/mL to 1300 IU/mL; AND
     - **iv.** FDA labeling and dose does not exceed 375 mg every 2 weeks; AND
     - **v.** Patient's weight is 20 kg to 150 kg; AND
     - **vi.** The patient has a baseline (prior to treatment with Xolair) positive skin test or *in vitro* test (i.e., a blood test) for allergen-specific immunoglobulin E (IgE) for one or more perennial aeroallergens AND/OR for one or more seasonal aeroallergens; AND
       Note: Examples of perennial aeroallergens are house dust mite, animal dander, cockroach, feathers, and mold spores. Examples of seasonal aeroallergens are grass, pollen, and weeds.
     - **vii.** Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b) unless contraindicated or intolerant to at least two inhaled corticosteroid containing medications
       - **a)** An inhaled corticosteroid; AND
       - **b)** At least one additional asthma controller/maintenance medication; AND
         Note: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-IL-4/13 therapy (Dupixent) used concomitantly with an inhaled corticosteroid for at least 3 consecutive months. Examples of additional asthma controller/maintenance medications are inhaled long-acting beta$_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor

antagonists, and theophylline. Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting beta$_2$-agonist would fulfil the requirement for both criteria a and b.

viii. Patient and prescriber agrees to continue asthma therapy with an asthma controller maintenance medication in conjunction with Xolair (inhaled ICS or ICS combination inhaler); AND

ix. Patient's asthma is uncontrolled or was uncontrolled prior to receiving any Xolair or anti-IL-4/13 therapy (Dupixent) therapy as defined by ONE of the following (a, b, c, d, or e):

a) The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR

b) The patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) visit in the previous year; OR

c) Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR

d) Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR

e) The patient's asthma worsens upon tapering of oral corticosteroid therapy.

x. Patient will not be concurrently receiving Xolair in combination with any anti-IL4, anti-IL5, TSLP inhibitor therapies such as Dupixent, Nucala, Cinqair, Fasenra, and Tezspire

B) Patients Continuing Xolair Therapy. Approve Xolair for 1 year if the patient meets the following criteria (i, ii, iii, iv, v, vi, and vii):

- MPC Renewal:

i. The patient has already received at least 4 months of therapy with Xolair; AND
Note: Patients who have received < 4 months of therapy or those who are restarting therapy with Xolair should be considered under criterion 1A (Asthma, Initial Therapy).

ii. Xolair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND

iii. FDA labeling and dose does not exceed 375 mg every 2 weeks; AND

iv. Patient's weight is 20 kg to 150 kg; AND

v. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND

vi. Patient will not be concurrently receiving Xolair in combination with any anti-IL4, anti-IL5, TSLP inhibitor therapies such as Dupixent, Nucala, Cinqair, Fasenra, and Tezspire

vii. The patient has responded to therapy as determined by the prescriber and has a documented clinical improvement or stabilization.
Note: Examples of a response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or medical clinic visits due to asthma; decreased reliever/rescue medication use; and improved lung function parameters.

- Non- MPC Renewal:

i. Patients who have previously been taking Xolair and are requesting a non-MPC renewal should be considered under criterion 1A (Asthma, Initial Therapy).
ii. Patient has not been receiving medication samples for Xolair; AND
iii. Patient has been established on therapy for at least 4 months and has had a documented clinically significant response, as determined by the prescriber.
Note: Examples of a response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or medical clinic visits due to asthma;decreased reliever/rescue medication use; and improved lung function parameters.

