Utilization Review Policy 132B

POLICY: Immunologicals – Xolair® (omalizumab injection for subcutaneous [SC] use – Genentech/Novartis)

EFFECTIVE DATE: 01/01/2020
LAST REVISED DATE: 04/24/2024

COVERAGE CRITERIA FOR: UCare Medicare Plans Only (UCare Medicare, UCare Medicare with M Health Fairview and North Memorial, EssentiaCare, Group Plans, MSHO, Connect + Medicare, UCare Your Choice)

OVERVIEW

Xolair, an anti-immunoglobulin (Ig)E monoclonal antibody, is indicated for the following uses:[1]

- **Asthma,** in patients ≥ 6 years of age with moderate to severe persistent disease 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 has been shown to decrease the incidence of asthma exacerbations in these patients. Limitations of Use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus. It is also not indicated for the treatment of other allergic conditions.
- **Chronic idiopathic urticaria**, in patients ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment. Limitation of Use: Xolair is not indicated for the treatment of other forms of urticaria.
- **Chronic rhinosinusitis with nasal polyps** (CRSwNP), as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids.
- **IgE-mediated food allergy**, in patients ≥ 1 year of age, for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. Xolair is to be used in conjunction with food allergen avoidance. Limitation of Use: Xolair is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

Dosing of Xolair for the treatment of asthma or nasal polyps is based on body weight and the serum total IgE level measured before the start of treatment.[1] Dosing for these indications is only provided for patients with a pretreatment serum IgE level ≥ 30 IU/mL. Dosing of Xolair in patients with chronic idiopathic urticaria is not dependent on serum IgE level or body weight.

Clinical Efficacy

Timing of efficacy assessments varied by indication across the numerous pivotal studies in which Xolair demonstrated benefit. In the majority of the asthma trials, efficacy with Xolair was assessed as early as 16 weeks.[1-11] In chronic idiopathic urticaria, one of the studies included a 12-week double-blind treatment period, while the other was longer with 24 weeks of double-blind treatment.[12,13] Across both studies evaluating Xolair in nasal polyps, efficacy was evaluated at Week 24.[14] Patients continued treatment with intranasal corticosteroids throughout the study. In the pivotal study of Xolair for food allergy, patients were required to have a positive skin prick test response to a food and to have a positive IgE test to food.[15] Patients were provided with an epinephrine auto-injector throughout the study.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2023) proposes a step-wise approach to asthma treatment.[16] Xolair is listed as an option for add-on therapy in patients ≥ 6 years of age with difficult-to-treat, severe eosinophilic asthma (i.e., patients with symptoms and/or exacerbations despite medium- or high-dose ICS/long-acting beta2-agonist [LABA] or who require maintenance oral corticosteroid). Allergy-driven symptoms and childhood-onset asthma may predict a good asthma response to Xolair.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), 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.[17,18] Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20;
2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;
3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: forced expiratory volume in 1 second (FEV_1) < 80% predicted after appropriate bronchodilator withholding.

Chronic Urticaria Guidelines

Guidelines for the definition, classification, diagnosis, and management of urticaria have been published by the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/Asia Pacific Association of Allergy, Asthma and Clinical Immunology (2022).[19] The American Academy of Dermatology was involved in the development of these guidelines and endorses their recommendations. Chronic spontaneous urticaria is defined as the appearance of wheals, angioedema, or both for > 6 weeks due to known or unknown causes. Signs and symptoms may be present daily/almost daily or have an intermittent recurrent course. Second generation H1-antihistamines taken regularly are the recommended first-line treatment for all types of urticaria following elimination of possible underlying causes. If standard doses do not eliminate urticaria signs and symptoms, the dose of the antihistamine should be increased up to 4-fold. If symptoms persist following 2 to 4 weeks of antihistamine therapy, the addition of Xolair may be considered. For patients with refractory chronic urticaria, the addition of Xolair may be considered. Short courses of rescue systemic corticosteroids are recommended for treatment of patients with acute exacerbations of chronic urticaria. However, guidelines recommend against the long-term use of systemic steroids.

Chronic Rhinosinusitis with Nasal Polyps Guidelines

The Joint Task Force on Practice Parameters (JTFPP) published a focused guideline update for the medical management of CRSwNP (2023), which updated recommendations regarding intranasal corticosteroids and biologic therapies.[20] Intranasal corticosteroids are recommended for the treatment of CRSwNP. Use of biologics (e.g., Xolair) are also recommended. However, in patients who derived a sufficient benefit from other therapies such as intranasal corticosteroids, surgery, or aspirin therapy after desensitization, biologics may not be preferred. Conversely, biologics may be preferred over other medical treatment options in patients who continue to have a high burden of disease despite receiving at least 4 weeks of treatment with an intranasal corticosteroid.

