REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Omalizumab (Xolair®) for subcutaneous use: History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Age -Prescribed by or in consultation with an allergist, immunologist, dermatologist or pulmonologist -Labs/diagnostics - Medication list (current and past) to include start and end dates of previous trials for all asthma, urticaria or rhinitis therapies.

BACKGROUND

Asthma is a common chronic inflammatory disease of the airways. For most patients asthma is well controlled with inhaled therapy but for those with severe asthma it can be associated with substantial morbidity, mortality, and economic effects.

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 aged ≥ 6 years 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. 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. Doses and dosing frequency in asthma are determined by serum total IgE level (which is measured before the start of therapy) and the patient’s body weight. Xolair is also indicated for the treatment of adults and adolescents (aged ≥ 12 years) with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment.

Dosing in patients with CIU does not depend on serum IgE (free or total) or on body weight. In CIU, 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 CIU symptoms is not known.

Xolair is not indicated for the following conditions:

- Treatment of other allergic conditions or other forms of urticaria
- Relief of acute bronchospasm or status asthmaticus
- Treatment of atopic dermatitis
DEFINITIONS-
None

INDICATIONS/Criteria
Coverage of Xolair is recommended in those who meet one of the following criteria:
FDA-Approved Indications

**Medicaid Members**: Per WA HCA Antiasthmatic Monoclonal Antibodies- Anti-IgE Antibodies Medical Policy no.44.60.30-2. Continue to clinical criteria below.

**Medicare Members**: Follow criteria from MCG: ACG: A-0315 (AC)

*Step-utilization of Part D drugs not required.*

1. **Moderate to Severe Persistent allergic asthma.**

   **A) Initial Therapy.** Approve for 12 months if the patient meets **ALL** of the following criteria:
   
   i. Severe persistent (allergic) asthma is defined by at least **ONE** of the following:
      
      a. FEV₁ less than (<) 80% predicted; OR
      b. Two or more bursts of systemic corticosteroids in the previous 12 months; OR
      c. Frequent (at least twice per year) additional medical treatment such as: emergency department (ED) visits, hospitalizations, mechanical ventilation, or unplanned (sick) office visits; OR
      d. Documentation of functional impairment due to poor asthma control or exacerbations: (e.g. activities of daily living (ADLs), nighttime awakening, or dyspnea)
   
   ii. Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT score consistently less than 20)
   
   iii. History of failure (remains symptomatic after 6 weeks), contraindication or intolerance to medium- to high-dose inhaled corticosteroids (ICS)
   
   iv. Positive skin prick test or in-vitro specific IgE test (such as RAST, MAST, FAST, ELISA) to one or more allergens, (or is currently receiving specific immunotherapy like allergy shots) which support the patient’s clinical history
   
   v. Pre-treatment serum IgE level between 30 and 700 IU/mL
   
   vi. Combination use with other monoclonal antibodies (e.g. benralizumab, mepolizumab, reslizumab) is considered not medically necessary
   
   vii. Prescribed by or in consultation with a specialist in allergy, pulmonology, or immunology
   
   viii. Greater than or equal to (≥) 6 years of age

   **B) Patients Continuing Xolair Therapy.** Approve for 12 months if:
   
   Clinical documentation of improved or sustained clinical benefit compared to baseline measures (e.g., reduced missed days from work or school, improved FEV₁, ACQ or ACT scores, decrease in burst of systemic corticosteroids, etc.) or stable asthma control
Xolair is indicated for use in patients aged ≥ 6 years with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair is not indicated for acute bronchospasm or status asthmaticus. Doses and dosing frequency are determined by serum total IgE level (which is measured before the start of therapy) and the patient’s body weight. Based on the prescribing information for Xolair, an IgE level of ≥ 30 IU/mL is required to calculate a dose. In addition, most of the clinical studies used a baseline IgE level of ≥ 30 IU/mL for inclusion. Serum total IgE levels increase during Xolair therapy due to formation of Xolair:IgE complexes and remain elevated for up to one year after Xolair is stopped. The 2014 ERS/ATS guidelines for the definition, evaluation, and treatment of severe asthma suggest a trial of Xolair may be considered when a patient’s total serum IgE level is ≥ 30 IU/mL and < 700 IU/mL (in addition to other qualifiers). The 2016 GINA guidelines also reference this IgE level requirement for a trial of Xolair therapy. The GINA guidelines and the 2007 NAEPP guidelines indicate that inhaled corticosteroids plus a LABA are the recommended controller medications for asthma patients prior to the potential addition of Xolair. The ERS/ATS guidelines reference the GINA guidelines for these therapy recommendations. The following agents are noted as alternatives to LABA therapy according to the GINA guidelines: sustained-release theophylline, tiotropium, or a LTRA (e.g., montelukast). However, tiotropium is not indicated in patients <12 years of age at this time, and therefore is not recommended in guidelines. If a patient is uncontrolled despite optimal therapy with the previously listed agents, the GINA guidelines support referral to a specialized physician for further investigation and consideration of additional therapies, such as Xolair.