2. **Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria).** Approve Xolair for the duration noted if the patient meets one of the following conditions (A or B):
A) Initial Therapy. Approve Xolair for 4 months if the patient meets the following criteria (i, ii, iii, iv, v, and vi):
i. Patient is ≥ 12 years of age; AND
ii. Patient has been evaluated for other causes of urticaria (bradykinin-related angioedema, auto-inflammatory disorders, urticarial vasculitis); AND
iii. Xolair is prescribed by, or in consultation with, an allergist, immunologist, or dermatologist; AND
iv. Xolair dosing does not exceed FDA approved indication; AND
v. Patient will not be concurrently receiving Xolair in combination with any anti-IL4, anti-IL5, TSLP inhibitor therapies such as Dupixent, Nucala, Cinqair, Fasenra, and Tezspire; AND
vi. Patient remains symptomatic despite a 4 week trial with at least one H1 antihistamine in combination with a leukotriene receptor antagonist (LTRA), or H2 antihistamine, or another H1 antihistamine with doses that have been titrated up to a maximum of four times the standard FDA-approved dose, unless contraindicated or intolerant
Note: Examples of H_1 antihistamine therapy are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.
B) Patients Continuing Xolair Therapy. Approve Xolair for 1 year if the patient meets the following criteria (i, ii, iii, iv, and v):
- MPC Renewal:
i. Patient has been evaluated for other causes of urticaria (bradykinin-related angioedema, auto-inflammatory disorders, urticarial vasculitis); AND
ii. Xolair is prescribed by, or in consultation with, an allergist, immunologist, or dermatologist; AND
iii. Xolair dosing does not exceed FDA approved indication; AND
iv. Patient will not be concurrently receiving Xolair in combination with any IL-4, IL-5, TSLP inhibitor therapies such as Dupixent, Nucala, Cinqair, Fasenra, and Tezspire; AND

v. The patient has a documented clinical response to therapy as determined by the prescriber.
Note: Examples of a response to Xolair therapy are decreased severity of itching, decreased number and/or size of hives.

- Non- MPC Renewal:

i. Patients who have previously been taking Xolair and are requesting a non-MPC renewal should be considered under criterion 2A (Chronic Idiopathic Urticaria, Initial Therapy).
ii. Patient has not been receiving medication samples for Xolair; AND
iii. Patient has been established on therapy for at least 4 months and has had a documented clinically significant response, as determined by the prescriber.
Note: Examples of a response to Xolair therapy are decreased severity ofitching, decreased number and/or size of hives.

3. Nasal Polyps. Approve Xolair for the duration noted if the patient meets one of the following conditions (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets the following criteria (i, ii, iii, iv, v, vi, vii, viii, and ix):

i. Patient is ≥ 18 years of age; AND
ii. Patient has chronic rhinosinusitis with nasal polyposis as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND
iii. Patient has experienced two or more of the following symptoms for at least 6 months: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND
iv. Patient has a baseline immunoglobulin E (IgE) level ≥ 30 IU/mL; AND
Note: "Baseline" is defined as prior to receiving any Xolair or anti-interleukin 4/13 therapy (i.e., Dupixent [dupilumab subcutaneous injection]).
v. Patient meets BOTH of the following (a and b):
a) Patient has received at least 3 months of therapy with an intranasal corticosteroid, unless contraindicated or intolerant to two products; AND
b) Patient will receive Xolair as an add on maintenance therapy in combination with an intranasal corticosteroid unless contraindicated or intolerant; AND
vi. Patient meets ONE of the following (a, b or c):
a) Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR
b) Patient has a contraindication to systemic corticosteroid therapy; OR
c) Patient has had prior surgery for nasal polyps; AND
vii. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] physician specialist); AND
viii. Patient will not concurrently be receiving Xolair with any anti-IL4, anti-IL5, or TSLP inhibitor such as Dupixent, Cinqair, Fasenra, or Tezspire; AND
ix. Dosing does not exceed FDA approved indication

B) Patient is currently receiving Xolair. Approve for 1 year if the patient meets the following criteria (i, ii, iii, iv, v, vi, vii, and viii):

- MPC Renewal:

i. Patient is ≥ 18 years of age; AND

ii. Patient has chronic rhinosinusitis with nasal polyposis as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND

iii. Patient has already received at least 4 months of therapy with Xolair; AND

Note: A patient who has received < 4 months of therapy or who is restarting therapy with Xolair should be considered under criterion 3A (Nasal Polyps, Initial Therapy).