The diagnosis of CRSwNP was not addressed in this focused guideline update. Previous guidelines have noted that 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 of chronic rhinosinusitis likely.[21-24] However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Oral corticosteroids and surgical intervention were not specifically addressed in this update. Prior guidelines

recommend short courses of oral corticosteroid as needed and consideration of surgical removal as an adjunct to medical therapy in patients with CRSwNP that is not responsive or is poorly responsive to medical therapy.[21,22,24]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Xolair. Approval is recommended for those who meet the **Criteria** and **Dosing** the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Indications with a ^ below are also covered (and, if applicable, further detailed/referenced) in the corresponding Commercial Care Continuum (CC) Policy. Note: Additional criteria requirements for coverage of the same indication as outlined in the Commercial CC Policy and this Medicare Advantage Care Continuum Policy may NOT be the same.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Xolair is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Asthma. ^

Criteria. 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, and iv):

- **i.** The patient is ≥ 6 years of age; AND
- **ii.** The patient has a baseline 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: "Baseline" is defined as prior to receiving any Xolair or another monoclonal antibody therapy that may interfere with allergen testing (e.g., Dupixent and Tezspire). Examples of perennial aeroallergens are house dust mite, animal dander, cockroach, feathers, and mold spores. Examples of seasonal aeroallergens are grass, pollen, and weeds.
- **iii.** Patient has received at least 3 consecutive months of therapy with an inhaled corticosteroid; AND
  Note: Use of a combination inhaler containing an inhaled corticosteroid would fulfill this requirement. Examples of inhaled corticosteroids include Aerospan, Alvesco, ArmonAir RespiClick, Arnuity Ellipta, Asmanex Twisthaler/HFA, Flovent Diskus/HFA, Pulmicort Flexhaler, Qvar/Qvar RediHaler, and budesonide suspension for inhalation (Pulmicort Respules, generics). Examples of combination inhalers containing an inhaled corticosteroid include Advair

Diskus (generic Wixela Inhub; authorized generics), Advair HFA, AirDuo RespiClick (authorized generics), Breo Ellipta, Dulera, and Symbicort.

iv. The patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, e, f, g, h, or i):
Note: "Baseline" is defined as prior to receiving Xolair or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Cinqair, Dupixent, Fasenra, Nucala, Tezspire, and Xolair.

- **a.** Daily symptoms or symptoms throughout the day;[40] OR
- **b.** Daily use of inhaled short-acting beta$_2$-agonist or use of inhaled short-acting beta 2-agonist several times per day; [40] OR
- **c.** Some limitation with normal activity or extremely limited normal activity; [40] OR
- **d.** The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
- **e.** The patient experienced one or more asthma exacerbation requiring a hospitalization, an emergency department (ED) visit, or an urgent care visit in the previous year; OR
- **f.** Nighttime symptoms greater than 1 time a week but not nightly or nighttime symptoms often 7x/week;[40] OR
- **g.** Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR
- **h.** Patient has an FEV_1/forced vital capacity (FVC) < 0.80 or the patient's FEV_1/forced vital capacity (FVC) is reduced by ≥ 5%;[40] OR
- **i.** The patient's asthma worsens upon tapering of oral corticosteroid therapy; OR

B) Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets the following criteria (i, ii, and iii):

- **i.** The 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 1A (Asthma, Initial Therapy).
- **ii.** Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND
- **iii.** The patient has responded to therapy, as determined by the prescriber; AND
  Note: Examples of a response to Xolair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department/urgent care, or medical clinic visits due to asthma; decreased reliever/rescue medication use; and improved lung function parameters.

Dosing. Approve up to a maximum dose of 375 mg administered subcutaneously (SC) not more frequently than once every 2 weeks.

**See Exhibit 1 for normal ranges of FEV1/FVC by age range*

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2. Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria). ^

Criteria. 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 and ii):

- **i.** The patient is ≥ 12 years of age; AND
- **ii.** Patient has/had urticaria for > 6 weeks (prior to treatment with Xolair), with symptoms present > 3 days per week despite daily non-sedating H_1 antihistamine therapy with doses that have been titrated up to a maximum of four times the standard FDA-approved dose.

Note: Examples of non-sedating H_1 antihistamine therapy are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.

B) Patient is Currently Receiving Xolair. Approve Xolair for 1 year if the patient meets the following criteria (i and ii):

- **i.** The 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 2A (Chronic Idiopathic Urticaria, Initial Therapy).
- **ii.** The patient has responded to therapy, as determined by the prescriber; AND
  Note: Examples of a response to Xolair therapy are decreased severity of itching, decreased number and/or size of hives.