In regard to assessing current clinical control (preferably over 4 weeks), the GINA guidelines state that uncontrolled asthma is demonstrated by at least three of the following: daytime symptoms more than twice per week, any limitation of activities, any nocturnal symptoms/awakening, or the need for reliever/rescue treatment more than twice per week. The NAEPP guidelines recommend patient referral to an asthma specialist for consultation or co-management if the patient is having difficulty achieving or maintaining control of asthma, if immunotherapy or Xolair are considered, or if the patient has had an exacerbation requiring hospitalization. Following initiation of Xolair therapy, the ERS/ATS guidelines also recommend a physician assessment of treatment response, taking into consideration asthma control, exacerbations, unscheduled healthcare utilization, and patient quality of life. These guidelines note that if a patient has not responded within 4 months of initiating treatment, further Xolair therapy is unlikely to be beneficial. The ERS/ATS guidelines define uncontrolled asthma in patients ≥ 6 years of age, as asthma that meets one of the following four criteria: poor symptom control; frequent severe exacerbations (two or more requiring systemic corticosteroids per year); serious exacerbations (one hospitalization in the previous year); or airflow limitation (FEV1 < 80% of predicted in the setting of reduced FEV1/FVC). Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids (high-dose ICs or systemic corticosteroids). In the professional opinion of specialist physicians reviewing the data, we have adopted the seasonal aeroallergens listed in the criteria above.

2. **Chronic Idiopathic Urticaria (Chronic Spontaneous Urticaria).**
Medicaid Members | Follow WA HCA Antiasthmatic Monoclonal Antibodies- Anti-IgE Antibodies Medical Policy no.44.60.30-2. Continue to clinical criteria below.
--- | ---
Medicare Members | Follow criteria from MCG: ACG: A-0315 (AC).

**A)** Initial Therapy. Approve for 12 months if the patient meets all of the following criteria:

i. Diagnosis of chronic idiopathic urticarial **AND** documentation that rules out all other causes of urticaria, including all potential triggers of urticaria

ii. Patient continues to have spontaneous urticarial flares, in the absence of potential triggers, and while on optimal management of all underlying conditions and potential triggers

iii. Documentation of functional impairment due to poor urticaria control or exacerbations: (e.g., activities of daily living (ADLs), insomnia, missing school or work)

iv. Patient shows a trial at least 2 weeks minimum with second-generation H1 antihistamines

v. Patient has tried at least **ONE** or more of the following:
   a. Dose increase of second-generation H1 antihistamine at the maximally tolerated dose, unless contraindicated; **OR**
   b. Addition of another second-generation H1 antihistamine; **OR**
   c. Addition of H2 antihistamine; **OR**
   d. Addition of leukotriene-receptor antagonist; **OR**
   e. Addition of first-generation H1 antihistamine at bedtime

vi. Patient is not using omalizumab with benralizumab or mepolizumab or reslizumab

vii. Patient is greater than or equal to (≥) 12 years of age

viii. Prescribed by or in consultation with a specialist in allergy, dermatology, immunology, or pulmonology

**B)** Patients Continuing Xolair Therapy. Approve for 12 months if:

Clinical documentation of improved or sustained clinical benefit from reduced urticaria symptoms (such as reduced missed days from work or school or insomnia due to itching)