iv. Patient will receive Xolair as an add on maintenance therapy in combination with an intranasal corticosteroid unless contraindicated or intolerant; AND

v. Patient has responded to Xolair therapy as determined by the prescriber; AND

Note: Examples of a response to Xolair therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, and/or improved sense of smell.

vi. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] physician specialist); AND

vii. Patient will not concurrently be receiving Xolair with any anti-IL4, anti-IL5, or TSLP inhibitor such as Dupixent, Cinqair, Fasenra, or Tezspire; AND

viii. Dosing does not exceed FDA approved indication

- Non-MPC Renewal:

i. Patients who have previously been taking Xolair and are requesting a non-MPC renewal should be considered under criterion 3A (Nasal Polyps, Initial Therapy).

ii. Patient has not been receiving medication samples for Xolair; AND

iii. Patient has been established on therapy for at least 4 months and has had a documented clinically significant response, as determined by the prescriber.

iv. Note: Examples of a response to Xolair therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, and/or improved sense of smell.

B. Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling.

C. Xolair will be considered investigational or experimental for any other use and will not be covered.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Xolair has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following

conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Atopic Dermatitis (AD).** There have been several case series/reports and two small randomized, double-blind, placebo-controlled pilot studies evaluating the efficacy and safety of Xolair for the treatment of patients with AD.[6,7] Efficacy data have been mixed. One systematic review and meta-analysis reported that of the studies reviewed (n = 103 patients total), 43% of patients achieved an excellent clinical response with Xolair, while 27.2% of patients had satisfying results and another 30.1% had no clinical change or worsening of their disease. However, these data are difficult to interpret due to the very small sample sizes in each case series/report and the non-controlled,non-randomized design of the majority of the available studies. Additional larger, well-designed clinical trials are needed to determine if Xolair has a role in the treatment of AD. AD guidelines from the American Academy Dermatology (AAD) [2014] note that data are limited to determine if Xolair is efficacious in the treatment of AD.[8] These guidelines do not make a recommendation regarding Xolair use in this patient population. European consensus guidelines for the treatment of AD (2018) from multiple European dermatology associations, including the European Dermatology Forum (EDF), the European Academy of Dermatology and Venereology (EADV), and the European Academy of Allergy and Clinical Immunology (EAACI) also note the mixed data and state that they cannot recommend Xolair for the treatment of AD.[9] There is currently one randomized, double-blind, placebo controlled study evaluating Xolair for the treatment of pediatric AD (Atopic Dermatitis Anti-IgE Paediatric Trial [ADAPT]).[10] This trial is ongoing and results are not yet available.

2. **Chronic Rhinosinusitis.** A small study assessed the effects of Xolair in patients (n = 14) with chronic rhinosinusitis.[11] The majority of patients had severe and refractory disease and presented with nasal polyposis; all had undergone endoscopic sinus surgery. After 6 months Xolair-treated patients showed reduced sinus inflammation (as determined by computed tomography [CT] imaging) while placebo-treated patients showed no change in inflammation; however, the net difference between groups was not statistically significant. A small, single arm study (n = 13) also demonstrated efficacy of Xolair in improving symptoms in patients with chronic rhinosinusitis with nasal polyps.[12] Further study is warranted. The 2015 Clinical Practice Guideline: Adult Sinusitis from the American Academy of Otolaryngology (AAO) does not mention Xolair or anti-IgE therapy in its recommendations.[13]

3. **Concurrent use of Xolair with an Anti-Interleukin (IL) Monoclonal Antibody.** The efficacy and safety of Xolair used in combination with IL antagonist monoclonal antibodies (e.g., Cinqair® [reslizumab injection for intravenous use], Fasenra™ [benralizumab injection for subcutaneous use], Nucala® [mepolizumab injection for subcutaneous use], Dupixent® [dupilumab subcutaneous injection]) have not been established. There very limited case reports describing the combination use of Nucala and Xolair for severe asthma as well as off-label indications.[14-16] Further investigation is warranted.