Dosing. Approve the following dosing regimens (A or B):
A) 150 mg administered subcutaneously (SC) once every 4 weeks; OR
B) 300 mg administered subcutaneously (SC) once every 4 weeks.

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3. Chronic Rhinosinusitis with Nasal Polyps. ^

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

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i, ii, iii and iv):

- **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 will receive therapy with an intranasal corticosteroid concomitantly with Xolair; AND
- **iv.** Patient meets ONE of the following (a, b or c):
  - **a.** Patient has had an inadequate response to an intranasal corticosteroid;[41] OR
  - **b.** Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR
  - **c.** Patient has a contraindication to systemic corticosteroid therapy; OR
  - **d.** Patient has had prior surgery for nasal polyps.

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

- **i.** Patient has already received at least 6 months of therapy with Xolair; AND
  Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 3A [Nasal Polyps, Initial Therapy]).
- **ii.** Patient continues to receive therapy with an intranasal corticosteroid; AND
- **iii.** Patient has responded to Xolair therapy as determined by the prescriber.
  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.

Dosing. Approve up to a maximum dose of 600 mg administered subcutaneously (SC) not more frequently than once every 2 weeks.

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4. Immunoglobulin (Ig)E-Mediated Food Allergy. ^

Criteria. Approve Xolair for 1 year if the patient meets ALL of the following (A, B and C):

A) Patient is ≥ 1 year of age; AND
B) Patient meets BOTH of the following (i and ii):

i. Patient has a positive skin prick test (SPT) response to one or more foods; AND
ii. Patient has a positive *in vitro* test (i.e., a blood test) for IgE to one or more foods; AND

C) According the prescriber, Xolair will be used in conjunction with a food allergen-avoidant diet.

Dosing. Approve up to a maximum dose of 600 mg administered subcutaneously not more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Xolair is not recommended in the following situations:

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

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EXHIBIT 1

Normal ranges by age for FEV_1/FVC are as follows (National Heart, Lung, and Blood Institute [NHLBI]):

- 8-19 years of age – 85%;
- 20-39 years of age – 80%;
- 40-59 years of age – 75%;
- 60-80 years of age – 70%

HISTORY

Type of Revision	Summary of Changes	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52448.	02/20/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52448.	12/11/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020

Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Determination L33394, Local Coverage Article A52448.	02/12/2020
Policy revision	• Asthma – changed wording for the indication, simplified to asthma. Also changed "moderate to severe requirement" to "uncontrolled or was uncontrolled prior to receiving any Xolair or anti-IL-4/13 therapy (Dupixent) therapy" and added additional options to meet that criteria, Added criteria requiring patient to continue therapy with an ICS or ICS-containing product for continuation of coverage. • All indications – removed requirement that Xolair be administered by a physician or incident to a physician's service in office/clinic setting. • Removed Allergic rhinitis as a covered condition • Removed self-administration of Xolair and acute bronchospasm or status asthmaticus from conditions not recommended for approval	3/26/2020
Policy revision	New indication - Nasal Polyps: criteria for this indication – for initial therapy includes an age requirement, current intranasal corticosteroid therapy, previous systemic therapy (or contraindication) or surgery for nasal polyps or previous inadequate response to an intranasal corticosteroid. For continuation therapy, requires patient has already received at least 6 months of therapy with Xolair, patient continues to receive therapy with an intranasal corticosteroid, and that pt has had a response to therapy.	01/06/2021
Policy revision	Nasal Polyps: Added criteria requiring patient have chronic rhinosinusitis with nasal polyposis as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan. Changed criteria requiring patient be currently receiving a nasal corticosteroid to Patient will receive therapy with an intranasal corticosteroid concomitantly with Xolair. Clarified the systemic corticosteroid criteria to require that the patient has received at least one course of systemic corticosteroids for at least 5 days in the previous 2 years.	07/20/2021
Policy revision	**Asthma:** Notes were also updated to include Xolair, Cinqair, Fasenra, Nucala, and Tezspire as examples of monoclonal antibody therapies for asthma. Criteria requiring the patient to have experienced one or more asthma exacerbation(s) requiring a hospitalization or an emergency department visit in the previous year, were updated to include an urgent care visit as well.	08/03/2022
Policy review	No criteria changes	03/22/2023
Policy revision	**Chronic Rhinosinusitis with Nasal Polyps:** Approval condition updated from "Nasal Polyps" to "Chronic Rhinosinusitis with Nasal Polyps". **IgE-Mediated Food Allergy:** New approval criteria for this indication were added.	04/24/2024