**Quantity and Dosage Limit:**

Urticaria: up to 300mg every 4 weeks

Xolair is indicated for the treatment of adults and adolescents aged ≥ 12 years with CIU who remain symptomatic despite H1 antihistamine treatment. Dosing in patients with CIU does not depend on serum IgE (free or total) or on body weight. Xolair is not indicated for other forms of urticaria. In studies and guidelines, patients with chronic urticaria are generally defined as those having symptoms (e.g., pruritus and hives) for > 3 days per week for > 6 consecutive weeks despite treatment with an H1 antihistamine. Guidelines recommend non-sedating (second-generation) H1 antihistamines at standard daily doses as first-line therapy for CIU. In patients who do not respond adequately to standard doses of non-sedating H1 antihistamines, the dosage should be increased up to four times the...
standard dose. Adding a second non-sedating antihistamine, an H2 antagonist, a LTRA, or a 1st generation antihistamine to be taken at bedtime may be considered for patients with refractory CIU despite non-sedating H1 antihistamine therapy. If the patient still has poorly controlled symptoms, treatment with hydroxyzine or doxepin may be considered as part of step-up therapy. Patients with refractory chronic urticaria despite treatment with the previously listed therapies for 1 to 4 weeks may consider alternative therapies, such as Xolair or cyclosporine. For any drug therapy, it is recommended to temporarily discontinue the drug to check for spontaneous remission. Adequate controlled clinical studies have not been conducted in patients less than 12 years of age with CIU. In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

SPECIAL CONSIDERATIONS
None.

LIMITATIONS/EXCLUSIONS
Please refer to a product line’s certificate of coverage for benefit limitations and exclusions for these services:

<table>
<thead>
<tr>
<th>PRODUCT LINE</th>
<th>LINK TO CERTIFICATE OF COVERAGE</th>
</tr>
</thead>
</table>

Citations & References

1. Xolair® subcutaneous injection [prescribing information]. South San Francisco, CA and East Hanover, NJ: Genentech, Inc. and Novartis Pharmaceuticals Corporation; May 2019.
3. Finn A, Gross G, van Bavel J, et al. Omalizumab improves asthma-related quality...


34. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology; the American College of Allergy, Asthma and Immunology; and the Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of rhinitis: An updated practice parameter. J Allergy Clin Immunol. 2008;122(2):S1-S84.


56. Schneider LC, Rachid R, LeBovidge J, et al. A pilot study of omalizumab to...


**OTHER REFERENCES UTILIZED**


---

**Revision History**

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Description</th>
<th>Revision Made By</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/14/2016</td>
<td>NEW</td>
<td>Sophia Yun, PharmD</td>
</tr>
<tr>
<td>02/24/2017</td>
<td>Approval</td>
<td>MMLT</td>
</tr>
<tr>
<td>11/25/2017</td>
<td>Clarification of criteria based on product line</td>
<td>Sonya Ou, PharmD</td>
</tr>
<tr>
<td>12/21/2017</td>
<td>Approval</td>
<td>MMLT</td>
</tr>
<tr>
<td>03/09/2018</td>
<td>Reassigned from UM to Pharmacy</td>
<td>Cindy Bush</td>
</tr>
<tr>
<td>05/04/2018</td>
<td>Transferred to new template</td>
<td>Cindy Bush</td>
</tr>
<tr>
<td>05/16/2018</td>
<td>Selected revisions</td>
<td>Catherine Vu, PharmD</td>
</tr>
<tr>
<td>Date</td>
<td>Action</td>
<td>Approved By</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>06/07/2018</td>
<td>Revised to HCA Policy</td>
<td>Jennifer Farley, PharmD</td>
</tr>
<tr>
<td>06/14/2018</td>
<td>Approval</td>
<td>UM Committee</td>
</tr>
<tr>
<td>03/12/2019</td>
<td>Revised, removed quantity limits</td>
<td>Ivan Figueira, PharmD</td>
</tr>
<tr>
<td>05/09/2019</td>
<td>Approval</td>
<td>UM Pharmacy Subcommittee</td>
</tr>
<tr>
<td>07/02/2019</td>
<td>Minor formatting revisions</td>
<td>Ivan Figueira, PharmD</td>
</tr>
<tr>
<td>04/08/2020</td>
<td>Extensive revisions to mirror update from HCA. For asthma, reduction of IgE level required, allow immunotherapy shots as evidence of allergens, defined “clinical benefit” for reauthorization. For urticaria, more specificity for trial of antihistamines and need for impairment due to condition. Defined “clinical benefit” for reauthorization.</td>
<td>Jennifer Farley, PharmD</td>
</tr>
<tr>
<td>04/23/2020</td>
<td>Approval</td>
<td>UM Pharmacy Subcommittee</td>
</tr>
</tbody>
</table>