4. **Eosinophilic Gastroenteritis (EG), Eosinophilic Esophagitis (EE), or Eosinophilic Colitis.** There are limited and conflicting data on the use of Xolair for the treatment of eosinophilic gastrointestinal conditions. In a case series evaluating patients with eosinophil-associated gastrointestinal disorders, Xolair was effective in decreasing absolute eosinophil count, allergen skin test wheal and erythema responses, and symptom scores.[17] Subsequently, a small (n = 15), open-label, single-arm, unblinded study (published) evaluated Xolair for the treatment of patients 12 to 75 years of age with EE.[18] Following 12 weeks of Xolair therapy (dose calculated in mg/kg per IU IgE units/mL), tissue IgE levels were significantly reduced in 13 of the 15 patients, with full remission (defined as histologic and clinical improvement) present in 33% of patients. Conversely, a prospective, randomized, double-blind, placebo-controlled trial (n = 30) also examined the effects of Xolair in patients 12 to 60 years of age with EE who were either refractory to or relapsed after a trial of topical corticosteroids.[18,19] Patients received either Xolair or placebo every 2 to 4 weeks for 16 weeks (dose of Xolair based on weight and serum IgE level). Xolair therapy was not found to improve the symptoms of EE (dysphagia scores) or eosinophil counts in biopsy samples when compared with placebo. An additional case series including two patients with multiple food allergies and EE reported an improvement in patient symptoms with Xolair therapy, but did not find an improvement in esophageal endoscopy and histology in short-term follow-up.[20] The 2013 American College of Gastroenterology guidelines for the diagnosis and management of esophageal eosinophilia and EE do not recommend Xolair therapy for these conditions; the guidelines note that Xolair was ineffective in a case series involving two patients

(referenced above). It is recognized that corticosteroids (systemic or topical administered by swallowing a formulation for inhalation) are the standard treatment for management of both EG and EE.[21,22] Adequate controlled clinical studies have not been conducted in patients less than 12 years of age with EG, EE, or eosinophilic colitis. A 2014 updated food allergy practice parameter from the AAAAI, ACAAI, and JCAAI Joint Task Force also addresses EE and EG, but does not address Xolair as a treatment for these conditions.[23]

5. **Latex Allergy in Health Care Workers with Occupational Latex Allergy.** A small European study assessed the effects of Xolair treatment in health care workers (n = 18) with occupational latex allergy.[24] Xolair use in these patients resulted in a reduction in mean conjunctival challenge test scores as compared with placebo-treated patients after 16-weeks of therapy. Also, three patients who did not respond to Xolair treatment during the double-blind phase responded during the 16-week open-label phase. Thus the overall ocular response rate for all patients in the open-label phase was 93.8% (n = 15/16). Also 11 of 15 patients in the open-label phase had a negative response to a latex glove challenge test (4 patients had a mild response). Well-controlled trials are needed.

6. **Peanut and Other Food Allergies.** Limited data are available regarding the use of Xolair to facilitate desensitization to food allergens. A Phase II multicenter clinical trial was initiated using Xolair in patients with peanut allergy; however, it was discontinued prematurely due to concerns regarding the safety of the oral peanut challenges in some patients.[25] Insufficient data were obtained to reach any conclusions about the efficacy of Xolair. Data are also available from a small pilot study examining the use of Xolair to facilitate rapid oral desensitization in high-risk peanut-allergic patients.[26] There are also minimal data (a Phase I study and a case series) on the use of Xolair to facilitate desensitization in patients with severe cow's milk allergy.[27-30] Additionally, a Phase I study and a Phase II study have evaluated the use of Xolair to facilitate desensitization in patients with multiple food allergies.[31,32] Guidelines for the diagnosis and management of food allergy in the US (published in 2010) indicate there are currently no medications recommended to prevent IgE-mediated or non-IgE- mediated food-induced allergic reactions from occurring in an individual with existing food allergies.[33] Allergen avoidance and use of antihistamines are recommended for treatment of food-induced allergic reactions. The updated food allergy practice parameter from the AAAAI, ACAAI, and JCAAI Joint Task Force (2014) also states that immunotherapies (such as the oral immunotherapy desensitization described above) show promise for the treatment of food allergy; however, there is currently inadequate evidence that the therapeutic benefit outweighs the risk.[23] Trials of these have been uncontrolled, small studies, which are subject to selection bias and uncertain safety profiles. However, treatment with anti-IgE monoclonal antibodies might increase the threshold for doses needed to stimulate an allergic reaction and

potentially may enhance the safety profile for patients. Additional well-controlled trials are needed.

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

HCPCS Codes:

Code	Description
J2357	Injection, Omalizumab, 5 MG

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HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Early Annual Revision	Removed the age requirement and specialist involvement from Continuation Criteria for Asthma, Chronic Idiopathic Urticaria, and Allergic Rhinitis. Added AirDuo RespiClick as an example of an ICS/LABA product. Noted generic availability of Astepro and Patanase.	04/11/2018
Selected Revision	Removed the requirement of a trial of a leukotriene modifier (e.g., montelukast) with a daily non-sedating H_1 antihistamine from the Chronic Idiopathic Urticaria criteria.	08/08/2018
Early Annual Revision	• Updated initial therapy criteria for "Asthma in Patients with Moderate to Severe Persistent Disease" to state that the baseline IgE level ≥ 30 IU/mL should be prior to treatment with Xolair or anti-IL-4/13 therapy (Dupixent). Previously criteria only noted the level should be prior to Xolair therapy. • Updated initial therapy criteria for "Asthma in Patients with Moderate to Severe Persistent Disease" to more concisely state the previous therapies required. Added the following note: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-IL-4/13 therapy (Dupixent) used concomitantly with an ICS for at least 3 consecutive months. • Updated initial therapy criteria for "Asthma in Patients with Moderate to Severe Persistent Disease" to state that the patient's asthma is uncontrolled or was uncontrolled prior to receiving any Xolair or anti-IL-4/13 therapy (Dupixent). Previously criteria only stated it should be uncontrolled prior to Xolair therapy.	01/23/2019
Annual Revision	• Asthma: Approval indication was changed from "Asthma in Patients with Moderate to Severe Persistent Disease" to "Asthma". Removed examples of *in vitro* allergen-specific IgE tests: enzyme-linked immunoabsorbant assay (ImmunoCAP™, ELISA] or the radioallergosorbent test [RAST]). Wording in reference to "according to the prescribing physician" was changed to "according to the prescriber".	02/12/2020

	Removed lists of examples of inhaled asthma controller/maintenance medications. • Chronic Idiopathic Urticaria: Wording in reference to "according to the prescribing physician" was changed to "according to the prescriber". • Allergic Rhinitis: Approval indication was changedfrom "Allergic Rhinitis, Seasonal or Perennial" to "Allergic Rhinitis". Updated requirement that patient have a positive skin test or in vitro test for allergen- specific IgE for "one or more relevant allergens" to "oneor more perennial aeroallergens AND/OR for one or more seasonal aeroallergens" (previously criteria listedboth perennial and aeroallergen examples as relevant allergens, updated wording to be consistent with Asthma approval criteria). Wording in reference to "second-generation/less-sedating antihistamines" was changed to "non-sedating H_1 antihistamines". Wording in reference to "according to the prescribing physician" was changed to "according to the prescriber". Removed lists of examples of intranasal antihistamines and intranasal corticosteroids.	
Selected Revision	• Removed Allergic Rhinitis as an "Other Use with Supported Evidence"	03/25/2020
Selected Revision	• Addition of dosing requirements and off-label restriction	12/2021
Annual review	• N/A	02/2022
Selected Revision	• Additional criteria added for asthma and chronic idiopathic urticaria indications • Criteria added for asthma indication for patient's weight requirement • Initial criteria added for treatment of nasal polyps and IgE requirements • Patient will not be concurrently receiving Xolair in combination with any anti-IL4, anti-IL5, TSLP inhibitor therapies such as Dupixent, Nucala, Cinqair, Fasenra, and Tezspire	06/2022

ICS – Inhaled corticosteroid; LABA – Long-acting $beta_2$-agonist; IgE – Immunoglobulin E; IL – Interleukin.